

MEDICAL RECORDS

International Medical Journal

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Department of Anatomy

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Outcomes of Reverse Shoulder Arthroplasty in the Management of Proximal Humerus Fractures Following Failed Internal Fixation

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Abstract

Aim: This research aims to assess the clinical and functional outcomes of reverse shoulder arthroplasty (RSA) in patients with proximal humerus fractures who underwent revision surgery following unsuccessful internal fixation. The influence of fracture classification and the timing of revision surgery on postoperative pain, range of motion (ROM), and functional outcomes was also evaluated.

Material and Method: A retrospective analysis was performed on patients aged 65 years or older who sustained fractures due to low-energy trauma, such as simple falls, and underwent RSA due to failed internal fixation of proximal humerus fractures between 2017 and 2020. Patients with intraoperatively identified irreparable rotator cuff tears were included in the study. Functional outcomes were measured using the American Shoulder and Elbow Surgeons (ASES) score, Constant-Murley score, the Disabilities of the Arm, Shoulder, and Hand Score (QuickDASH), and Visual Analog Scale (VAS). Additionally, ROM, including flexion, abduction, internal rotation, and external rotation, was assessed. Statistical comparisons were conducted based on fracture classification (Neer Type 3 vs. Neer Type 4) and the interval between the initial fixation and revision surgery.

Results: Patients with Neer Type 4 fractures had poorer functional outcomes and higher pain levels than those with Neer Type 3 fractures. The VAS score was higher (3.2 ± 1.8 vs. 0.9 ± 0.9), and the Constant-Murley score was lower (50.7 ± 10.4 vs. 61.8 ± 9.0) in Neer Type 4 patients. Delayed revision surgery led to greater functional decline, increased pain, and restricted motion. Flexion ($102.9 \pm 23.1^\circ$) and abduction ($99.4 \pm 19.2^\circ$) were better preserved in Neer Type 3 fractures than in Neer Type 4 ($80.0 \pm 22.8^\circ$ and $73.3 \pm 22.5^\circ$). However, RSA effectively reduced postoperative pain (VAS 1.5 ± 1.5) and improved functional scores (ASES 59.0 ± 21.3).

Conclusion: RSA serves as a reliable reconstructive option for managing complications arising from unsuccessful surgical stabilization of proximal humerus fractures, especially in cases where the rotator cuff damage is beyond repair. Early revision surgery is linked to superior functional recovery, whereas delayed intervention may result in heightened pain and restricted shoulder movement.

Keywords: Reverse shoulder arthroplasty, proximal humerus fractures, failed internal fixation, functional outcomes, revision surgery

INTRODUCTION

Proximal humerus fractures represent one of the most frequently encountered upper limb fractures, especially in older adults and individuals with osteoporosis (1). These fractures typically result from low-energy trauma, especially falls, and can lead to significant functional impairment if not treated appropriately in the early period (2). Treatment options include conservative management, internal fixation (plates, screws, or intramedullary nailing), and arthroplasty (3). However, complications following internal fixation, such as impaired bone healing, mechanical failure of the implant, and loss of vascular supply to the humeral head, may require revision surgery.

In patients requiring revision surgery following failed internal fixation, determining the appropriate surgical strategy is of critical importance. In proximal humerus fractures, particularly when rotator cuff integrity is compromised, traditional hemiarthroplasty has been associated with suboptimal outcomes (4). Unlike conventional prostheses, reverse shoulder arthroplasty (RSA) relies on the deltoid muscle as the primary driver of movement, leading to enhanced clinical outcomes and improved shoulder function in individuals with rotator cuff insufficiency (5). Consequently, RSA has gained prominence as a favored therapeutic approach, especially for individuals with extensive rotator cuff damage following unsuccessful internal fixation (6).

CITATION

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Various studies in the literature have analyzed the clinical effectiveness of RSA, whether implemented as an initial intervention or as a secondary procedure following proximal humerus fractures (7). These studies indicate that RSA is effective in pain control and facilitates a faster return to daily activities. Nevertheless, the effectiveness of RSA may differ based on variables such as patient age, fracture classification, timing of surgery, and the surgical approach utilized. Therefore, evaluating the sustained clinical effectiveness of RSA in cases of failed internal fixation is essential for informing clinical practice and enhancing patient management.

This research aims to assess the clinical and imaging outcomes of RSA in individuals with osteoporotic proximal humerus fractures who experienced complications following internal fixation and were diagnosed with irreparable rotator cuff tears during revision surgery. Furthermore, it explores the practicality and therapeutic efficacy of this surgical approach.

MATERIAL AND METHOD

Study Design and Patient Selection

This retrospective study was conducted at the Orthopedics and Traumatology Clinics of Adana City Training and Research Hospital between January 1, 2017, and November 30, 2020. The study included patients aged 65 years or older who sustained fractures due to low-energy trauma, such as simple falls, and underwent internal fixation for osteoporotic proximal humerus fractures. Patients who subsequently required revision surgery due to complications and had intraoperatively confirmed irreparable rotator cuff insufficiency, necessitating RSA, were evaluated. The selection of the 2017–2020 study period was based on the availability of a sufficiently large and homogenous patient cohort that met the inclusion criteria, ensuring comprehensive and standardized data collection. This timeframe also allowed for a minimum follow-up period of 24 months, enabling a thorough assessment of postoperative functional and clinical outcomes. Ethical approval for the study was obtained from the Adana City Training and Research Hospital Clinical Research Ethics Committee (Approval No. 1122, dated December 16, 2020).

Inclusion and Exclusion Criteria

The inclusion criteria for the study consisted of patients aged 65 years or older who had sustained fractures due to low-energy trauma, such as simple falls, and had undergone internal fixation for osteoporotic proximal humerus fractures. Patients who developed complications necessitating revision surgery and were found to have irreparable rotator cuff tears during revision were included. Additionally, a minimum follow-up period of 24 months was required for inclusion in the study. Patients were excluded if they had a history of open fractures, previous septic arthritis or similar infections in the glenohumeral

joint, multiple fractures in the same extremity, or any neurological deficits. These criteria were established to ensure a homogeneous study population and enhance the reliability of the outcome assessments.

Sample Size and Power Analysis

The sample size was determined based on a moderate effect size difference in parameter means, with an alpha significance level of 0.05 and a power of 95%, resulting in a total sample size of 19 participants. The power analysis was conducted using the PASS 13.0.6 software (NCSS, LLC, USA-2014). The margin of error was set at 5%, with a statistical power of 99% and an effect size of 0.68. During the study period, 28 patients who underwent RSA due to rotator cuff insufficiency following failed internal fixation were identified. After applying exclusion criteria, five patients were excluded, and the final analysis was completed with 23 patients.

Surgical Procedure

All primary and revision procedures were conducted by a single surgical team utilizing the deltopectoral approach. In the primary procedure, patients underwent internal fixation with proximal humerus plates or screws. During revision surgery, patients were placed in the supine position under general anesthesia, and a deltopectoral incision was used for surgical exploration. After careful removal of internal fixation materials, the proximal humerus was assessed, and RSA was performed in cases where the rotator cuff tear was deemed irreparable. This determination was made intraoperatively based on the extent of tendon retraction and its mobilization capacity, as well as the presence of extensive scar tissue preventing reapproximation of the torn edges. Additionally, cases where the deltoid muscle was unable to develop a functional compensatory mechanism were also considered unsuitable for rotator cuff repair, necessitating RSA. Following glenoid preparation and debridement, appropriate prosthetic components were implanted, ensuring stability before closing the joint capsule. In the postoperative period, patients were immobilized with a shoulder sling, and early passive range of motion (ROM) exercises were initiated. The rehabilitation process was individually tailored to optimize functional recovery.

Functional and Clinical Assessment

Postoperatively, patients included in the study were evaluated in terms of functional and clinical outcomes. Functional assessment was conducted using the American Shoulder and Elbow Surgeons (ASES) score, Constant-Murley score, and the Disabilities of the Arm, Shoulder, and Hand Score (QuickDASH). Pain levels were measured using the Visual Analog Scale (VAS). Additionally, ROM was assessed, including flexion, abduction, external rotation, and internal rotation. These evaluations were conducted to determine the impact of RSA on patients' functional recovery and overall clinical outcomes.

Radiological Assessment

In the period before the internal fixation surgery, direct radiographs taken after the fracture occurred were analyzed to classify the fractures according to the Neer classification system. Patients were categorized as having Neer Type 3 or

Neer Type 4 fractures. In the period following revision surgery with RSA, prosthesis positioning and bone healing were radiologically evaluated, and any potential complications were recorded. The proper placement of the prosthesis and implant stability were also assessed (Figure 1).

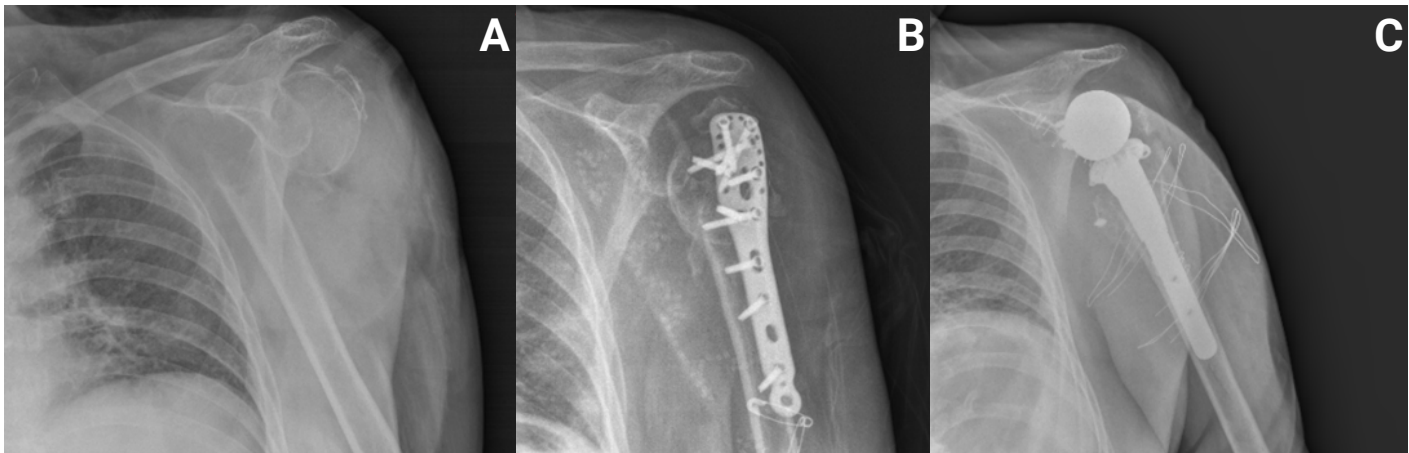


Figure 1. Sequential radiographs demonstrating the progression of treatment; (A) Preoperative anteroposterior radiograph showing a proximal humerus fracture; (B) Radiograph showing implant failure after internal fixation with a locking plate; (C) Final radiograph after revision surgery with reverse shoulder arthroplasty

Evaluated Parameters

In this study, patients' demographic data, fracture types, surgical procedures, and postoperative functional outcomes were assessed. Limb laterality was recorded as right or left extremity, and basic demographic characteristics such as age and gender were analyzed. Fracture classification was performed based on the Neer system, categorizing patients as Neer Type 3 or Neer Type 4, while the duration between the primary surgery and revision surgery was examined. The total follow-up period was calculated to assess long-term outcomes. For postoperative functional assessment, the ASES scores were recorded for both the operated and unaffected arms. QuickDASH score was used to evaluate upper extremity functional impairment, and the VAS was utilized to measure pain levels. Overall shoulder function was assessed using the Constant-Murley score. Postoperative ROM was extensively analyzed, including flexion, abduction, external rotation, and internal rotation. These parameters were used to determine movement limitations and evaluate the functional effectiveness of the prosthesis. Based on all these assessments, the clinical and functional efficacy of RSA following failed internal fixation was investigated.

RESULTS

The mean age of the patients included in the study was 70.0±3.1 years (range: 65–77 years). The average time between the primary surgery and revision was 71.6±27.4 days, while the mean follow-up duration was recorded as 28.3±3.1 months. In functional assessment, the ASES score was found to be 59.0±21.3 for the operated arm and 94.8±7.5 for the unaffected arm. The QuickDASH score,

which indicates upper extremity functional limitation, had a mean value of 36.7±19.9, while the VAS score for pain assessment was calculated as 1.5±1.5. The Constant-Murley score, evaluating shoulder function, was found to be 58.9±10.4. Regarding ROM, the mean flexion was 97.0±24.8 degrees, abduction was 92.6±22.8 degrees, external rotation was 25.0±10.3 degrees, and internal rotation was 19.8±7.0 degrees (Table 1).

Table 1. Demographic, surgical, and functional outcomes of patients	
	Mean±S.D.
Age (years)	70.0±3.1
Revision Interval (days)	71.6±27.4
Follow-up Duration (months)	28.3±3.1
ASES operated arm	59.0±21.3
ASES healthy arm	94.8±7.5
QuickDASH	36.7±19.9
VAS score	1.5±1.5
Constant-Murley	58.9±10.4
Flexion (degrees)	97.0±24.8
Abduction (degrees)	92.6±22.8
External rotation (degrees)	25.0±10.3
Internal rotation (degrees)	19.8±7.0
The data in the table are presented as mean±standard deviation (Mean±S.D.); ASES: American Shoulder and Elbow Surgeons Score, VAS: Visual Analog Scale, QuickDASH : The Disabilities of the Arm, Shoulder, and Hand Score	

In 52.2% of the patients, surgery was performed on the right shoulder, while 47.8% underwent surgery on the left

shoulder. Among the study participants, 69.6% were female, and 30.4% were male. Regarding fracture classification, 73.9% of the patients had Neer Type 3 fractures, whereas 26.1% had Neer Type 4 fractures (Table 2).

Table 2. Side, gender, and fracture type characteristics of the patients

		Count	Column N (%)
Side	Right	12	52.2
	Left	11	47.8
Gender	Female	16	69.6
	Male	7	30.4
Fracture type	Neer type 3	17	73.9
	Neer type 4	6	26.1

The data in the table are presented as count (percentage)

The mean age of female patients was calculated as 69.8 ± 2.9 years, while for male patients, it was 70.6 ± 3.7 years, with no statistically significant difference between the two groups ($p=0.570$). The mean duration between primary surgery and revision was 76.1 ± 28.5 days in female patients and 61.1 ± 23.1 days in male patients, but this difference was not statistically significant ($p=0.198$). In functional assessment, the ASES score for the operated arm was 56.0 ± 22.2 in female patients and 65.7 ± 19.1 in male patients. The QuickDASH score was 39.5 ± 20.2 in females and 30.5 ± 19.3 in males, with no statistically significant

difference between the groups ($p=0.222$). The VAS score, used for pain assessment, was 1.8 ± 1.7 in females and 0.7 ± 0.8 in males, but the difference was not statistically significant ($p=0.154$). Regarding ROM, the mean flexion was 93.8 ± 25.0 degrees in female patients and 104.3 ± 24.4 degrees in male patients, with no statistically significant difference ($p=0.376$). Similarly, abduction was measured as 88.1 ± 23.7 degrees in females and 102.9 ± 18.0 degrees in males ($p=0.159$). External and internal rotation values also did not show a statistically significant difference between the groups (Table 3).

Table 3. Gender-based comparison of demographic, surgical, and functional outcomes

	Female (n=16)	Male (n=7)	p value
	Mean $\pm$ S.D.	Mean $\pm$ S.D.	
Age (years)	69.8 ± 2.9	70.6 ± 3.7	0.570 ^a
Revision interval (days)	76.1 ± 28.5	61.1 ± 23.1	0.198 ^b
Follow-up duration (months)	27.8 ± 2.9	29.4 ± 3.2	0.198 ^b
ASES operated arm	56.0 ± 22.2	65.7 ± 19.1	0.278 ^b
ASES healthy arm	94.4 ± 8.5	95.7 ± 4.5	0.922 ^b
QuickDASH	39.5 ± 20.2	30.5 ± 19.3	0.222 ^b
VAS score	1.8 ± 1.7	0.7 ± 0.8	0.154 ^b
Constant-Murley	56.7 ± 10.9	63.9 ± 7.7	0.131 ^a
Flexion (degrees)	93.8 ± 25.0	104.3 ± 24.4	0.376 ^b
Abduction (degrees)	88.1 ± 23.7	102.9 ± 18.0	0.159 ^a
External rotation (degrees)	23.1 ± 9.3	29.3 ± 12.1	0.249 ^b
Internal rotation (degrees)	18.7 ± 6.7	22.1 ± 7.6	0.341 ^b

The data in the table are presented as mean $\pm$ standard deviation (Mean $\pm$ S.D.); Mann-Whitney U test is denoted by b, while a represents the Independent Samples t-test. ASES: American Shoulder and Elbow Surgeons Score, VAS: Visual Analog Scale, QuickDASH: The Disabilities of the Arm, Shoulder, and Hand Score

No statistically significant differences were observed between the two groups regarding age, time between primary and revision surgery, follow-up duration, ASES Healthy Arm score, QuickDASH score, and ASES Operated Arm score ($p=0.172$, $p=0.609$, $p=0.919$, $p=0.201$, $p=0.117$,

$p=0.135$, respectively). In functional assessment, the VAS score, which indicates pain levels, was significantly higher in Neer Type 4 patients (3.2 ± 1.8) compared to Neer Type 3 patients (0.9 ± 0.9) ($p=0.010$). Similarly, the Constant-Murley score was significantly lower in the Neer Type 4 group

(50.7±10.4) compared to the Neer Type 3 group (61.8±9.0) (p=0.021). Regarding ROM, flexion was significantly reduced in Neer Type 4 patients (80.0±22.8°) compared to Neer Type 3 patients (102.9±23.1°) (p=0.002). Likewise, abduction was lower in Neer Type 4 patients (73.3±22.5°) compared to Neer Type 3 patients (99.4±19.2°) (p=0.012).

External rotation was also significantly lower in Neer Type 4 patients (17.5±6.9°) compared to Neer Type 3 patients (27.6±10.2°) (p=0.030). Similarly, internal rotation was significantly lower in Neer Type 4 patients (15.0±4.5°) compared to Neer Type 3 patients (21.5±7.0°) (p=0.047) (Table 4).

Table 4. Fracture type-based comparison of demographic, surgical, and functional parameters

	NEER type 3 (n=17)	NEER type 4 (n=6)	p value
	Mean±S.D.	Mean±S.D.	
Age (years)	69.5±3.2	71.5±2.2	0.172 ^a
Revision interval (days)	69.6±28.4	77.0±25.9	0.609 ^b
Follow-up duration (months)	28.1±2.4	28.8±4.7	0.919 ^b
ASES operated arm	63.4±18.7	46.3±25.0	0.135 ^b
ASES healthy arm	96.8±3.9	89.2±12.0	0.201 ^b
QuickDASH	33.0±17.5	47.2±24.2	0.117 ^b
VAS score	0.9±0.9	3.2±1.8	0.010^b
Constant-Murley	61.8±9.0	50.7±10.4	0.021^a
Flexion (degrees)	102.9±23.1	80.0±22.8	0.002^b
Abduction (degrees)	99.4±19.2	73.3±22.5	0.012^a
External rotation (degrees)	27.6±10.2	17.5±6.9	0.030^b
Internal rotation (degrees)	21.5±7.0	15.0±4.5	0.047^b

Mann-Whitney U test is denoted by b, while a represents the Independent Samples t-test; the data in the table are presented as mean±standard deviation (Mean±S.D.); statistically significant p-values are indicated in bold; ASES: American Shoulder and Elbow Surgeons Score, VAS: Visual Analog Scale, QuickDASH : The Disabilities of the Arm, Shoulder, and Hand Score

A strong negative correlation was found between revision interval and both ASES Operated Arm score and Constant-Murley score, indicating that as the revision interval increased, these scores decreased (r=-0.784, p<0.001 and r=-0.866, p<0.001, respectively). A strong positive correlation was observed between the revision interval and QuickDASH score, showing that longer revision intervals were associated with higher QuickDASH scores, indicating greater upper extremity functional impairment (r=0.808, p<0.001). Similarly, a

moderate positive correlation was detected between the revision interval and VAS score, suggesting that longer revision times were associated with higher pain levels (r=0.455, p=0.029). Regarding ROM, significant negative correlations were found between the revision interval and flexion, abduction, external rotation, and internal rotation, demonstrating that longer revision times resulted in reduced joint mobility (r=-0.818, p<0.001; r=-0.802, p<0.001; r=-0.638, p=0.001; r=-0.739, p<0.001, respectively) (Table 5).

Table 5. Correlation between revision interval and functional outcomes

	Revision interval (r)	p value
ASES operated arm	-0.784	<0.001
QuickDASH	0.808	<0.001
VAS	0.455	0.029
Constant-Murley	-0.866	<0.001
Flexion (degrees)	-0.818	<0.001
Abduction (degrees)	-0.802	<0.001
External rotation (degrees)	-0.638	0.001
Internal rotation (degrees)	-0.739	<0.001

The data in the table are presented as correlation coefficients (r) and p-values; statistically significant p-values are indicated in bold; ASES: American Shoulder and Elbow Surgeons Score, VAS: Visual Analog Scale, QuickDASH : The Disabilities of the Arm, Shoulder, and Hand Score

DISCUSSION

In this study, the functional status and treatment results of individuals who underwent RSA after unsuccessful internal fixation were assessed. The findings indicated that patients with Neer Type 4 fractures experienced greater pain and had lower functional scores compared to those with Neer Type 3 fractures. Additionally, ROM was significantly more restricted in Neer Type 4 patients. Furthermore, a prolonged interval between the initial surgery and revision was associated with a marked decline in both functional capacity and ROM. Delayed revision surgery may contribute to increased degenerative changes in the shoulder joint and weakening of muscle function. Notably, pain levels and losses in joint mobility appeared to be directly influenced by the timing of revision surgery. These findings suggest that early intervention with RSA may improve functional outcomes and that Neer Type 4 fractures may require a more aggressive surgical approach for optimal management.

Proximal humerus fractures constitute nearly 6% of all adult fractures, with osteoporosis and advanced age being significant risk factors (8,9). The Neer classification is commonly utilized to evaluate proximal humerus fractures (10,11). With the growing prevalence of osteoporosis, the occurrence of proximal humerus fractures is anticipated to rise as well (12). Treating these fractures presents challenges for orthopedic surgeons due to patients' demographic characteristics and associated comorbidities, with nearly half of these fractures classified as displaced and requiring surgical intervention (13,14).

In recent years, RSA has been increasingly employed as a surgical solution for managing complicated proximal humerus fractures in osteoporotic patients (15). Originally designed to address extensive rotator cuff deficiencies, this prosthesis has gradually broadened its indications, yielding favorable outcomes in proximal humerus fractures, arthroplasty revisions, and cases of unsuccessful internal fixation (16,17). Compared to hemiarthroplasty, RSA offers significant advantages, including improved joint stability by shifting the biomechanical center of the shoulder inferiorly and medially, as well as enhancing deltoid muscle function (18,19). Hemiarthroplasty remains a viable option in select cases, particularly in patients with preserved rotator cuff integrity, minimal glenoid erosion, and sufficient bone stock. Additionally, younger patients with good healing potential or those requiring future revision surgery may benefit from hemiarthroplasty due to its bone-preserving nature. While RSA is the preferred choice in most complex cases, surgical decisions should be tailored to individual patient factors.

In our study, the post-surgical functional performance of individuals who received RSA was found to align with findings from similar studies in the literature. Prior research analyzing individuals undergoing primary RSA and those requiring revision surgery due to unsuccessful internal fixation has indicated comparable functional

results without statistically meaningful variation (20). Likewise, individuals diagnosed with Neer Type 2, 3, and 4 fractures who underwent RSA exhibited functional scores comparable to those documented in previous studies (21,22).

When assessing the post-surgical functional performance of individuals undergoing RSA after unsuccessful internal fixation, the Constant-Murley scores reported in prior studies were found to be consistent with those in our research (23,24). Comparisons between RSA and hemiarthroplasty indicate that RSA provides better functional outcomes and lower complication rates (25). Consistent with these findings, our study also demonstrated that patients with Neer Type 4 fractures experienced greater functional loss and higher pain levels.

When assessing ROM, the mobility levels of individuals who received RSA were observed to be comparable to findings documented in previous studies (21-23,26). In a study by Wright et al., individuals who received primary RSA demonstrated improved ROM compared to those who underwent revision surgery after unsuccessful internal fixation (27). However, the alignment of post-revision functional outcomes in our research with previously published findings supports the notion that RSA serves as a viable treatment approach for this patient population (28). Research comparing RSA with hemiarthroplasty in the management of proximal humerus fractures has indicated that both procedures yield comparable ASES scores (29). Although individuals who received RSA due to glenohumeral instability exhibited slightly greater flexion, external rotation, and abduction values compared to those in our study, the achieved outcomes are deemed satisfactory (30).

When assessing pain levels, the VAS scores of individuals who received RSA for rotator cuff degeneration or arthroplasty revision were observed to be comparable to those in our study (31). Some studies have reported higher VAS scores (32). However, in our study, postoperative pain levels were found to be within acceptable limits. Nevertheless, functional performance and joint mobility were reduced among revision patients compared to those who underwent primary RSA. This may be related to deficiencies in the rehabilitation process or the inability to achieve optimal shoulder function after the initial surgery. The prolongation of the interval between primary surgery and revision is considered a negative factor affecting functional outcomes, which aligns with findings reported in other studies in the literature (33). While our results suggest that earlier revision leads to improved functional outcomes, further research is required to define an optimal time frame for intervention.

Study Limitations

This study has some limitations. First, since it has a retrospective design, there may be certain constraints in the data collection process. To obtain stronger evidence, prospective and randomized controlled studies would be

beneficial. Second, the sample size is relatively limited. As our study focuses on a specific patient group, future studies with larger populations would help confirm these findings. Third, while the follow-up period is sufficient for evaluating mid-term outcomes, longer follow-up is necessary to determine long-term results. The durability of the prosthesis and the sustainability of functional improvements could be better assessed in future long-term studies. Fourth, detailed data on the rehabilitation process are not available. Postoperative physical therapy programs may vary among individuals, potentially affecting functional outcomes. Further studies investigating the impact of rehabilitation would provide more insights into this aspect. Finally, the lack of a comparative control group restricts the ability to directly contrast the findings with those of patients undergoing initial reverse shoulder replacement or alternative operative approaches. Nevertheless, this research offers important perspectives on the clinical and functional results observed in this particular patient group. Despite these limitations, our study contributes important findings regarding the evaluation of functional and clinical outcomes in patients undergoing RSA following failed internal fixation. Subsequent research involving larger patient populations and extended follow-up durations could offer more in-depth insights into this topic.

CONCLUSION

The findings of this research highlight that individuals who undergo RSA due to irreparable rotator cuff failure following unsuccessful surgical stabilization of osteoporotic proximal humerus fractures experience substantial functional gains. While prolonged revision intervals were associated with decreased functional outcomes and increased pain levels, early intervention may contribute to better postoperative recovery. Moreover, individuals with Neer Type 4 fractures demonstrated greater restrictions in joint mobility and higher pain levels when compared to those with Neer Type 3 fractures. The results emphasize the significance of early detection and sound surgical decision-making in improving patient outcomes. Subsequent research involving larger cohorts and extended follow-up durations is suggested to confirm these findings and enhance treatment approaches for this patient group.

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Ethical approval: Ethical approval for this study was obtained from the Clinical Research Ethics Committee of Adana City Training and Research Hospital (Approval Date: 16.12.2020, Approval Number: 1122). Informed consent was obtained from all patients included in the study. This study adheres to the ICMJE Recommendations and STROBE guidelines. Sex and gender considerations were addressed in accordance with the SAGER guidelines, and the manuscript follows the EASE Guidelines for Authors and Translators.

REFERENCES

- Jacobs AN, Umlauf JA, Kniss JR. Proximal humerus fracture following arthroscopic biceps tenodesis. *J Orthop Sports Phys Ther.* 2020;50:649.
- Koeppel J, Stolberg-Stolberg J, Fischhuber K, et al. The incidence of proximal humerus fracture-an analysis of insurance data. *Dtsch Arztebl Int.* 2023;120:555-6.
- Rudran B, Little C, Duff A, Poon H, Tang Q. Proximal humerus fractures: anatomy, diagnosis and management. *Br J Hosp Med (Lond).* 2022;83:1-10.
- Marigi EM, Bartels DW, Aibinder WR, Cofield RH, Sperling JW, Sanchez-Sotelo J, et al. Hemiarthroplasty for proximal humerus fractures and for fracture sequelae: did not differ in their outcomes. *JSES Int.* 2023;7:239-46.
- Chawla H, Gamradt S. Reverse total shoulder arthroplasty: technique, decision-making and exposure tips. *Curr Rev Musculoskelet Med.* 2020;13:180-5.
- Luster TG, Dean RS, Trasolini NA, et al. Predictive factors influencing internal rotation following reverse total shoulder arthroplasty. *J Shoulder Elbow Surg.* 2024;33:1200-8.
- Galvin JW, Kim R, Ment A, et al. Outcomes and complications of primary reverse shoulder arthroplasty with minimum of 2 years' follow-up: a systematic review and meta-analysis. *J Shoulder Elbow Surg.* 2022;31:e534-44.
- Perritt S, Roberts M. Flexural-slip structures in the bushveld complex, South Africa?. *Journal of Structural Geology.* 2007;29:1422.
- Brorson S, Rasmussen JV, Olsen BS, et al. Reverse shoulder arthroplasty in acute fractures of the proximal humerus: a systematic review. *Int J Shoulder Surg.* 2013;7:70-8.
- Neer CS 2nd. Displaced proximal humeral fractures. I. Classification and evaluation. *J Bone Joint Surg Am.* 1970;52:1077-89.
- Lanting B, MacDermid J, Drosdowech D, Faber KJ. Proximal humeral fractures: a systematic review of treatment modalities. *J Shoulder Elbow Surg.* 2008;17:42-54.
- Palvanen M, Kannus P, Niemi S, Parkkari J. Update in the epidemiology of proximal humeral fractures. *Clin Orthop Relat Res.* 2006;442:87-92.
- García-Fernández C, Lopiz Y, Rizo B, et al. Reverse total shoulder arthroplasty for the treatment of failed fixation in proximal humeral fractures. *Injury.* 2018;49:S22-6.
- Dezfuli B, King JJ, Farmer KW, et al. Outcomes of reverse total shoulder arthroplasty as primary versus revision procedure for proximal humerus fractures. *J Shoulder Elbow Surg.* 2016;25:1133-7.
- Savin DD, Zamfirova I, Iannotti J, et al. Survey study suggests that reverse total shoulder arthroplasty is becoming the treatment of choice for four-part fractures of the humeral head in the elderly. *Int Orthop.* 2016;40:1919-25.
- Familiari F, Rojas J, Nedim Doral M, et al. Reverse total shoulder arthroplasty. *EFORT Open Rev.* 2018;3:58-69.
- Patel DN, Young B, Onyekwelu I, et al. Reverse total shoulder arthroplasty for failed shoulder arthroplasty. *J Shoulder Elbow Surg.* 2012;21:1478-83.

18. Juhan T, Stone M, Jalali O, et al. Irreparable rotator cuff tears: current treatment options. *Orthop Rev (Pavia)*. 2019;11:8146.
19. Farshad M, Gerber C. Reverse total shoulder arthroplasty- from the most to the least common complication. *Int Orthop*. 2010;34:1075-82.
20. Kristensen MR, Rasmussen JV, Elmengaard B, et al. High risk for revision after shoulder arthroplasty for failed osteosynthesis of proximal humeral fractures. *Acta Orthop*. 2018;89:345-50.
21. Obert L, Saadnia R, Tournier C, et al. Four-part fractures treated with a reversed total shoulder prosthesis: Prospective and retrospective multicenter study. Results and complications. *Orthop Traumatol Surg Res*. 2016;102:279-85.
22. Grubhofer F, Wieser K, Meyer DC, et al. Reverse total shoulder arthroplasty for acute head-splitting, 3- and 4-part fractures of the proximal humerus in the elderly. *J Shoulder Elbow Surg*. 2016;25:1690-8.
23. Grubhofer F, Wieser K, Meyer DC, et al. Reverse total shoulder arthroplasty for failed open reduction and internal fixation of fractures of the proximal humerus. *J Shoulder Elbow Surg*. 2017;26:92-100.
24. Cacak N, Klobucar H, Medancic N. Reverse shoulder arthroplasty in acute fractures provides better results than in revision procedures for fracture sequelae. *Int Orthop*. 2015;39:343-8.
25. Shannon SF, Wagner ER, Houdek MT, et al. Reverse shoulder arthroplasty for proximal humeral fractures: outcomes comparing primary reverse arthroplasty for fracture versus reverse arthroplasty after failed osteosynthesis. *J Shoulder Elbow Surg*. 2016;25:1655-60.
26. Constant CR, Murley AH. A clinical method of functional assessment of the shoulder. *Clin Orthop Relat Res*. 1987;160-4.
27. Wright JO, Ho A, Kalma J, et al. Uncemented reverse total shoulder arthroplasty as initial treatment for comminuted proximal humerus fractures. *J Orthop Trauma*. 2019;33:e263-9.
28. Sebastia-Forcada E, Lizaur-Utrilla A, Cebrian-Gomez R, et al. Outcomes of reverse total shoulder arthroplasty for proximal humeral fractures: primary arthroplasty versus secondary arthroplasty after failed proximal humeral locking plate fixation. *J Orthop Trauma*. 2017;31:e236-40.
29. Boileau P, Seeto BL, Clowez G, et al. SECEC Grammont Award 2017: the prejudicial effect of greater tuberosity osteotomy or excision in reverse shoulder arthroplasty for fracture sequelae. *J Shoulder Elbow Surg*. 2020;29:2446-58.
30. Wolfensperger F, Grüniger P, Dietrich M, et al. Reverse shoulder arthroplasty for complex fractures of the proximal humerus in elderly patients: impact on the level of independency, early function, and pain medication. *J Shoulder Elbow Surg*. 2017;26:1462-8.
31. Pastor MF, Kieckbusch M, Kaufmann M, et al. Reverse shoulder arthroplasty for fracture sequelae: Clinical outcome and prognostic factors. *J Orthop Sci*. 2019;24:237-42.
32. Nielsen KP, Amundsen A, Olsen BS, Rasmussen JV. Good long-term patient-reported outcome after shoulder arthroplasty for cuff tear arthropathy. *JSES Int*. 2022;6:40-3.
33. Anakwenze OA, Zoller S, Ahmad CS, Levine WN. Reverse shoulder arthroplasty for acute proximal humerus fractures: a systematic review. *J Shoulder Elbow Surg*. 2014;23:e73-80.



Demographic Evaluation of Patients Treated Under General Anesthesia in Dentistry

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Abstract

Aim: This study aims to evaluate the demographic characteristics of patients treated under general anesthesia in dentistry and the reasons for their admission to general anesthesia.

Material and Method: Patients treated under general anesthesia at Eskişehir Osmangazi University Faculty of Dentistry Department of Oral and Maxillofacial Surgery between May 20, 2013, and April 1, 2023, were analyzed. The relationships between age, gender, systemic diseases, reasons for general anesthesia, and dental treatment parameters under general anesthesia were evaluated for those who met the inclusion criteria. Descriptive statistics, including standard deviation, mean, minimum and maximum values, percentages, cross tables, and frequencies, were used. The chi-square test was used to evaluate relationships between groups. Post-hoc analyses were performed using the chi-square distribution's right-tailed probability to identify significant differences between groups. A significance level of $p < 0.05$ was used to determine statistical significance.

Results: The data of 550 patients treated under general anesthesia were analyzed. The patients' ages ranged from 1 to 79 years, with a mean age of 16.41. The most common treatments were tooth extraction and restorative procedures. No significant relationship was found between gender and the reason for general anesthesia ($p > 0.05$). However, there was a strong relationship between systemic conditions and reasons for general anesthesia ($p < 0.05$). Dental phobia was more common among patients with mental retardation. Significant differences were observed in the reasons for general anesthesia across age groups ($p < 0.05$).

Conclusion: The most frequent treatments under general anesthesia were tooth extraction and restorative procedures. The primary reasons for undergoing general anesthesia were anesthesia requirements, dental phobia, and gag reflex. Demographic factors such as age and systemic health significantly influence the causes and outcomes of treatments. These findings highlight the need for specific strategies to improve the effectiveness and accessibility of dental care under general anesthesia.

Keywords: General anesthesia, demographic, dentistry, dental phobia

INTRODUCTION

Anesthesia is a preferred practice to prevent the patient from feeling pain and moving (1). General anesthesia is a medical practice used to ensure that you do not feel pain and remain motionless during surgical procedures. The anesthetic agent is usually administered intravenously or by inhalation. These drugs slow down brain activity, reducing pain sensitivity and causing loss of consciousness (2). General anesthesia is used in dental practice for many reasons. While local anesthesia is often required in the practice of dental procedures, some patients may need to be placed under general anesthesia due to dental phobias or other special health conditions

(3). Treatments performed under general anesthesia: restoration (including stainless steel crowns), tooth extractions, endodontic procedures (pulpotomy and root canal treatments) and surgical interventions (surgical tooth extractions, tongue and lip frenulum surgeries, surgical removal of cystic lesions, odontomas and oral soft tissue It includes procedures such as benign lesions, tooth replacements, autotransplantations, hyperplastic tissue excisions (4). Surgical interventions performed under general anesthesia have an important place in oral surgery practice. There may be reasons why general anesthesia is preferred over local anesthesia, such as painful complex surgical procedures, anatomical variation, and acute infection (5). The operations

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performed are mainly cyst/tumor, Le Fort I and sagittal split ramus osteotomies (SSRO). There may be many reasons for surgery, such as cancer, midface fractures, and better appearance (3,6). The aim of this study is to analyze the demographic characteristics of patients treated under general anesthesia to help these patients receive better care and achieve better outcomes. The hypothesis of our research is that general anesthesia is used more frequently in people with dental phobia and individuals with special needs.

MATERIAL AND METHOD

Data Collection

550 patients treated under general anesthesia at Eskişehir Osmangazi University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery were included in this study. Informed consent forms were obtained from all patients and their parents before general anesthesia. The ethical compliance of our study, T.R. Approval was given by Eskişehir Osmangazi University Non-invasive Clinical Research Ethics Committee with the decision numbered 2023-15. Patients who were given an indication for general anesthesia and had complete clinical and radiological data were included in the study. Patients who were treated with local anesthesia and whose clinical and radiological data were not available were excluded from the study. Patients who underwent the procedure under general anesthesia were evaluated retrospectively and demographically. In demographic evaluation; The age, gender, systemic diseases of the patients, the procedure performed and the reason for general anesthesia were evaluated. Systemic diseases; They were classified as healthy, mentally retarded, cerebral palsy, autism, cardiovascular diseases, diabetes, thyroid, epilepsy, asthma, physical disability, Down syndrome, history of anaphylaxis and bipolar disorder. Procedures performed under general anesthesia were classified as tooth extraction, impacted tooth extraction, restorative procedures, cyst, tumor, apical resection, orthognathic surgery, sinus lift and implant, and oroantral fistula treatment. Reasons for undergoing general anesthesia: It was classified as anesthesia requirement, dental phobia, and nausea reflex.

Statistical Analysis

IBM SPSS (Statistical Package for the Social Sciences) Statics 27.0 program (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp) was used in statistical analysis. Normality of distributions was calculated using the Shapiro-Wilk test. In descriptive statistics, standard deviation, mean, minimum values, maximum values, percentages, cross tables and frequencies were used. Chi-square test was used to determine the relationships between groups. Post-hoc analyses were performed using the chi-square distribution's right-tailed probability to identify significant differences between groups. Statistical significance level was measured as $p < 0.05$.

RESULTS

In this study, a total of 550 patients, 332 women (58.5%) and 228 men (41.5%), aged between 1 and 79, with an average age of 16.41 ± 13.36 , were treated under general anesthesia at Eskişehir Osmangazi University Faculty of Dentistry. data were examined. The average age of the patients in the study was 15.05 ± 12.66 for women and 18.34 ± 14.09 for men. The patients in the study were mostly under the age of 20, with 370 people (67.3%), while 1 person (0.2%) was at least over 70 years old. The frequencies and percentages of patients in age groups are given in Table 1. Of the patients in the study, 352 were healthy (64%), 65 had mental retardation (11.8%), 22 had cerebral palsy (4%), 36 had autism (6.5%), and 23 had cardiovascular disease (4.2%). 6 with diabetes (1.1%), 3 with thyroid disease (0.5%), 21 with epilepsy (3.8%), 9 with asthma (1.6%), 4 with physical disability (0.7%), 1 with a history of anaphylaxis (0.2%), and 1 with bipolar disorder (0.2%). 47 of the general anesthetics were performed due to the need for anesthesia (8.5%), 423 due to dental phobia (76.9%) and 80 due to nausea reflex (14.5%). Due to the need for anesthesia, 24 males (7.5%) and 23 females (10.1%); 259 men (80.4%) and 164 women (71.9%) due to dental phobia; Due to nausea reflex, 39 men (12.1%) and 41 women (18%) were taken under general anesthesia. In the chi-square test performed to examine the relationship between gender and the reason for undergoing general anesthesia, the p value was higher than 0.05. There is no significant difference between gender and the reason for undergoing general anesthesia. When we examine the reasons for undergoing general anesthesia according to systemic conditions, the healthy group is the most prevalent in all three reasons. The second most common systemic condition group in patients undergoing general anesthesia due to dental phobia is patients with mental retardation, and the third most common is patients with autism (Table 2). In the chi-square test performed to examine the relationship between systemic status and the reason for undergoing general anesthesia. There is a significant difference between the reason for undergoing general anesthesia and the systemic condition ($p < 0.05$). Post-hoc analysis was performed with the right-tailed probability of the chi-square distribution to look at the differences between the groups ($p = 0.001$ significance value was determined). The number of patients in the healthy group in the group that required general anesthesia was significantly higher than expected ($p < 0.001$). Among the groups that underwent general anesthesia due to dental phobia, the healthy group ($p < 0.001$) and the diabetes group ($p < 0.001$) were significantly less than expected, while the mental retardation ($p < 0.001$) and autism group ($p < 0.001$) were significantly more than expected. has come out. In the group taken under general anesthesia with nausea reflex, the mental retardation group ($p < 0.001$) was significantly lower than expected, while

the diabetes group ($p<0.001$) was significantly higher than expected. When we examine the reasons for undergoing general anesthesia according to age groups, the need for anesthesia is highest in the group between the ages of 20 and 30, dental phobia is highest in the group under the age of 20, then in the group between the ages of 20 and 30, and nausea reflex is highest in the group between the ages of 30 and 40, and then in the group between the ages of 20 and 20. It is in the 30-year age group (Table 3).

Table 1. Distributionof patients by age groups		
Age groups	N	%
Under 20	370	67.3
Between 20-30 years	81	14.7
Between 30-40 years	55	10
Between 40-50 years	31	5.6
Between 50-60 years	10	1.8
Between 60-70 years	2	0.4
Over 70 years old	1	0.2

Table 2. Reasons for undergoing general anesthesia according to systemic conditions					
Systemic status		Reason for general anesthesia			Total
		Requirement for anesthesia	Dental phobia	Nausea reflex	
Healthy	N	41	249	62	352
	%	11.6	70.7	17.6	100.0
Mentally retarded	N	0	65	0	65
	%	0.0	100.0	0.0	100.0
Cerebral palsy	N	0	22	0	22
	%	0.0	100.0	0.0	100.0
Autism	N	0	36	0	36
	%	0.0	100.0	0.0	100.0
Cardiovascular disease	N	3	15	5	23
	%	13.0	65.2	21.7	100.0
Diabet	N	1	0	5	6
	%	16.7	0.0	83.3	100.0
Thyroid disease	N	0	2	1	3
	%	0.0	66.7	33.3	100.0
Epilepsy	N	0	14	7	21
	%	0.0	66.7	33.3	100.0
Asthma	N	0	9	0	9
	%	0.0	100.0	0.0	100.0
Physically disabled	N	2	2	0	4
	%	50.0	50.0	0.0	100.0
Down syndrome	N	0	7	0	7
	%	0.0	100.0	0.0	100.0
History of anaphylaxis	N	0	1	0	1
	%	0.0	100.0	0.0	100.0
Bipolar disorder	N	0	1	0	1
	%	0.0	100.0	0.0	100.0
Total	N	47	423	80	550
	%	8.5	76.9	14.5	100.0

Table 3. Age-based comparison of reasons for general anesthesia

Age groups		Reason for general anesthesia			Total
		Requirement for anesthesia	Dental phobia	Nausea reflex	
Under 20	N	7	360	3	370
	%	1.9	97.3	0.8	100.0
20-30 years between	N	15	41	25	81
	%	18.5	50.6	30.9	100.0
30-40 years between	N	9	13	33	55
	%	16.4	23.6	60.0	100.0
40-50 years between	N	8	7	16	31
	%	25.8	22.6	51.6	100.0
50-60 years between	N	6	2	2	10
	%	60.0	20.0	20.0	100.0
60-70 years between	N	1	0	1	2
	%	50.0	0.0	50.0	100.0
Over 70 years old	N	1	0	0	1
	%	100.0	0.0	0.0	100.0
Total	N	47	423	80	550
	%	8.5	76.9	14.5	100.0

In the chi-square test performed to examine the relationship between age groups and the reason for undergoing general anesthesia, p was <0.001 . Post-hoc analysis was performed with the right-tailed probability of the chi-square distribution to look at the differences between the groups ($p=0.0023$ significance value was determined). While the group under the age of 20, who underwent general anesthesia due to the need for anesthesia, was significantly lower than expected ($p<0.0023$), the group between the ages of 20-30, the group between the ages of 40-50, the group between the ages of 50-60 and the group over the age of 70 were significantly higher than expected ($p<0.0023$). Among the groups that underwent general anesthesia due to dental phobia, the group under the age of 20 was significantly higher than expected ($p<0.0023$), while the group between the ages of 20-30, the group between the ages of 30-40, the group between the ages of 40-50, the group between the ages of 50-60. It was significantly higher than expected ($p<0.0023$). In the groups under general anesthesia due

to nausea reflex, the group under the age of 20 was significantly less than expected ($p<0.0023$), while the group between the ages of 20-30, the group between the ages of 30-40 and the group between the ages of 40-50 were significantly higher than the expected ($p<0.0023$). Of the treatments performed under general anesthesia, 93 were tooth extraction (16.9%), 92 were impacted tooth extraction (16.7%), 318 were tooth extraction (57.8%) and restorative procedures, 18 were cysts (3.3%), 6 were cysts (3.3%), and 6 were cysts (3.3%). 1 tumor (1.1%), 9 cyst and apical resection (1.6%), 12 orthognathic surgery (2.2%), 1 sinus lift and implant (0.2%), 1 of which is the treatment of oroantral fistula (0.2%). When we examine the treatments performed under general anesthesia by gender, men are mostly in the tooth extraction and restorative procedure, impacted tooth extraction and tooth extraction groups, respectively. Women are mostly found in the tooth extraction and restorative procedure, tooth extraction and impacted tooth extraction groups, respectively (Table 4).

Table 4. Treatments performed under general anesthesia according to gender

Dental treatment under general anesthesia	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Tooth extraction	51	15.8	42	18.4	93	16.9
Impacted tooth extraction	55	17.1	37	16.2	92	16.7
Tooth extraction and restorative process	190	59.0	128	56.1	318	57.8
Cyst	7	2.2	11	4.8	18	3.3
Tumor	2	0.6	4	1.8	6	1.1
Cyst and apical resection	8	2.5	1	0.4	9	1.6
Orthognathic surgery	7	2.2	5	2.2	12	2.2
Sinus lift and implant	1	0.3	0	0.0	1	0.2
Oroantral fistula treatment	1	0.3	0	0.0	1	0.2

In the chi-square test performed to examine the relationship between gender and treatment under general anesthesia, $p>0.05$ was found. There is no significant difference between treatment performed under general anesthesia and gender. When we

examined the treatments performed under general anesthesia according to systemic conditions, the most frequent tooth extractions and restorative procedures were performed in all systemic diseases except bipolar disorder (Table 5).

Table 5. Treatments performed under general anesthesia for systemic conditions											
Systemic status		Dental treatment under general anesthesia									Total
		Tooth extraction	Impacted tooth extraction	Tooth extraction and restorative treatment	Cyst	Tumor	Cyst and apical resection	Orthognathic surgery	Sinus lift and implant	Orontral fistula treatment	
Healthy	N	72	62	177	14	6	9	11	1	0	352
	%	20.5	17.6	50.3	4.0	1.7	2.6	3.1	0.3	0.0	100.0
Mentally retarded	N	5	11	49	0	0	0	0	0	0	65
	%	7.7	16.9	75.4	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Cerebral palsy	N	2	1	19	0	0	0	0	0	0	22
	%	9.1	4.5	86.4	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Autism	N	2	6	28	0	0	0	0	0	0	36
	%	5.6	16.7	77.8	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Cardiovascular disease	N	6	2	13	2	0	0	0	0	0	23
	%	26.1	8.7	56.5	8.7	0.0	0.0	0.0	0.0	0.0	100.0
Diabet	N	0	2	2	1	0	0	0	0	1	6
	%	0.0	33.3	33.3	16.7	0.0	0.0	0.0	0.0	16.7	100.0
Thyroid disease	N	0	1	2	0	0	0	0	0	0	3
	%	0.0	33.3	66.7	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Epilepsy	N	5	5	11	0	0	0	0	0	0	21
	%	23.8	23.8	52.4	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Asthma	N	0	0	9	0	0	0	0	0	0	9
	%	0.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Physically disabled	N	0	1	1	1	0	0	1	0	0	4
	%	0.0	25.0	25.0	25.0	0.0	0.0	25.0	0.0	0.0	100.0
Down syndrome	N	0	1	6	0	0	0	0	0	0	7
	%	0.0	14.3	85.7	0.0	0.0	0.0	0.0	0.0	0.0	100.0
History of anaphylaxis	N	0	0	1	0	0	0	0	0	0	1
	%	0.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Bipolar disorder	N	1	0	0	0	0	0	0	0	0	1
	%	100.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	100.0
Total	N	93	92	318	18	6	9	12	1	1	550
	%	16.9	16.7	57.8	3.3	1.1	1.6	2.2	0.2	0.2	100.0

In the chi-square test performed to examine the relationship between systemic status and dental treatment under general anesthesia, p was <0.001 . Post-hoc analysis was performed with the right-tailed probability of the chi-square distribution to look at the differences between the groups ($p=0.00042$ significance value was determined). While the healthy group was significantly lower than expected in tooth extraction and restorative procedures ($p<0.00042$), the diabetes group was significantly higher than expected in oroantral fistula treatment ($p<0.00042$). When we examined the dental treatments performed under general anesthesia according to age groups, the most tooth extraction

and restorative procedures were performed, except for the group between the ages of 50-60 and over the age of 70. In the 20-year age group, which has the largest number of samples, the most frequent tooth extractions, restorative procedures, tooth extractions and impacted tooth extractions were performed (Table 6).

In the chi-square test performed to examine the relationship between age groups and dental treatment under general anesthesia, p was <0.001 . Post-hoc analysis was performed with the right-tailed probability of the chi-square distribution to look at the differences between the groups ($p=0.00079$ significance value was determined). In the groups that underwent general anesthesia due to

tooth extraction, the group under 20 years of age was significantly higher than expected ($p<0.00079$), while the group between 20-30 years of age was significantly lower than expected ($p<0.00079$). In the groups that underwent general anesthesia due to impacted tooth extraction, the group under 20 years of age was significantly lower than expected ($p<0.00079$), while the group between 20-30 years of age was significantly higher than expected ($p<0.00079$).

In the groups under general anesthesia due to tooth extraction and restorative procedures, the group under 20 years of age was significantly higher than expected ($p<0.00079$). In the groups that underwent general

anesthesia due to cyst treatment, the group under the age of 20 was significantly lower than expected ($p<0.00079$), while the group between the ages of 50-60 and the group over 70 years of age was significantly higher than expected ($p<0.00079$). In the groups that underwent general anesthesia due to cysts and apical resection, the group under 20 years of age was significantly lower than expected ($p<0.00079$), while the group between 20-30 years of age was significantly higher than expected ($p<0.00079$). In the groups that underwent general anesthesia due to orthognathic surgery, the group under 20 years of age was significantly lower than expected ($p<0.00079$), while the group between 20-30 years of age was significantly higher than expected ($p<0.00079$).

Table 6. Dental treatments performed under general anesthesia by age groups								
Dental treatment under general anesthesia	Age groups							Total
	Under 20	20-30 between ages	30-40 between ages	40-50 between ages	50-60 between ages	60-70 between ages	Over 70 years old	
Tooth extraction	80	3	3	6	1	0	0	93
Impacted tooth extraction	40	27	15	8	1	1	0	92
Tooth extraction and restorative treatment	245	35	25	10	2	1	0	318
Cyst	2	4	2	4	5	0	1	18
Tumor	3	1	1	1	0	0	0	6
Cyst and apical resection	0	1	5	2	1	0	0	9
Orthognathic surgery	0	10	2	0	0	0	0	12
Sinus lift and implant	0	0	1	0	0	0	0	1
Oroantral fistula treatment	0	0	1	0	0	0	0	1
Total	370	81	55	31	10	2	1	550

When we compare the reasons for undergoing general anesthesia compared to dental treatments performed under general anesthesia, the need for anesthesia was mostly in cyst patients, while dental phobia and nausea reflex occurred mostly in tooth extraction and restorative procedure patients (Table 7).

In the chi-square test performed to examine the relationship between the reasons for undergoing general anesthesia and the dental treatment performed under general anesthesia, p was <0.001 . Post-hoc analysis was performed with the right-tailed probability of the chi-square distribution to look at the differences between the groups ($p=0.0018$ significance value was determined). In the groups where tooth extraction was performed under general anesthesia, there were significantly fewer patients who were taken under general anesthesia due to the need for anesthesia ($p<0.0018$), while those who were taken due to dental phobia were significantly more ($p<0.0018$). In the groups where impacted tooth extraction was performed under general anesthesia, there were significantly fewer patients taken under general anesthesia due to dental phobia ($p<0.0018$), while there were significantly more patients taken due to nausea reflex ($p<0.0018$). In the group where tooth extraction and restorative procedures were performed under general anesthesia, the group taken

due to the need for anesthesia was significantly lower than expected ($p<0.0018$), while the group taken due to dental phobia was significantly higher than expected ($p<0.0018$). In the groups where cyst treatment was performed under general anesthesia, those removed due to the need for anesthesia were significantly higher than expected ($p<0.0018$), while those removed due to dental phobia were significantly less than expected ($p<0.0018$). In the groups where tumor treatment was performed under general anesthesia, the number of patients taken due to the need for anesthesia was significantly higher than expected ($p<0.0018$), while the number of patients taken due to dental phobia was significantly lower than expected ($p<0.0018$). In patients who underwent cyst and apical resection treatment under general anesthesia, the number of patients taken under general anesthesia due to the need for anesthesia was significantly higher than expected ($p<0.0018$), while the number of patients taken due to dental phobia was significantly lower than expected ($p<0.0018$). Among patients who underwent orthognathic surgery under general anesthesia, the number of patients taken under general anesthesia due to the need for anesthesia was significantly higher than expected ($p<0.0018$), while the number of patients taken under general anesthesia due to dental phobia was significantly lower than expected ($p<0.0018$).

Table 7. Relationship between causes and types of treatments performed under general anesthesia

	Reason for general anesthesia							
	Requirement for anesthesia		Dental phobia		Nausea reflex		Total	
	N	%	N	%	N	%	N	%
Tooth extraction	0	0.0	85	20.1	8	10.0	93	16.9
Impacted tooth extraction	5	10.6	54	12.8	33	41.3	92	16.7
Tooth extraction and restorative treatment	0	0.0	281	66.4	37	46.3	318	57.8
Cyst	18	38.3	0	0.0	0	0.0	18	3.3
Tumor	6	12.8	0	0.0	0	0.0	6	1.1
Cyst and apical resection	7	14.9	2	0.5	0	0.0	9	1.6
Orthognathic surgery	11	23.4	1	0.2	0	0.0	12	2.2
Sinus lift and implant	0	0.0	0	0.0	1	1.3	1	0.2
Oroantral fistula treatment	0	0.0	0	0.0	1	1.3	1	0.2
Total	47	100.0	423	100.0	80	100.0	550	100.0

DISCUSSION

The most common reasons for dental treatments performed under general anesthesia are lack of cooperation and multiple systemic diseases (7-10). 45% of dental treatments performed under general anesthesia were performed due to lack of cooperation due to autism, dementia, mental retardation and other mental problems (7,11,12). Patients with autism spectrum disorder should be examined individually when choosing local anesthesia, sedation or general anesthesia because cooperation varies from patient to patient. Depending on their learning difficulties and cooperation, repeated learning can increase their cooperation and allow them to be treated without general anesthesia (10,13). More teeth may be extracted in patients with autism spectrum disorder due to cooperation problems and poor oral hygiene (14,15). Due to different cooperation difficulties in patients with mental retardation, general anesthesia preferences should be made individually for the patient (16). Cerebral palsy is one of the most common reasons for dental treatments performed under general anesthesia due to muscle paralysis, muscle weakness, involuntary movements, poor coordination and other motor dysfunctions (17).

Patients with special needs have a higher prevalence of oral diseases because it is more difficult for them to maintain oral hygiene compared to other patients (18). While untreated caries is 22.7% in the general population, it is 32.2% in those with mental and/or developmental disabilities, edentulism is 7.6% in the general population and 10.9% in those with mental and/or developmental disabilities, while the average missing tooth is 3.6 in the general population and 6.7% in those with mental and/or developmental disabilities (19). However, some studies have shown that patients with psychiatric problems have poorer oral hygiene than adult patients with physical or mental disabilities (20,21). The most common dental treatment performed under general anesthesia is tooth extraction, as opposed to longer and more complex

treatments such as root canal treatment (21,22).

In a retrospective study on dental treatments under general anesthesia conducted in Türkiye in 2015, the average age of the patients was 16.78±12.7 years. Gender distribution is 59.3% male and 40.7% female among 467 people. 51.2% of the dental treatments applied to patients are tooth extraction, 40.9% are fillings and tooth extractions, and 7.9% are maxillofacial surgery. 24.4% of the patients in the study had mental retardation, 7.1% cerebral palsy, 3.9% epilepsy, 6% autism, 2.4% Down syndrome, 1.5% schizophrenia, 0.2% morbid obesity, 12.2%. 100% with mental retardation and epilepsy, 0.6% with cerebral palsy and mental retardation, 5.1% with epilepsy and While 1.7% have mental retardation, epilepsy and cerebral palsy, 34.9% have no known disease. 45.6% of dental treatments were performed under general anesthesia due to lack of cooperation, 38.9% for mental retardation, 5.9% for autism, 1.7% for schizophrenia, and 7.9% for maxillofacial surgery. The average duration of dental treatments administered to patients under general anesthesia is 114.53±35.4 minutes. The average time it takes for patients to recover after general anesthesia is 40.47±6.0 minutes (12). In our study, the data of 550 patients, 332 women (58.5%) and 228 men (41.5%), whose ages ranged from 1 to 79 years old and whose average age was 16.41 years, were examined. In our study, dental treatment was performed under general anesthesia mostly on mentally retarded individuals, apart from the healthy group. Patients mostly underwent dental treatment under general anesthesia due to dental phobia. More male patients were treated under general anesthesia due to dental phobia. General anesthesia durations were not examined in our study. In 2016, Shin et al. (23) In his study, the ages of the patients ranged from 1 to 16 and 176 were males (66.9%) and 87 were females (33.1%). The average duration of general anesthesia for patients was 132.7±77.6 minutes, and the average duration of treatment was 101.9±71.2 minutes. Of the 380 treatments performed, 106 were surgical, 33 were prosthetic, 158 were restorative,

11 were preventive, and 72 were endodontic treatments. Of the treatments performed, 127 were for dental anxiety, 38 for mental retardation, 29 for age-related non-cooperation, 29 for mental illness, 26 for autism, 18 for developmental disorder, 10 for nausea reflex, 6 for physical therapy disability, 4 due to asthma and 3 due to epilepsy. Similarly, in our study, the most commonly applied treatment under general anesthesia is tooth extraction and restorative procedures. Similarly, in our study, the reason for taking general anesthesia was mostly due to dental phobia.

In the study of Schnabl et al. (20) on 444 adult patients with an average age of 37.37 ± 13.78 years who received dental treatment under general anesthesia, there were 245 males (55.2%) and 199 females (44.8%). 226 (56.2%) of the men have a physical or mental disability, and 19 (45.2%) have a psychiatric disease. Of the women, 176 (43.8%) have a physical or mental disability and 23 (54.8%) have a psychiatric disease. Among patients treated under general anesthesia, those with physical or mental disabilities are significantly more likely than those with psychiatric illnesses. While the average number of teeth restored under general anesthesia in each of 402 patients with physical or mental disabilities was 5.34 ± 4.41 , the average number of teeth extracted was 2.6 ± 3.96 . While the average number of teeth restored under general anesthesia in each of the 42 patients with psychiatric illness was 7.98 ± 5.4 , the average number of teeth extracted was 4.86 ± 4.51 . The number of teeth restored under general anesthesia was significantly higher than the number of teeth extracted, both in patients with physical or mental disabilities and in patients with psychiatric diseases. In our study, apart from healthy individuals, tooth extraction and restorative procedures performed under general anesthesia were mostly performed on mentally retarded and autistic individuals. In our study, the number of extracted and restored teeth was not compared.

Choi and Doh (24), in their review of dental treatments performed under general anesthesia in 2021, they found autism, mental retardation, dementia, panic attack due to cooperation problems, cerebral palsy due to motor dysfunction, epilepsy, Parkinson's, other neurological disorders, skeletal muscle diseases; They stated that Down syndrome and other genetic diseases due to craniofacial anomalies are indications for dental treatment performed under general anesthesia.

According to the study conducted by Mastilovic et al. (25) in 2021, 257 patients aged between 18 and 68.8 had an average of 8.69 ± 13.1 dentist appointments in 10 years, 3.64 ± 4.42 of them had dental restoration and 6.64 ± 5.95 had tooth extraction, and the average treatment time of these patients was 1.47 months. ± 0.8 have been shown to be performed under general anesthesia. Among these patients, mentally retarded patients showed a significant decrease in dentist appointments compared to other patients (5.00 ± 5.66) and a significant increase in tooth extraction treatment compared to other patients

(12.0 ± 8.49). It has also been shown that the patient's condition and mental retardation cause a significant increase in dental restoration and extraction performed under general anesthesia. In our study, individuals with mental retardation received more dental treatment under general anesthesia than those with other systemic conditions.

Marinho et al. (26) in 2022, the distribution products it makes with technologies, which are special treatments for dental treatment under general anesthesia in private and public health services, are in the 6-80 age range and 100 of them are accessible, 62% are men and 38% are women. The most commonly diagnosed treatable medical diseases are autistic spectrum disorder (33%), followed by mental retardation (27%) and cerebral palsy (10%). The most common International Association of Disability and Oral Health (IADH) categories are behavioral and psychiatric disorders (41%), followed by mental and physical disabilities (39%). Anesthesiologists, technicians and medical personnel adopted a general anesthesia sequence similar to the literature, using inhalation sedation together with intravenous drug administration, followed by nasotracheal intubation and sevoflurane gas. The duration of general anesthesia was determined as 3 hours on average for each patient, and it was reported that no complications were observed related to general anesthesia and no problems occurred in recovery. It was reported that 52% of private health institutions and 5% of patients with special needs admitted by public hospitals received dental treatment before general anesthesia. While dental complaints reported by patients or their relatives were dental pain in the private sector (65%), it was reported as 54% in public hospitals. In our study, public and private health services were not compared, and the group most frequently receiving dental treatment under general anesthesia is the mental retardation group, not the autism group.

Kasemkhun et al. (27) in their study titled retrospective comparison of dental treatments performed under general anesthesia and non-pharmacological approach in patients with special health needs in 2022, there were 261 patients with an average age of 14.22 ± 8.64 years and ages ranging from 2.2 to 43.1 years. The ratio between cases treated under general anesthesia and non-pharmacological treatment was determined as 1.6:1. The general anesthesia group was significantly higher in mean age, caries experience, lack of cooperation and need for treatment than the non-pharmacological treatment group. Additionally, control rates in the general anesthesia group were significantly lower compared to the non-pharmacological treatment group, but no significant difference was observed in terms of regularity. After 24 months of follow-up, the frequency of new cavities and the time to detection of cavities were found to be faster in the general anesthesia group, as well as significant behavioral changes. In our study, general anesthesia and non-pharmacological treatments were not compared.

In the literature review, Karaduran et al. (28) reported that general anesthesia in dentistry is a procedure that can be applied to uncooperative patients, those with health risks, or individuals with disabilities. They noted a significant relationship between complications that may occur during or after general anesthesia and factors such as treatment duration, treatment procedures, and the potential need for repeat general anesthesia. The authors emphasized that patients and their families should be thoroughly informed about the risks and complications of general anesthesia beforehand. As a conclusion, they highlighted the importance of implementing preventive measures and ensuring regular follow-ups after dental treatments performed under general anesthesia.

CONCLUSION

It has been observed that the most common reasons for the need for general anesthesia are the need for anesthesia, dental phobia and nausea reflex. Among the patients who were taken under general anesthesia due to dental phobia, individuals with mental retardation were the most common ones. It has been determined that the most frequently performed dental treatments under general anesthesia are tooth extraction, impacted tooth extraction and restorative procedures. It has been observed that the need for anesthesia occurs mostly in cyst patients, and dental phobia and nausea reflex occur in patients with tooth extraction and restorative procedures.

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REFERENCES

- Kepekçi AH, Kepekçi AB. Surgery and the Operating Room From Past to Present. Journal of Medical Sciences. 2023;4:15-20.
- Breen P, Park KW. General anesthesia versus regional anesthesia. Int Anesthesiol Clin. 2002;40:61-71.
- Balaji S, Balaji PP. Textbook of Oral and Maxillofacial Surgery-E-Book. 4th edition . Elsevier Health Sciences. 2023;199-227.
- Savanheimo N, Sundberg SA, Virtanen JI, Vehkalahti MM. Dental care and treatments provided under general anaesthesia in the Helsinki Public Dental Service. BMC Oral Health. 2012;12:45.
- Andreeva R. Indications for dental treatment under general anesthesia. Scripta Scientifica Medica. 2018;50:15-8.
- Arbağ H, Uyar Y, Öztürk K, Ülkü ÇH. The evaluation of the le fort I osteotomy approach. KBB-Forum. 2004;3:110-4.
- Wang YC, Lin IH, Huang CH, Fan SZ. Dental anesthesia for patients with special needs. Acta Anaesthesiol Taiwan. 2012;50:122-5.
- Hulland S, Sigal MJ. Hospital-based dental care for persons with disabilities: a study of patient selection criteria. Spec Care Dentist. 2000;20:131-8.
- Silvestre-Rangil J, Silvestre FJ, Espín-Gálvez F. Hospital dental practice in special patients. Med Oral Patol Oral Cir Bucal. 2014;19:163-9.
- Sacoar S. Anaesthesia and sedation for the autistic patient. SAAD Dig. 2017;33:40-3.
- Mallineni SK, Yiu CK. Dental treatment under general anesthesia for special-needs patients: analysis of the literature. J Investig Clin Dent. 2016;7:325-31.
- Özkan AS, Erdoğan MA, Şanlı M, et al. Retrospective evaluation of dental treatment under general anaesthesia. Turk J Anaesthesiol Reanim. 2015;43:332-6.
- van der Walt JH, Moran C. An audit of perioperative management of autistic children. Paediatr Anaesth. 2001;11:401-8.
- Chang J, Kim HY. Does caries risk assessment predict the incidence of caries for special needs patients requiring general anesthesia?. Acta Odontol Scand. 2014;72:721-8.
- Rada RE. Treatment needs and adverse events related to dental treatment under general anesthesia for individuals with autism. Intellect Dev Disabil. 2013;51:246-52.
- Miyawaki T, Kohjitani A, Maeda S, et al. Intravenous sedation for dental patients with intellectual disability. J Intellect Disabil Res. 2004;48:764-8.
- Kuban KC, Leviton A. Cerebral palsy. N Engl J Med. 1994;330:188-95.
- Stanková M, Buček A, Dostálová T, et al. Patients with special needs within treatment under general anesthesia - meta-analysis. Prague Med Rep. 2011;112:216-25.
- Morgan JP, Minihan PM, Stark PC, et al. The oral health status of 4,732 adults with intellectual and developmental disabilities. J Am Dent Assoc. 2012;143:838-46.
- Schnabl D, Guarda A, Guarda M, et al. Dental treatment under general anesthesia in adults with special needs at the University Hospital of Dental Prosthetics and Restorative Dentistry of Innsbruck, Austria: a retrospective study of 12 years. Clin Oral Investig. 2019;23:4157-62.
- Jockusch J, Hopfenmüller W, Ettinger R, Nitschke I. Outpatient, dental care of adult vulnerable patients under general anaesthesia-a retrospective evaluation of need for treatment and dental follow-up care. Clin Oral Investig. 2021;25:2407-17.
- Fernández-Feijoo J, Carro B, Branco A. The effect of dentist experience on the treatment of individuals with disability under general anesthesia. Spec Care Dentist. 2019;39:281-6.
- Shin B, Yoo S, Kim J, et al. A survey of dental treatment under general anesthesia in a Korean university hospital pediatric dental clinic. J Dent Anesth Pain Med. 2016;16:203-8.
- Choi J, Doh RM. Dental treatment under general anesthesia for patients with severe disabilities. J Dent Anesth Pain Med. 2021;21:87-98.

25. Mastilovic G, Petrovic B, Peric T, et al. Dental treatment and oral rehabilitation for adults with intellectual disability under general anesthesia. *Journal of Policy and Practice in Intellectual Disabilities*. 2021;18:306-12.
26. Marinho MA, Ramos FCT, Cardoso AL, et al. Dental treatment under general anesthesia in patients with special needs provided by private and public healthcare services-a retrospective, comparative study. *Healthcare (Basel)*. 2022;10:1147.
27. Kasemkhun P, Smutkeeree A, Jirattanasopha V. A retrospective comparison of dental treatment under general anesthesia versus non-pharmacological approach in patient with special health care needs. *J Dent Sci*. 2022;17:1238-43.
28. Karaduran B, Kumas Solak S, Koruyucu M. Dental treatments under general anesthesia. *Yeditepe J Dent*. 2024;20:60-4.



What Affects the Lives of Patients with Adolescent Idiopathic Scoliosis More, Brace or Surgery?

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Abstract

Aim: Scoliosis is a deformity characterized by lateral curvature and rotation of the spine. Scoliosis treatment modalities include observation, exercise, bracing, and surgery. This study aimed to compare the effects of bracing and surgery with posterior spinal instrumentation and posterior fusion (PSIPF) on pain, activities of daily living, and depression in individuals with scoliosis.

Material and Method: In this prospectively planned study, 105 patients who met the criteria were included among 184 scoliosis patients who were diagnosed with adolescent idiopathic scoliosis (AIS) and followed up regularly in our clinic between January 2023 and December 2024. The patients who met the inclusion criteria were randomly divided into two groups Brace and Surgery Group. Visual Analog Scale (VAS), Beck Depression Scale (BDS), and Scoliosis Research Society 22 (SRS-22) questionnaire were administered to both groups by the same researchers and the data were compared statistically. A p-value <0.05 was considered statistically significant.

Results: There was no significant difference between the two groups in terms of descriptive characteristics of the participants ($p>0.05$). VAS and BDS data were significantly decreased in the Surgery Group compared to the Brace Group ($p<0.05$). Among the sub-parameters of SRS-22, function, pain, and satisfaction data were significantly improved in the surgery group compared to the brace group ($p<0.05$).

Conclusion: In the treatment of scoliosis, surgical treatment with the PSIPF method seems to be more effective in physical and psychological recovery compared to brace treatment.

Keywords: Adolescent idiopathic scoliosis, instrumentation, braces, spine, deformity

INTRODUCTION

Scoliosis is a deformity characterised by lateral curvature and rotation of the spine with a major curvature angle of at least 10° in the coronal plane (1). Treatment modalities for scoliosis include observation, exercise, bracing and surgery. The criteria taken into account when deciding on the appropriate treatment are the age of the patient, the degree of curvature, and the maturation of the skeletal bones (2). Brace, which is one of the conservative treatment methods of scoliosis, aims to stop the progressive curve and reduce the degree of scoliosis (3). The brace should be used as long as growth continues and is recommended if the patient has progressed 5-10 degrees in the last six months and should be used for an average of 2-4 years (4). Spinal correction surgery is considered in scoliosis patients with complete skeletal ossification and curves with a major curvature angle greater than 45° . The main aims of surgical treatment are to terminate the progression of idiopathic scoliosis, to minimise the risk of progression, to eliminate pulmonary dysfunction, to

relieve uncontrollable low back and back pain, to provide psychological relief by achieving a proper posture and to reduce the rate of short and long-term complications that may occur (5,6). Many techniques have been defined for the correction of curvature in scoliosis surgery, and the most common surgical treatment applied today is posterior spinal instrumentation and posterior fusion (PSIPF) (7,8). Scoliosis surgery is a procedure that requires a great deal of difficulty and patience for the patient and the patient's relatives in terms of operation time, incision size and postoperative follow-up. Therefore, some patients may prefer brace as an alternative to surgical treatment (9). However, the effectiveness of brace and its psychosocial effects on the patient are still a matter of debate (10). In addition, the long-term effects of both treatment methods on patients need to be compared in terms of factors such as pain level, activities of daily living and mental status.

The aim of this study was to compare and evaluate the effects of brace treatment and surgery with PSIPF method on pain, quality of life and depression in individuals with

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adolescent idiopathic scoliosis (AIS). It is aimed that the findings to be obtained will be a guide for patients and physicians in the scoliosis treatment process.

MATERIAL AND METHOD

In this prospective study, 105 patients who met the criteria were included among 184 scoliosis patients who were diagnosed with AIS and followed up regularly in our Orthopaedics and Traumatology Clinic between January 2023 and December 2024. Patients whose informed consent was obtained were included in the study. Ethical approval numbered 03.01.2023/775 was received from the Kayseri City Hospital Ethics Committee for the study. The principles of the Declaration of Helsinki were adhered to at all stages of the study.

Inclusion criteria: (I) diagnosis of adolescent idiopathic scoliosis in our clinic, (II) age between 12-18 years, (III) Patients who have been using a brace for 23 hours a day for at least 1 year and whose Cobb angle is between 20°-45° or who have had PSIPF surgery in our clinic and whose Cobb angle is over 45° with at least 1 year of follow-up, (IV) complete data.

Exclusion criteria: (I) incomplete follow-up and records, (II) the patient had undergone another surgical treatment other than scoliosis during the follow-up period, (III) unwillingness to participate in the study.

The patients who met the inclusion criteria were divided into two groups. Patients who underwent conservative treatment with bracing were included in the Brace Group. Patients who underwent PSIPF were included in the Surgical Group. Each patient included in the study was assigned a patient follow-up number. For each number, the patient's name, surname, gender, age, file number, and date of surgery were recorded. In addition, all physicians participating in the study were ensured to follow uniform treatment and assessment guidelines to minimise the effect of individual differences on treatment outcomes. Visual Analogue Scale (VAS), Beck Depression Scale (BDS) and Scoliosis Research Society 22 (SRS-22) questionnaires were administered to all patients by the same investigator.

VAS: A pain rating scale, often used in epidemiologic and clinical research to measure pain intensity or frequency. It categorizes pain as mild, moderate and severe. In the scale, pain intensity is expressed by numbers between

0-10 on the line segment and is evaluated as no pain at 0 and severe pain at 10 (11).

BDS: It was developed to measure behavioral findings related to depression in adolescents or adults. A score between 0-13 on the BDS questionnaire indicates no depression, a score between 14-19 indicates low depression, a score between 20-28 indicates moderate depression, and a score between 29-63 indicates high depression (12).

SRS-22 questionnaire: Function, Pain, Self Image, Mental Health and Satisfaction with Treatment is an easy and practical quality of life questionnaire consisting of 5 sub-parameters and a total of 22 questions, designed specifically for scoliosis to evaluate the current condition of the spine and widely used all over the world. A scoring system was created so that the total score to be obtained from each sub-parameter would be between 1 and 5. 5 points means the highest score and 1 point means the lowest score (13).

Statistical Analysis

Statistical evaluation of the data was performed using SPSS 22 package program. Normality of the data was examined by Kolmogrov-Simirnov test. Since the data were normally distributed, ANOVA analysis was used in the comparison of more than two group averages by using the independent t-test for two group mean comparisons. The level of error was taken as 0.05.

RESULTS

Of the 105 patients included in the study, 74 were female and 31 were male with an average age of 14.58±1.68 years. Of the cases, 57 were Lenke Type-1, 37 were Lenke Type-2 and 11 were Lenke Type-3. The mean age of 54 patients (39 F, 15 M) included in the Brace Group was 13.52±1.69 years and the mean Cobb angle was 31.81°±3.73, while the mean age of 51 patients (35 F, 16 M) included in the Surgery Group was 15.65±1.68 years and the mean Cobb angle was 60.14°±9.51. VAS value indicating pain level and BDS data indicating behavioural findings of depression were found to be significantly decreased in the surgery group compared to the brace group (p<0.05). Function, pain and satisfaction data, which are sub-parameters of SRS-22, were significantly improved in the surgery group compared to the brace group (p<0.05), (Table 1).

Table 1. Comparison of brace group and surgery group data of adolescent idiopathic scoliosis patients			
	Brace group (n=54) (Mean±SD)	Surgery group (n=51) (Mean±SD)	Sig (p)
VAS	4.7±1.1	3.8±0.9	.005
Beck Depression Scale	18.5±9.4	15.4±6.9	.019
SRS-22			
Function	3.8±0.6	4.2±0.8	.022
Pain	3.6±0.9	4.3±0.3	.002
Self Image	4.0±0.8	4.2±0.7	.059
Mental Health	4.0±0.6	4.1±0.7	.392
Satisfaction	3.9±0.6	4.5±0.8	.016
Mean	3.9±0.7	4.3±0.7	.032

VAS: Visual Analog Scale, SRS-22: Scoliosis Research Society 22, SD: standard deviation, Sig: significant

DISCUSSION

In this study, the effects of surgical and bracing methods on pain, physical function and depression in the treatment of AIS were compared. Our findings show that surgical treatment, especially when applied with the PSIPF method, reduces behavioural symptoms of pain and depression and improves physical function more than bracing treatment. It is also reported in the literature that surgery is recommended in scoliosis patients, especially in cases with a Cobb angle of 40° and above, to protect pulmonary functions, relieve chronic pain and improve psychological well-being (5,7).

On the other hand, although surgical treatment is effective in halting the progression of scoliosis, brace treatment is also considered as an important alternative in certain patient groups. In recent years, brace treatment has gained popularity in the management of scoliosis, especially in infancy, because it involves lower risks compared with surgery (9). However, there are different opinions in the literature regarding the effectiveness of bracing. Some studies have demonstrated that daily brace use for 20-23 hours slows the progression of scoliosis and reduces the necessity for surgery (10,14), whereas some studies have reported that brace treatment has no significant effect on scoliosis (9).

In this context, the findings of our study support that surgery provides more significant functional improvements in the treatment of scoliosis compared to bracing. However, it should be kept in mind that the success of bracing depends on factors such as flexibility of the curve, duration of use and patient compliance (15,16). Considering the findings that bracing and exercise therapy may reduce the need for surgery, especially in patients with a high risk of progression (17), it can be said that patient-based individualised approaches should be adopted in the treatment of scoliosis.

The effects of scoliosis surgery on pain, physical function and psychosocial health have been extensively studied in the literature and most studies have emphasised the positive effects of surgery. In our study, significant improvements were observed in the pain scores, physical function and psychosocial health of scoliosis patients who underwent surgical treatment with the PSIPF method. Especially pain scores were found to decrease significantly after surgery, and this finding was consistent with previous studies (18-21). In addition, factors determining quality of life such as physical functionality and self-confidence have also been found to improve after surgery (22-24).

The main reason for patients to seek treatment is the negative effect of spinal deformity on body image (25). Body image and mental health are affected by the progression of scoliosis (26). Patients are seriously concerned about the negative effect of scoliosis deformity on body image. They also feel a decrease in self-confidence, shame and even a sense of inferiority. Lack of

self-confidence may lead to pessimism and anxiety and may cause impairment in social functioning and isolation (22). Surgical correction of the deformity in scoliosis does not only correct the curvature. It significantly improves the quality of life of the person. Moreover, it provides significant psychological improvements (23).

Bunge et al. reported a significant improvement in the functional/activity scores of the operated patients. They also found that a slight improvement was observed in mental health scores (24). In contrast, Carreon et al. (27) did not find any significant change in mental health scores. Mariconda et al (22) showed that patients who underwent scoliosis surgery continued to show poorer physical conditions and role limitations compared to scoliosis-free individuals with similar or superior mental health characteristics (28-30). Mens et al reported a significant decrease in functioning, self-image and pain and very few adverse events at two-year follow-up after PSIPF (31).

In the present study, it was observed that scoliosis patients who underwent surgical treatment with the PSIPF method showed significant improvement in physical function and behavioral findings of depression. In line with these findings, it can be said that scoliosis surgery not only corrects the spinal curvature but also plays an important role in improving the overall quality of life of the individual. The good results seen after surgical treatment, especially in scoliosis patients with a Cobb angle of 45° and above, may be due to the patients being in a more painful and distressed state before surgery.

However, our study has some limitations. These include the relatively small size of the study group and the lack of long-term follow-up of the patients. Future long-term follow-up studies with larger patient groups will help to better evaluate the long-term efficacy of the PSIPF method in scoliosis surgery. In addition, the fact that scoliosis curvatures are not of similar types is another limitation of the study.

CONCLUSION

This study demonstrates that surgical treatment with posterior spinal instrumentation and fusion is more effective than bracing in the treatment of scoliosis. Surgical intervention provides significant advantages not only in the correction of spinal curvature but also in the improvement of physical function and quality of life of patients. In addition, the positive effects of surgery on mental well-being have also been found to be remarkable. In conclusion, in appropriate patient selection, PSIPF method can be considered as a treatment option with the potential to provide a more comprehensive and permanent improvement in the treatment of scoliosis.

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Ethical approval: The Kayseri City Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (03.01.2023/number: 775).

REFERENCES

- Cheng JC, Castelein RM, Chu WC, et al. Adolescent idiopathic scoliosis. *Nat Rev Dis Primers*. 2015;1:15030.
- Maruyama T, Kitagawa T, Takeshita K, et al. Conservative treatment for adolescent idiopathic scoliosis: can it reduce the incidence of surgical treatment?. *Pediatr Rehabil*. 2003;6:215-9.
- SOSORT guideline committee; Weiss HR, Negrini S, Rigo M, et al. Indications for conservative management of scoliosis (guidelines). *Scoliosis*. 2006;1:5.
- Mohamed M, Jayesh T, Neil D, Sudarshan M. Adolescent idiopathic scoliosis: a review of current concepts. *Orthopaedics and Trauma*. 2020;34:338-45.
- Addai D, Zarkos J, Bowey AJ. Current concepts in the diagnosis and management of adolescent idiopathic scoliosis. *Childs Nerv Syst*. 2020;36:1111-9.
- Weinstein SL, Dolan LA, Cheng JC, et al. Adolescent idiopathic scoliosis. *Lancet*. 2008;371:1527-37.
- Hoernschemeyer DG, Boeyer ME, Robertson ME, et al. Anterior vertebral body tethering for adolescent scoliosis with growth remaining: a retrospective review of 2 to 5-year postoperative results. *J Bone Joint Surg Am*. 2020;102:1169-76.
- Jada A, Mackel CE, Hwang SW, et al. Evaluation and management of adolescent idiopathic scoliosis: a review. *Neurosurg Focus*. 2017;43:E2.
- Richards BS, Bernstein RM, D'Amato CR, Thompson GH. Standardization of criteria for adolescent idiopathic scoliosis brace studies: SRS Committee on Bracing and Nonoperative Management. *Spine (Phila Pa 1976)*. 2005;30:2068-77.
- Negrini S, Donzelli S, Jurenaite G, et al. Efficacy of bracing in early infantile scoliosis: a 5-year prospective cohort shows that idiopathic respond better than secondary-2021 SOSORT award winner. *Eur Spine J*. 2021;30:3498-508.
- Delgado DA, Lambert BS, Boutris N, et al. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. *J Am Acad Orthop Surg Glob Res Rev*. 2018;2:e088.
- Bock K, Bendstrup E, Hilberg O, Løkke A. Screening tools for evaluation of depression in chronic obstructive pulmonary disease (COPD). A systematic review. *Eur Clin Respir J*. 2017;4:1332931.
- Alanay A, Cil A, Berk H, et al. Reliability and validity of adapted Turkish Version of Scoliosis Research Society-22 (SRS-22) questionnaire. *Spine (Phila Pa 1976)*. 2005;30:2464-8.
- Negrini S, Donzelli S, Aulisa AG, et al. 2016 SOSORT guidelines: orthopaedic and rehabilitation treatment of idiopathic scoliosis during growth. *Scoliosis Spinal Disord*. 2018;13:3.
- Cheung JPY, Cheung PWH. Supine flexibility predicts curve progression for patients with adolescent idiopathic scoliosis undergoing underarm bracing. *Bone Joint J*. 2020;102-B:254-60.
- Parent S, Newton PO, Wenger DR. Adolescent idiopathic scoliosis: etiology, anatomy, natural history, and bracing. *Instr Course Lect*. 2005;54:529-36.
- Negrini S, Atanasio S, Zaina F, et al. End-growth results of bracing and exercises for adolescent idiopathic scoliosis. Prospective worst-case analysis. *Stud Health Technol Inform*. 2008;135:395-408.
- Upasani VV, Caltoun C, Petcharaporn M, et al. Adolescent idiopathic scoliosis patients report increased pain at five years compared with two years after surgical treatment. *Spine (Phila Pa 1976)*. 2008;33:1107-12.
- Helenius L, Diarbakerli E, Grauers A, et al. Back pain and quality of life after surgical treatment for adolescent idiopathic scoliosis at 5-year follow-up: comparison with healthy controls and patients with untreated idiopathic scoliosis. *J Bone Joint Surg Am*. 2019;101:1460-6. Erratum in: *J Bone Joint Surg Am*. 2021;103:e13.
- Djurasovic M, Glassman SD, Sucato DJ, et al. Improvement in Scoliosis Research Society-22R pain scores after surgery for adolescent idiopathic scoliosis. *Spine (Phila Pa 1976)*. 2018;43:127-32.
- Newton PO, Ohashi M, Bastrom TP, et al. Prospective 10-year follow-up assessment of spinal fusions for thoracic AIS: radiographic and clinical outcomes. *Spine Deform*. 2020;8:57-66.
- Mariconda M, Andolfi C, Cerbasi S, Servodidio V. Effect of surgical correction of adolescent idiopathic scoliosis on the quality of life: a prospective study with a minimum 5-year follow-up. *Eur Spine J*. 2016;25:3331-40.
- Duramaz A, Yilmaz S, Ziroğlu N, et al. The effect of deformity correction on psychiatric condition of the adolescent with adolescent idiopathic scoliosis. *Eur Spine J*. 2018;27:2233-40.
- Bunge EM, Juttmann RE, de Kleuver M, et al.; NESICIO group. Health-related quality of life in patients with adolescent idiopathic scoliosis after treatment: short-term effects after brace or surgical treatment. *Eur Spine J*. 2007;16:83-9.
- Wang L, Wang YP, Yu B, et al. Relation between self-image score of SRS-22 with deformity measures in female adolescent idiopathic scoliosis patients. *Orthop Traumatol Surg Res*. 2014;100:797-801.
- Asher M, Min Lai S, Burton D, Manna B. The reliability and concurrent validity of the scoliosis research society-22 patient questionnaire for idiopathic scoliosis. *Spine (Phila Pa 1976)*. 2003;28:63-9.
- Carreon LY, Sanders JO, Diab M, et al. The minimum clinically important difference in scoliosis research Society-22 appearance, activity, and pain domains after surgical correction of adolescent idiopathic scoliosis. *Spine (Phila Pa 1976)*. 2010;35:2079-83.
- Andersen MØ, Thomsen K, Kyvik KO. Perceived health status in self-reported adolescent idiopathic scoliosis: a survey based on a population of twins. *Spine (Phila Pa 1976)*. 2010;35:1571-4.
- Tones M, Moss N, Polly DW Jr. A review of quality of life and psychosocial issues in scoliosis. *Spine (Phila Pa 1976)*. 2006;31:3027-38.

30. Danielsson AJ. What impact does spinal deformity correction for adolescent idiopathic scoliosis make on quality of life? Spine (Phila Pa 1976). 2007;32:S101-8.
31. Mens RH, Bisseling P, de Kleuver M, van Hooff ML. Relevant impact of surgery on quality of life for adolescent idiopathic scoliosis: a registry-based two-year follow-up cohort study. Bone Joint J. 2022;104-B:265-73.



The Relationship of Sarcopenia with Disease Stage and Activities of Daily Living in Parkinson's Patients

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Abstract

Aim: Parkinson's disease (PD) is the second most common progressive neurodegenerative disease, presenting with motor and nonmotor findings. The relationship between clinical features and sarcopenia in Parkinson's patients is not clear, and the evaluation of this relationship is imperative in terms of preventing falls and disabilities. Our study aimed to describe the demographic and clinical characteristics of patients with PD and to evaluate the relationship between sarcopenia screening test and disease stage, walking speed, hand grip muscle strength, and activities of daily living.

Material and Method: Male and female patients with clinically confirmed PD aged 50 years and older were included in the cross-sectional descriptive study. Disease staging was evaluated using the Hoehn-Yahr scale, walking speed with the Time Up and Go test (TUG), muscle strength with a hand dynamometer, activities of daily living with the Barthel Index, and the SARC-F test for sarcopenia.

Results: Of the 52 patients included in the study, 40.4% were female and 59.6% were male, and the mean age was 69.86±8.14 years. SARC-F score was high in 51.4% of the patients. The disease stage was associated with an increase in SARC-F scores. The increase in SARC-F scores was positively correlated with the increase in the TUG test ($p=0.028$, $r=0.306$), while the SARC-F score was negatively correlated with activities of daily living. ($p=0.000$, $r=-0.684$). Eighty-one-point three percent of the women with low hand muscle strength had high SARC-F scores, and the difference between them was statistically significant.

Conclusion: Our findings indicated that sarcopenia was prevalent among patients with PD, with its prevalence increasing in direct proportion to the progression of the disease. Furthermore, patients exhibiting high sarcopenia levels demonstrated reduced walking speed and impaired daily living abilities. These observations underscore the critical importance of incorporating sarcopenia evaluations into the development of rehabilitation programs for patients.

Keywords: Parkinson's disease, sarcopenia, disease stage, daily living activities

INTRODUCTION

Parkinson's disease (PD) is a chronic and degenerative neurological disease that affects the central nervous system, often leading to progressive deterioration in motor functions. The basic pathophysiology of PD involves the loss of dopaminergic neurons. It causes motor and non-motor symptoms. The primary motor symptoms of PD include bradykinesia, tremor, and postural instability. Cognitive disorders, sleep disorders, autonomic dysfunction, and musculoskeletal changes

have an essential place among non-motor symptoms. Non-motor symptoms such as cognitive impairment, sleep disturbances, autonomic dysfunction, and musculoskeletal changes significantly impact patients (1). These symptoms lead to severe limitations in the activities of daily living of Parkinson's patients (2). Sarcopenia refers to the age-related decline in skeletal muscle mass and function.

Recent studies have reported that sarcopenia and PD share common pathogenetic features. In patients

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with PD, disruption of the basal ganglia—a group of subcortical nuclei responsible for movement initiation—and interleukin-6-mediated neuroinflammation lead to motor dysfunction. As a result of motor dysfunction, insufficient muscle use due to bradykinesia, rigidity, and tremors leads to a decrease in muscle mass (3,4). Additionally, factors such as nutritional deficiencies, difficulty swallowing, loss of appetite, and substance use can lead to insufficient protein intake and negatively impact muscle health. Recent research has also revealed mitochondrial dysfunction in sarcopenia and Parkinson's disease. Mitochondrial abnormalities are more common in sarcopenic muscles than in healthy aged muscles (5). This can contribute to muscle degeneration by disrupting energy metabolism. As a result, patients' quality of life decreases, the risk of falls increases, and their functional independence is threatened. In recent years, it has become increasingly imperative to develop new strategies to optimize the health status of individuals with PD. The role of sarcopenia in terms of maintaining muscle health and ensuring the sustainability of functional capacity in PD has been a topic of increasing interest (6).

This study aims to characterize the demographic and clinical features of Parkinson's patients and investigate the relationship between sarcopenia (as assessed by the SARF-C screening test) and key functional parameters, including disease stage, gait speed, handgrip strength, and activities of daily living.

MATERIAL AND METHOD

This study was approved by the Ethics Committee of İzmir Bakırçay University (Ethics approval number: 656). All participants provided written informed consent by the Declaration of Helsinki. An observational cross-sectional study was conducted between January and July 2024 among patients who visited the Physical Medicine and Rehabilitation Outpatient Clinic and were diagnosed with PD by a neurologist.

A total of 60 patients were included in the study, but 8 patients were excluded due to stage 5. The study was completed with 52 patients. Patients aged 50 years or older, of both sexes, who provided written informed consent and were classified as Hoehn-Yahr stage 1-4 were included in the study. Patients with orthopedic and rheumatologic problems that would affect hand grip strength in the upper extremity and walking function in the lower extremity, those who did not sign the informed consent form, those who could not perform commands due to cognitive dysfunction, patients with Hoehn and Yahr scale stage 5, and patients with Parkinson's plus syndrome were excluded from the study. Cognitive functions were evaluated with a mini-mental test, and patients with a score above twenty-five were included.

Demographic information and clinical examinations of the patients who signed the informed consent were recorded. A physical therapy and rehabilitation physician made all evaluations.

Disease staging was evaluated using the Hoehn-Yahr scale. Walking speed was assessed with the Timed Up and Go test. Muscle strength was measured using a hand dynamometer. Daily living activities were evaluated with the Barthel test, and sarcopenia was assessed through the SARC-F test.

The Hoehn and Yahr scales evaluate the clinical course of PD. They assess the severity and progression of motor symptoms, which consist of five stages (7).

Stage 1: Symptoms are only unilateral.

Stage 2: Symptoms become bilateral.

Stage 3: Postural instability is evident

Stage 4: Severe motor dysfunctions are seen.

Stage 5: The patient becomes completely dependent.

The SARC-F scale is a simple, rapid and self-reported screening test developed to assess the risk of sarcopenia in elderly individuals. SARC-F evaluates five main parameters on individuals' muscle function and physical performance. These parameters include strength, need for walking assistance, ability to get up from a chair, ability to climb stairs, and risk of falling. The total score on the scale ranged from 0 to 10, with a score of ≥ 4 considered a high risk of sarcopenia. This test provides a critical starting point for planning interventions for managing and preventing sarcopenia. Turkish validity and reliability study was conducted by Bahat et al. (8).

The Time Up and Go test evaluates individuals' balance, gait, and overall mobility levels. The patient is seated in a standard-height chair on a flat, stable surface. It covers the time it takes for the person to get up from the chair, walk 3 meters, turn around, walk back to the starting point, and sit back in the chair. In recent studies, 13.5 seconds or more in Parkinson's patients are considered significant regarding falling and mobility impairment (9).

Hand grip strength is a reliable indicator of upper extremity muscle strength and is a crucial parameter for assessing physical functional capacity. Hand grip muscle strength was evaluated using a Jamar hand dynamometer. The patient was seated in a flat chair with back support, in a wrist position that was either neutral or slightly extended, with the shoulder in a neutral position and the elbow in 90° flexion. For each hand, usually, three measurements were made, and the average value was recorded in kilograms. Hand grip strength of more than 30 kg for men and 20 kg for women is considered normal. Dynopenia is defined as a hand grip strength of less than 30 kg in men and less than 20 kg in women. Decreased hand grip strength, sarcopenia, and fragility have been reported as increased risk symptoms. The test has validity and reliability in Turkish (6,10-12).

The Barthel Index evaluates individuals' performance in ten basic activities of daily living. Each activity is scored based on the individual's level of independence, with a

total score ranging from 0 to 100. The Barthel Index is a reliable scale that objectively evaluates the level of independence of individuals with PD in activities of daily living. The test has a validity reliability in Turkish (13).

Statistical Method

Statistical analysis was performed with SPSS version 21 for Windows. The normality of the data was assessed using the Shapiro-Wilk test. Data with a normal distribution were presented as mean $\pm$ standard deviation. Correlations between variables were evaluated using the Pearson test, as appropriate. The chi-square test was used to assess associations between categorical variables. A p-value of lower than 0.05 was regarded as statistically significant.

RESULTS

The study included 52 patients, comprising 21 females (40%) and 31 males (60%). The mean age of the patients was 69.86 ± 8.14 years. Demographic data of Parkinson's patients are shown in Table 1, and clinical data are shown in Table 1 and Table 2.

Table 1. Demographic data of Parkinson's patients	
Demographic data	n (%)
Gender	
Woman	21 (40.4)
Male	31 (59.6)
Age	
50-59 years	6 (11.5)
60-69 years	18 (34.6)
70-79 years	10 (38.5)
80 years and older	8 (15.4)
Education	
Illiterate	4 (7.7)
Secondary	26 (50.7)
Higher education	28 (62.3)
Body mass index	
Weak	1 (1.9)
Normal	15 (28.8)
Weight	25 (48.1)
Overweight	9 (17.3)
Obesity	2 (3.8)
Comorbidity	
Yes	9 (17.3)
No	43 (82.7)

n: number of patients, %: percentage

Table 2. Clinical data of Parkinson's patients	
Clinical data	n (%)
Disease stage	
Stage 1	20 (38.5)
Stage 2	7 (13.5)
Stage 3	14 (26.9)
Stage 4	11 (21.1)
Tremor	
No	12 (23.1)
Yes	40 (76.9)
Rigidity	
No	32 (61.5)
Yes	20 (38.5)
Barthel Index	
Independent	33 (63.5)
Moderately dependent	13 (25.0)
Highly dependent	4 (7.7)
Totally dependent	2 (3.8)
Bradykinesia	
No	11 (21.2)
Yes	41 (78.8)
Dorsal kyphosis	
No	14 (26.9)
Yes	38 (73.1)
Imbalance	
No	25 (48.1)
Yes	27 (51.9)
SARC-F score	
≥ 4	27 (51.9)
< 4	25 (48.1)
Time up to go test (second)	
≥ 13.5	40 (76.9)
< 13.5	12 (23.1)
Dominant hand/muscle strength/female (kilogram)	
≥ 20	5 (24)
< 20	16 (76)
Dominant hand/hand muscle strength/male (kilogram)	
≥ 30	28 (90.3)
< 30	3 (9.7)

n: number of patients, %: percentage

The relationship between the SARC-F score and the stage of the disease was evaluated, and it was positively correlated with the increase in PD stage and the increase in SARC-F score. The relationship between the Disease Stage and SARC-F is shown in Figure 1. When the SARC-F score and the TUG test were evaluated, their relationship was statistically significant ($p=0.028$, $r=0.306$). There was a negative correlation between SARC-F and the Barthel Index ($p=0.000$, $r=0.684$) when dominant hand muscle strength was evaluated with SARC-F. While there was a statistically significant correlation between hand muscle strength and SARC-F scores in women ($p=0.025$), there was no relationship in men ($p=0.71$).

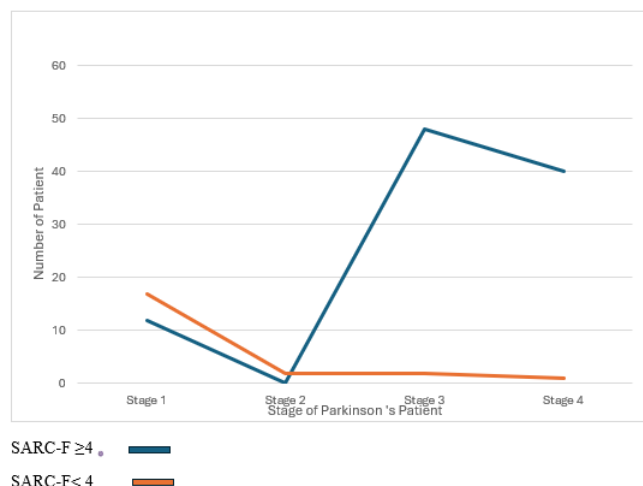


Figure 1. Relationship between disease stage and SARC-F

There was a statistically significant correlation between SARC-F scores and Timed Up and Go test results ($p=0.028$, $r=0.306$), indicating a link between sarcopenia risk and mobility impairment in Parkinson's patients. A significant negative correlation was found between SARC-F scores and Barthel Index scores ($p=0.000$, $r=0.684$), suggesting that sarcopenia negatively impacts daily living activities.

Eighty-one percent of women with low dominant hand muscle strength ($n=16$) had high SARC-F scores, and the difference between them was statistically significant ($p=0.011$). In males, the dominant hand ($n=28$) muscle strength, SARC-F scores were 64.8% ($n=18$) standard, 35.7% ($n=10$) lower, and no significant difference was found between them ($p=0.935$).

DISCUSSION

Our study demonstrated a high prevalence of sarcopenia in Parkinson's patients, with an increasing risk as the disease progresses. It has been determined that sarcopenia has adverse effects on walking speed, activities of daily living, and general functional capacity. Especially in female patients with Parkinson's disease, a 76% decrease in hand muscle strength has been observed. These findings are consistent with the loss of stamina, frailty, and disability caused by motor and non-motor symptoms in PD.

In a meta-analysis conducted by F. Petermann-Rocha et al., the prevalence of sarcopenia in the general population was

reported as 22%, 10%, and 15% according to the EWGSOP, EWGSOP2, and AWGS criteria, respectively (14). However, various studies conducted on Parkinson's patients indicate that the prevalence of sarcopenia ranges from 23.9% to 66.7% (6).

In contrast, Barichello et al. reported that the prevalence of sarcopenia was less than 6% in their study of 235 patients with a clinic for Parkinsonism (12). This difference in prevalence may be due to the diagnostic criteria, sample size, and study methodology used. However, in five studies of Parkinson's patients, Parkinson's patients were reported to have a higher prevalence of sarcopenia compared to control groups (13,14). Studies have reported that the reasons for the increased frequency of sarcopenia in PD are that dopamine deficiency weakens the control of motor functions, mitochondrial dysfunction disrupts cell energy metabolism, and chronic inflammation accelerates muscle protein degradation. It is also emphasized that nutritional problems also contribute (13-15).

Our study found that the risk of developing sarcopenia increases as the disease stage progresses. Previous research has similarly shown that sarcopenia is associated with longer disease duration, more severe motor symptoms (Hoehn and Yahr stage), and loss of functional independence (16).

However, the literature contains conflicting findings regarding the relationship between sarcopenia and motor symptoms (Unified Parkinson's Disease Rating Scale-Motor Examination Scores). This means that the mechanisms of sarcopenia in Parkinson's disease are not fully understood and may differ from person to person (17).

Reduced hand muscle strength is a common issue among older adults and individuals exhibiting symptoms of Parkinsonism. As the disease worsens, patients with Parkinson's face a decline in fine motor skills, a loss of muscle strength, and a decrease in hand dexterity (12-17).

The study shows that low hand grip strength is common among Parkinson's patients, especially women. Gender is an important predictor of muscle strength and SARC-F scores. The tremor, stiffness, and bradykinesia associated with the disease affect hand function and can adversely affect muscle strength by reducing their use (18).

The fact that sarcopenia is more pronounced in women can be attributed to hormonal differences and gender-related variations in muscle mass (17,18). This situation highlights the need for developing individualized treatment approaches based on gender for Parkinson's patients. Weakening hand muscles can restrict patients' independence by complicating daily activities.

The negative correlation between the Barthel Index and SARC-F scores indicates that sarcopenia increases dependence on daily living activities. This highlights the detrimental effects of sarcopenia on functional independence. This finding suggests that sarcopenia is a direct factor affecting the quality of life for patients with PD.

The test duration was high in 76% of the PD and was consistent with the risk of falling. Recent studies have reported that individuals with sarcopenia face a higher risk of falls and fractures, along with a decline in their daily living activities (19). In a systematic review of patients with PD, Ying et al. found that the incidence of falls among those with sarcopenia was more significant than in those without it, recommending early evaluation of sarcopenia in PD to prevent falls and disability (20).

PD, Sen et al. It has been reported that the quality of life of individuals decreases in specific periods, which leads to an increase in the care needs of patients and dependence on caregivers. It is emphasized that this situation increases the burden of care on both the patient and his family (21).

CONCLUSION

Considering the impact of sarcopenia on functional decline in PD, regular screening using the SARC-F test may facilitate early intervention. Furthermore, gender-specific rehabilitation strategies should be developed to address the unique needs of male and female patients. Future research with larger cohorts is needed to establish robust clinical guidelines for managing sarcopenia in Parkinson's patients.

Limitations of the Study

The primary limitation is the small patient sample size and the lack of a control group.

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REFERENCES

- Jankovic J. Parkinson's disease: clinical features and diagnosis. *J Neurol Neurosurg Psychiatry*. 2008;79:368-76.
- Hart A, Cordova-Rivera L, Barker F, Sayer AA, et al. The prevalence of sarcopenia in Parkinson's disease and related disorders-a systematic review. *Neurol Sci*. 2023;44:4205-17.
- Braak H, Del Tredici K, Rüb U, et al. Staging of brain pathology related to sporadic Parkinson's disease. *Neurobiol Aging*. 2003;24:197-211.
- Drey M, Hasmann SE, Krenovsky JP, et al. Associations between early markers of Parkinson's disease and sarcopenia. *Front Aging Neurosci*. 2017;9:53.
- Bua EA, McKiernan SH, Wanagat J, et al. Mitochondrial abnormalities are more frequent in muscles undergoing sarcopenia. *J Appl Physiol* (1985). 2002;92:2617-24.
- McMillan JM, Michalchuk Q, Goodarzi Z. Frailty in Parkinson's disease: a systematic review and meta-analysis. *Clin Park Relat Disord*. 2021 May 25;4:100095.
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology*. 1967;17:427-42.
- Bahat G, Yilmaz O, Kılıç C, et al. Performance of SARC-F in regard to sarcopenia definitions, muscle mass and functional measures. *J Nutr Health Aging*. 2018;22:898-903.
- Barry E, Galvin R, Keogh C, Horgan F, Fahey T. Is the Timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. *BMC Geriatr*. 2014;14:14.
- de Medeiros LC, da Luz MCL, da Costa Pereira JP, et al. Nutritional status and dynapenia in people living with Parkinson's disease: a cross-sectional study. *Neurol Sci*. 2022;43:2509-17.
- Bohannon RW. Considerations and practical options for measuring muscle strength: a narrative review. *Biomed Res Int*. 2019;2019:8194537.
- Barichella M, Pinelli G, Iorio L, et al. Sarcopenia and dynapenia in patients with parkinsonism. *J Am Med Dir Assoc*. 2016;17:640-6.
- Trevisan C, Vetrano DL, Calvani R, et al. Twelve-year sarcopenia trajectories in older adults: results from a population-based study. *J Cachexia Sarcopenia Muscle*. 2022;13:254-63.
- Petermann-Rocha F, Balntzi V, Gray SR, et al. Global prevalence of sarcopenia and severe sarcopenia: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2022;13:86-99.
- Vetrano DL, Pisciotto MS, Laudisio A, et al. Sarcopenia in Parkinson disease: comparison of different criteria and association with disease severity. *J Am Med Dir Assoc*. 2018;19:523-7.
- Lima DP, de Almeida SB, Bonfadini JC, et al. Clinical correlates of sarcopenia and falls in Parkinson's disease. *PLoS One*. 2020;15:e0227238.
- Rolland Y, Dupuy C, Van Kan GA, et al. Sarcopenia screened by the SARC-F questionnaire and physical performances of elderly women: a cross-sectional study. *J Am Med Dir Assoc*. 2017;18:848-52.
- Yılmaz N, Özmen G. Gender-assessment of attention functions in parkinson's patients: an fMRI study. *European Journal of Science and Technolog*. 2021;28:843-8.
- Allen NE, Canning CG, Almeida LRS, et al. Interventions for preventing falls in Parkinson's disease. *Cochrane Database Syst Rev*. 2022;6:CD011574.
- Cai Y, Feng F, Wei Q, et al. Sarcopenia in patients with Parkinson's disease: a systematic review and meta-analysis. *Front Neurol*. 2021;12:598035.
- Şen A, Azizoğlu F, İlhan SE. Quality of life in Parkinson's patients roles of nurses and care givers. *Uludağ Üniversitesi Tıp Fakültesi Dergisi*. 2023;49:417-24.



The Relationship Between Nutrition and Exercise Habits and Biochemical Parameters in Non-Smoking Elderly Individuals

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Abstract

Aim: The aim of this study is to examine the relationship between nutrition, physical activity and biochemical parameters in non-smokers aged 65 and over.

Material and Method: The study was completed with 180 participants in the cardiovascular surgery outpatient clinic of a public hospital located in Central Anatolia, Türkiye. Data were collected using a questionnaire form prepared by the researchers. Independent sample t-test and Pearson correlation test were used in the analysis of the data.

Results: The mean age of the participants was 72.36±5.65 years, 56.7% were illiterate, 60% had less income than expenses, and 73.3% had chronic diseases. It was determined that individuals who consumed at least one serving of fruit/vegetables per day had significantly lower glucose ($p<0.05$) and HDL ($p<0.05$) levels compared to those who consumed more. Participants who exercised for at least 30 minutes three times a week had significantly higher B9 levels ($p<0.05$). Fish consumption was associated with lower glucose, creatinine, cholesterol, HDL and B12 levels ($p<0.05$).

Conclusion: The study emphasizes that regular nutrition and physical activity have a significant effect on biochemical parameters in elderly individuals. It is recommended that social policies be implemented to improve nutrition and exercise habits in order to promote healthy aging, improve quality of life and support better health outcomes among the elderly population.

Keywords: Nutritional status, health services for the aged, diet, healthy, biochemistry, exercise

INTRODUCTION

The number of elderly people worldwide is rapidly increasing. According to the United Nations' 2022 report, the global population aged 60 and over is around 1.1 billion, and this number is expected to reach 2.1 billion by 2050 (United Nations, 2022) (1). A similar increase is observed in Türkiye, as well; according to data from the Turkish Statistical Institute (TÜİK), as of 2023, the population aged 65 and over is approximately 9.5 million, constituting 11.6% of the total population (TÜİK, 2023) (2). These figures indicate that Türkiye has a rapidly aging population, emphasizing the growing importance of efforts to protect the health and improve the quality of life of elderly individuals.

The aging process is influenced by many variables, including biological, environmental, genetic, and socioeconomic factors (3). Lifestyle factors such as dietary habits, level of physical activity, presence of chronic diseases, and use of tobacco and alcohol can determine the pace of aging and the quality of life of individuals (4). Additionally, genetic predisposition and environmental factors also shape the biological processes of aging. For example, healthy dietary habits and regular exercise contribute to healthier aging by reducing inflammation and oxidative stress levels in the body of elderly individuals (5).

With the aging process, individuals' nutrition and physical activity habits play a critical role in determining their health status (6). Regular nutrition and exercise

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habits have a significant impact on regulating various biochemical parameters, especially in elderly individuals who do not smoke (7). While smoking can contribute to the development of many diseases by triggering oxidative stress and inflammation processes (8), the impact of nutrition and exercise on the biochemical parameters of non-smoking individuals has not yet been fully understood.

Studies have shown that healthy nutrition and regular physical activity have positive effects on cardiovascular health, metabolic balance, and overall quality of life in elderly individuals (9). Additionally, exercise is known to have beneficial effects on biochemical parameters such as blood glucose, cholesterol, and triglycerides (10). Therefore, examining the relationship between nutrition and exercise habits and biochemical parameters in non-smoking elderly individuals can play an important role in supporting the healthy aging process of this group.

In this study, the aim is to investigate the relationship between nutrition and exercise habits and certain biochemical parameters in non-smoking elderly individuals, in order to obtain scientific data that will support strategies for improving the quality of life and healthy aging of elderly individuals.

MATERIAL AND METHOD

Study Desing and Ethical Considerations

This research is a cross-sectional study.

The study protocol was approved by the clinical ethics committee of the hospital where the research was conducted (Yozgat Bozok University Clinical Research Ethics Committee date: 22/09/2022, number: 2017-KAEK-189_2022.09.22_02). Informed voluntary consent was obtained from all participants (prepared in 24-point Times New Roman font for the elderly to read, read slowly and in an understandable manner by the researcher accompanied by the participants) and the rules of the Declaration of Helsinki were followed.

Population and Sample

The study population consisted of elderly individuals who visited the cardiovascular surgery outpatient clinic of a research and practice hospital in Central Anatolia between January and March 2024. In this cross-sectional study, 240 elderly patients visited the clinic during the specified period. The study sample included all patients (n=180) who met the inclusion criteria and agreed to participate in the research. Patients were enrolled in the study based on the order of their outpatient clinic visits.

Data Collection

Data were collected between January and March 2024 using a two-stage process. The first stage involved a questionnaire on sociodemographic characteristics, nutrition, and exercise habits, conducted face-to-face by the researcher. Participants were asked survey questions, and

their responses were recorded. Their height and weight were measured, and their Body Mass Index (BMI) was calculated. To ensure clarity for elderly participants, questionnaires were prepared in 24-point Times New Roman font and read aloud slowly. Individuals with any food intolerance, those using medications affecting vitamin absorption (e.g., Methotrexate, Carbamazepine, Sulfonamides), those taking medications for gastrointestinal conditions (e.g., Crohn's Disease, Ulcerative Colitis, and Proton Pump Inhibitors), and individuals with conditions such as cancer or rheumatic diseases were excluded from the study. In the second stage, blood samples were taken, and biochemical parameters such as glucose, cholesterol, creatinine, HDL, B9, and B12 were analyzed. Blood samples were collected by nurses in the hospital's blood collection unit and analyzed by the primary researcher in the hospital's laboratory.

Data Collection Forms

The data collection forms included questionnaires that gathered sociodemographic information (such as age, education level, income, chronic disease status, etc.) as well as details about participants' nutritional and exercise habits. Nutrition habits and physical activity levels were assessed through self-reported questionnaires. Participants were asked to provide information on the foods they consumed and the exercises they performed over a specific period. The data related to nutrition and physical activity were collected in a way that accurately reflects the participants' habits (Daily portions of fruits and vegetables consumed, pasta consumption, regular weekly fish consumption, breakfast habits, and weekly exercise duration). In addition, blood values were analyzed to measure biochemical parameters.

Data Analysis

Data were analyzed using SPSS 25. Descriptive statistics (frequency, percentage, mean, standard deviation) were used. Normality was tested using the Shapiro-Wilk test, and comparisons between nutrition/exercise habits and biochemical parameters were made with an independent sample t-test. Pearson correlation was applied for continuous variables, with statistical significance set at $p < 0.05$.

RESULTS

The demographic characteristics of non-smoking elderly individuals are presented in Table 1. The average age of the participants is 72.36 ± 5.65 years, and the average BMI is 28.68 ± 4.62 . 56.7% of the individuals are illiterate and live in the city center, 83.2% are not employed, 60% have an income less than their expenses, and 73.3% have a chronic illness. Among the elderly with chronic illnesses, 45.4% have both hypertension and diabetes (Table 1).

Table 2 presents the comparison of certain health behaviors of the participants with their blood parameters. Individuals who regularly consume at least one portion

of fruit per day have statistically significantly lower blood glucose, cholesterol, and HDL levels compared to those who consume more fruit ($p<0.05$). The frequency of consuming at least one portion or more of fruit daily does not affect the blood creatinine, B9, and B12 levels of the participants ($p>0.05$).

Individuals who regularly consume at least one portion of vegetables per day have lower B12 and glucose levels and higher HDL and B9 levels compared to those who consume more vegetables, and this difference is statistically significant ($p<0.05$). The frequency of consuming at least one portion or more of vegetables daily does not affect the creatinine and cholesterol levels of the individuals ($p>0.05$). Participants who consume at least one portion of fish per week have statistically significantly lower glucose, creatinine, cholesterol, HDL, and B12 levels compared to those who do not consume fish ($p<0.05$). The frequency of consuming at least one portion of fish per week does not affect the B9 levels of the participants ($p>0.05$).

Participants who regularly have breakfast have statistically significantly lower HDL and B12 levels compared to those who do not ($p<0.05$). The habit of having breakfast

does not affect the glucose, creatinine, cholesterol, and B9 levels of the participants ($p>0.05$). Participants who engage in physical activity for at least 30 minutes three times a week have statistically significantly higher B9 levels compared to those who do not exercise ($p<0.05$). The regular exercise habit (at least 30 minutes three times a week) does not affect the glucose, creatinine, cholesterol, HDL, and B12 levels of the participants ($p>0.05$) (Table 2).

The correlation of participants' age and BMI with certain biochemical parameters is presented in Table 3. There is a statistically significant weak positive relationship between individuals' ages and cholesterol levels, and a statistically significant weak negative relationship with B9 and B12 levels ($p<0.05$). There is no statistically significant relationship between participants' ages and creatinine or HDL levels ($p>0.05$). A statistically significant weak negative relationship was found between individuals' BMI and creatinine levels, a weak positive relationship with B9 levels, and a moderate positive relationship with cholesterol and HDL levels ($p<0.05$). There is no statistically significant relationship between participants' BMI and B12 levels ($p>0.05$).

Table 1. Distribution of some demographic characteristics of the participants			
Characteristics		n	%
Average age (Min.-Max.)		72.36±5.65 (65-89) years	
Average BMI (Min.-Max.)		28.68±4.62 (20.20-36.74) kg/m ²	
Education	Illiterate	102	56.7
	Primary education	78	43.3
Place of residence	Village/district	78	43.3
	City	102	56.7
Employment status	Yes	30	16.7
	No	150	83.3
Income status	Income less than expenses	108	60.0
	Income equal to expenses	66	36.7
	Income more than expenses	6	3.3
Chronic illness status	Present	132	73.3
	Absent	48	26.7
Chronic diseases*	Heart disease	24	18.2
	Hypertension	30	27.7
	Diabetes	12	9.1
	Hypertension-hypothyroid	6	4.5
	Hypertension-diabetes	60	45.4
*It has been calculated based on n=132			

Table 2. Comparison of certain health behaviors with blood parameters of the participants

Parameters	n	%	Glucose, mg/dL, N (74–109)	Creatinine, mg/dL, N (0.7–1.2)	Cholesterol, mg/dL, N (3–200)	HDL, mg/dL, N (35–55)	VitB9 (ng/ml) N (3–17)	VitB12 (pg/ml) N (200–800)
			Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Regularly consuming at least one portion of fruit per day								
Consumers	102	56.7	119.13±24.88	0.80±0.16	176.83±37.67	49.28±9.45	7.33±3.71	358.99±123.21
Higher consumers	78	43.3	182.51±139.16	0.85±0.18	199.97±22.18	55.74±9.56	7.25±3.39	364.01±133.81
Test/p			-2.924, 0.006	-1.480, 0.141	-3.383, 0.001	-2.984, 0.004	0.138, 0.890	-0.261, 0.794
Regularly consuming at least One portion of vegetables per day								
Consumers	114	63.4	118.67±21.53	0.79±0.16	185.82±36.08	53.22±11.07	8.07±3.56	344.20±113.36
Higher consumers	66	36.6	215.98±153.40	0.85±0.19	177.73±32.31	47.52±4.17	6.35±3.04	394.65±151.82
Test/p			-3.461, 0.002	-1.812, 0.072	0.853, 0.396	3.422, 0.001	3.026, 0.003	-2.473, 0.014
Consuming at least one portion of fish per week								
Consumers	54	30.0	120.01±22.68	0.75±0.11	166.18±37.15	48.30±5.45	6.88±2.93	316.26±116.04
Non-consumers	126	70.0	155.59±111.95	0.85±0.18	195.06±29.18	53.42±11.34	7.46±3.79	380.41±127.87
Test/p			-2.606, 0.011	-4.092, 0.000	-3.617, 0.001	2.787, 0.007	-1.057, 0.293	-3.169, 0.002
Having breakfast								
Breakfast eaters	108	60.0	156.02±116.65	0.82±0.14	178.55±30.25	48.18±4.22	7.19±3.70	344.09±149.13
Non-breakfast eaters	72	40.0	127.44±47.28	0.82±0.20	190.25±39.74	55.00±12.57	7.44±3.41	386.78±80.03
Test/p			1.745, 0.085	0.071, 0.944	-1.473, 0.145	-3.328, 0.002	-0.449, 0.654	-2.486, 0.014
Regular exercise (at least three days a week, at least 30 minutes)								
Exercisers	24	13.3	128.93±22.04	0.84±0.19	182.05±9.97	56.50±7.83	10.22±3.68	381.80±56.30
Non-exercisers	156	86.7	145.02±99.06	0.82±0.17	184.30±38.09	50.77±10.05	6.81±3.32	357.99±135.08
Test/p			-1.416, 0.160	0.527, 0.599	0.409, 0.684	1.876, 0.064	4.593, 0.000	1.508, 0.136

Table 3. Correlation of age and BMI with certain biochemical parameters					
	Creatinine (mg/dL), N (0.7–1.2)	Cholesterol (mg/dL), N (3–200)	HDL (mg/dL), N (35–55)	VitB9 (ng/ml) N (3–17)	VitB12 (pg/ml) N (200–800)
Age (year)	r=0.116	r=0.249	r=0.204	r=-0.217	r=-0.187
	p=0.184	p=0.028	p=0.073	p=0.005	p=0.012
BMI kg/m²	r=-0.262	r=0.588	r=0.346	r=0.165	r=-0.028
	p=0.002	p=0.000	p=0.002	p=0.032	p=0.713
*The relationship between blood glucose levels has not been examined due to some participants having diabetes; **N=normal range					

DISCUSSION

It was determined that elderly individuals who consume at least one serving of fruit per week appear to be healthier in terms of certain biochemical parameters compared to those who consume larger amounts. Studies have shown that fruit consumption plays an important role in regulating blood glucose levels and reducing the risk of cardiovascular diseases (11,12). In particular, antioxidants and flavonoids found in fruits can help control blood sugar levels by increasing insulin sensitivity (13,14). Additionally, the high fiber content of fruits contributes positively to the blood lipid profile by reducing cholesterol absorption. There are also studies indicating that regular consumption of fruits and vegetables lowers LDL cholesterol levels (15,16).

However, some studies have shown that excessive fruit consumption, especially those high in fructose, can lead to an increase in insulin levels and consequently cause fluctuations in blood glucose (17). In our study, elderly individuals who consumed more than one serving of fruit per day were found to have higher levels of HDL, cholesterol, and blood glucose. Therefore, maintaining a balanced and moderate fruit intake is important for the healthy management of blood glucose, HDL, and cholesterol levels.

In our study, consuming one serving of fruit per day or more did not affect B12 and B9 levels. While regular fruit/vegetable consumption has been reported to increase B9 levels in the literature, it does not have a direct impact on B12 levels (18,19). However, in this study, individuals who consumed more than one serving of vegetables per day had higher B12 levels but lower B9 levels. This may be due to the fact that the B9 and B12 levels of the elderly participants were already within normal reference ranges, as well as factors such as the diversity of dietary habits, diet balance, consumption practices, and food sources among elderly individuals.

Participants who consumed at least one serving of fish per week were found to have lower levels of glucose, creatinine, cholesterol, HDL, and B12 compared to those who did not consume fish ($p<0.05$). Fish is rich in omega-3 fatty acids, which have the potential to reduce inflammation and improve heart health. Omega-3 fatty acids lower triglyceride levels, increase HDL levels, and reduce the risk of cardiovascular disease (20). In one study, it was found

that individuals who consumed at least one serving of fish per week had a significantly reduced risk of developing heart disease (21,22). These findings support the positive effects of fish consumption on metabolic health in elderly individuals.

In this study, fish consumption was found not to affect B12 levels. This may be related to the decreased absorption of B12 in elderly individuals. During the aging process, changes in the gastrointestinal system, especially the reduction in stomach acid production and alterations in intestinal motility, can negatively impact B12 absorption (23). Reduced stomach acid makes it more difficult for vitamin B12 to be released from proteins, leading to decreased absorption (24). Additionally, certain health issues common in elderly individuals and the use of certain medications (e.g., proton pump inhibitors) can also adversely affect B12 absorption. Therefore, despite consuming a diet that contains sufficient amounts of vitamin B12 (such as fish), B12 levels may remain below the expected range due to absorption issues (25).

In our study, individuals who regularly had breakfast were found to have significantly lower HDL and B12 levels compared to those who did not have breakfast ($p<0.05$). The reason for the low B12 levels may be due to insufficient consumption of B12-rich foods during breakfast or absorption problems seen in the elderly. Reduced B12 absorption related to stomach acid and intrinsic factor deficiency in elderly individuals may explain this situation (26). The lower HDL levels in those who had breakfast could be due to the consumption of processed carbohydrates or insufficient intake of healthy fats and proteins during breakfast (27). The fact that glucose, creatinine, cholesterol, and B9 levels were not affected by breakfast consumption ($p>0.05$) indicates that breakfast did not have a significant impact on these parameters. Although the literature suggests that breakfast has positive effects on glucose metabolism, this effect was not observed in the elderly participants of this study (28).

In our study, participants who engaged in at least 30 minutes of exercise three times a week had significantly higher B9 levels compared to those who did not exercise ($p<0.05$). This finding suggests that physical activity positively influences folate metabolism and contributes

to maintaining folate levels in an active lifestyle. It is indicated that physical activity may help tissues better absorb essential vitamins like folic acid by increasing blood circulation in the body (29).

However, it was observed that regular exercise did not affect glucose, creatinine, cholesterol, HDL, and B12 levels ($p>0.05$). The effects of physical activity on biochemical parameters, especially in elderly individuals, can be complex. Due to the slower metabolic rate in the elderly and the lower intensity of physical activity compared to younger individuals, it may not have created a significant impact on these biochemical parameters (30). Additionally, the participants' existing dietary and lifestyle habits may have also contributed to these results.

Limitations

This study has some limitations. The research was conducted in a specific region, and the generalizability of the findings may be limited due to the lack of consideration of other demographic variables.

CONCLUSION

This study examined the relationship between health behaviors and biochemical values in elderly individuals, highlighting the positive effects of a balanced diet and regular physical activity on overall health. The findings underscore the critical importance of preventive medicine and health counseling in maintaining and improving the well-being of older adults. In particular, family medicine services play a vital role in helping elderly individuals monitor their health regularly and adopt healthy lifestyle habits. Family physicians not only support individuals in maintaining their health but also contribute to preventing more severe health problems.

Therefore, it is essential to encourage elderly individuals to attend regular medical check-ups and pay attention to their lifestyles. Projects and awareness campaigns that aim to enhance health literacy within the community could be a significant step forward. Our study demonstrates that preventive medicine practices and health counseling are key to ensuring a healthy and high-quality life for older adults.

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Ethical approval: The ethical approval for the study was obtained from the clinical ethics committee of the hospital where the study was conducted (Yozgat Bozok University Clinical Research Ethics Committee date: 22/09/2022, number: 2017-KAEK-189_2022.09.22_02).

REFERENCES

- World Health Organization (WHO). Population ageing 2022. <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health> access date: 20.08.2024.
- Turkish Statistical Institute (TÜİK). Population projections, 2023-2100. <https://data.tuik.gov.tr/Bulten/Index?p=Population-Projections-2023-2100-53699&dil=2#:~:text=If%20the%20current%20trends%20of,thousand%20618%20people%20in%202050> access date: 22.08.2024.
- Niccoli T, Partridge L. Ageing as a risk factor for disease. *Curr Biol*. 2012;22:R741-52.
- Fries JF. Aging, natural death, and the compression of morbidity. *Bulletin of the World Health Organization*. 2002;80:245-50.
- López-Otín C, Blasco MA, Partridge L, et al. The hallmarks of aging. *Cell*. 2013;153:1194-217.
- Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. *Lancet*. 2018;392:1147-59.
- Kahleova H, Znayenko-Miller T, Motos G, et al. Dietary advanced glycation end-products and their associations with body weight on a Mediterranean diet and low-fat vegan diet: a randomized, cross-over trial. *Front Nutr*. 2024;11:1426642.
- Alberg AJ, Shopland DR, Cummings KM. The 2014 Surgeon General's report: commemorating the 50th Anniversary of the 1964 Report of the Advisory Committee to the US Surgeon General and updating the evidence on the health consequences of cigarette smoking. *Am J Epidemiol*. 2014;179:403-12.
- Shlisky J, Bloom DE, Beaudreault AR, et al. Nutritional considerations for healthy aging and reduction in age-related chronic disease. *Advances in nutrition*. 2017;8:17-26.
- Shepherd SO, Wilson OJ, Taylor AS, et al. Low-volume high-intensity interval training in a gym setting improves cardio-metabolic and psychological health. *PloS One*. 2015;10:e0139056.
- Alissa EM, Ferns GA. Dietary fruits and vegetables and cardiovascular diseases risk. *Crit Rev Food Sci Nutr*. 2017;57:1950-62.
- Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ*. 2014;349:g4490.
- Petersen KS, Kris-Etherton PM. Diet quality assessment and the relationship between diet quality and cardiovascular disease risk. *Nutrients*. 2021;13:4305.
- Halvorsen RE, Elvestad M, Molin M, Aune D. Fruit and vegetable consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of prospective studies. *BMJ Nutr Prev Health*. 2021;4:519-31.
- Kimble R, Keane KM, Lodge JK, Howatson G. Dietary intake of anthocyanins and risk of cardiovascular disease: a systematic review and meta-analysis of prospective cohort studies. *Crit Rev Food Sci Nutr*. 2019;59:3032-43.
- Gan ZH, Cheong HC, Tu Y-K, Kuo P-H. Association between plant-based dietary patterns and risk of cardiovascular disease: a systematic review and meta-analysis of prospective cohort studies. *Nutrients*. 2021;13:3952.

17. Tappy L, Lê KA. Metabolic effects of fructose and the worldwide increase in obesity. *Physiol Rev.* 2010;90:23-46.
18. Tsang B, Sandalin F, De-Regil LM. Folate supplementation in women of reproductive age. *Cochrane Database Syst Rev.* 2015;2015:CD011766.
19. Scholl TO, Johnson WG. Folic acid: influence on the outcome of pregnancy. *Am J Clin Nutr.* 2000;71:1295S-303S.
20. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation.* 2002;106:2747-57. Erratum in: *Circulation.* 2003;107:512.
21. Mozaffarian D, Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and the benefits. *JAMA.* 2006;296:1885-99. Erratum in: *JAMA.* 2007;297:590.
22. Yurko-Mauro K, McCarthy D, Rom D, et al. Beneficial effects of docosahexaenoic acid on cognition in age-related cognitive decline. *Alzheimers Dement.* 2010;6:456-64.
23. Wong C. Vitamin B12 deficiency in the elderly: is it worth screening. *Hong Kong Med J.* 2015;21:155-64.
24. Stabler SP. Vitamin B12. Present knowledge in nutrition. Elsevier; 2020:257-71.
25. Gupta L, Gupta RK, Gupta PK, et al. Assessment of brain cognitive functions in patients with vitamin B12 deficiency using resting state functional MRI: a longitudinal study. *Magn Reson Imaging.* 2016;34:191-6.
26. Andrès E, Serraj K, Zhu J, Vermorken AJ. The pathophysiology of elevated vitamin B12 in clinical practice. *QJM.* 2013;106:505-15.
27. Asif M. The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. *J Educ Health Promot.* 2014;3:1.
28. Betts JA, Richardson JD, Chowdhury EA, et al. The causal role of breakfast in energy balance and health: a randomized controlled trial in lean adults. *Am J Clin Nutr.* 2014;100:539-47.
29. Chaudhary D, Sharma N, Senapati S. Serum homocysteine could be used as a predictive marker for chronic obstructive pulmonary disease: a meta-analysis. *Front Public Health.* 2019;7:69.
30. American College of Sports Medicine; Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc.* 2009;41:1510-30.



The Impact of Thoracic CT Findings, Adiposity Parameters, and Laboratory Data on COVID-19 Prognosis

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Abstract

Aim: Numerous studies have been conducted concerning the clinical, laboratory, and radiological methods and markers to predict the prognosis of Coronavirus disease 2019 (COVID-19). In this study, we aim to explore the impact of COVID-19 severity scores, adiposity parameters, and laboratory findings on the prognosis of COVID-19.

Material and Method: A retrospective study was performed with 98 patients who were both computed tomography (CT) and polymerase chain reaction positive. Clinical outcomes, laboratory findings, thorax CT findings, and adiposity parameters (such as hepatic steatosis and visceral fat amount) obtained from thorax CTs were evaluated.

Results: The frequency of hepatic steatosis, lung severity score, and C-reactive protein (CRP) levels were higher, whereas lymphocyte count was lower in hospitalized patients than in patients treated at home. Among hospitalized patients, in addition to previous laboratory and radiological findings d-dimer and ferritin levels were higher in patients requiring intensive care. Among patients admitted to intensive care unit (ICU), the visceral to subcutaneous adipose tissue ratio was higher in patients who died than in patients who survived; none of the other parameters showed a significant difference.

Conclusion: COVID-19 CT score, adiposity parameters, and laboratory results were related to the prognosis of COVID-19. These results align with those of other recent research. A formula based on patient age, CT score, and CRP levels can be employed to determine if the patient requires hospital admission.

Keywords: COVID-19, quantitative evaluation, tomography, visceral adipose tissue, subcutaneous adipose tissue

INTRODUCTION

The World Health Organization stated in March 2020 that the Coronavirus disease 2019 (COVID-19) outbreak had reached pandemic levels, leading to a rapid increase in global cases. Numerous risk factors, such as male gender, smoking, and pre-existing conditions like cardiovascular disease and diabetes, have been recognized as potential contributors to severe pneumonia, hospitalization, and death during the pandemic.

According to various studies, patients who have higher Body Mass Index (BMI) are more severely affected by COVID-19 and tend to develop more severe forms of illness, obesity has been linked to an increased risk of hospitalization and mortality in COVID-19 patients (1-3). Several studies have also explored the connection between visceral adiposity and the severity of COVID-19,

it has been suggested that visceral fat tissue area is associated with COVID-19 severity and may predict the need for intensive care (4-6).

Laboratory data is crucial in diagnosing and monitoring COVID-19 (7). These data include viral load, inflammation markers, organ functions, and other critical parameters. A detailed analysis of these parameters is crucial for comprehending the gravity of the disease and anticipating potential complications.

In our study, radiological markers of obesity, such as hepatic steatosis, waist circumference, visceral and subcutaneous fatty tissue amount, radiological extent of COVID pneumonia, and laboratory findings were evaluated to investigate their relationship with COVID severity and their potential effects on hospitalization, intensive care unit (ICU) admission, or mortality.

CITATION

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MATERIAL AND METHOD

Population and Study Design

This retrospective study was conducted at our hospital's radiology department between December 30, 2022, and February 15, 2023. The study received approval from Karamanoğlu Mehmetbey University's Institutional Ethics and Research Committee (approval number: 10-2022/07, approval date: 08.11.2022).

We retrospectively examined patients who applied to the pandemic clinic with flu-like symptoms and underwent non-contrast chest computed tomography (CT) between June 1, 2020, and July 15, 2020. All CT images were assessed using the guidelines set forth by the Radiological Society of North America (RSNA) (8). One hundred twenty-four patients with typical and indeterminate results according to RSNA classification were further evaluated. A total number of 98 patients who also had a positive real-time reverse transcription polymerase chain reaction (PCR) test were included in the study. Laboratory results and clinical outcomes were collected from hospital records. Patients were categorized according to their clinical outcome (Figure 1). Two main groups were established at the beginning of the study: "home treatment" and "hospital admission." Subsequently, the Hospital Admission cohort was further categorized into "COVID ward admission" and "ICU admission". Finally, the ICU admission group was divided into "ICU-mortality" and "ICU-survival" subgroups.

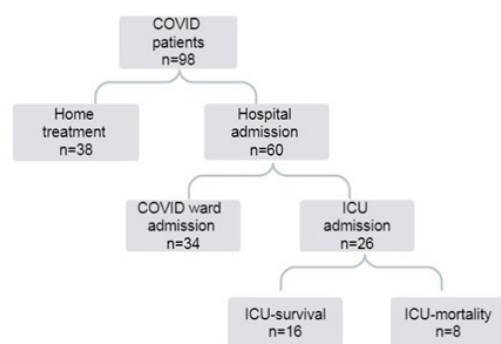


Figure 1. Flow chart of the study population

CT Acquisition and Evaluation

A non-contrast chest CT scan was performed on each patient as part of their initial clinical assessment in the emergency department. Images were obtained on a 16-detector CT scanner (Toshiba, Alexion) with the patients in supine position at full inspiration. CT scan parameters are as follows: X-ray tube parameters, 100 KVP; automatic tube current modulation (145–300 mAs); rotation time, 0.5 s; pitch, 1.43; section thickness, 5 mm.

The CT images were reviewed by a team of two radiologists (GMA and TG), each with eight and seven years of experience. The final agreement was made by consensus.

Chest CT scans were examined to detect the ground-glass opacities, consolidations, crazy paving appearance, and atoll sign.

The extent of pneumonia was visually scored following the previous method, "Total Severity Score (TSS)" (9). The

technique involved evaluating each lobe and giving it a rating on a 4-point scale depending on the degree of lobar involvement: 0 for no involvement, 1 for 1-25%, 2 for 25-50%, 3 for 51-75%, and 4 for 76-100% involvement. TSS was equal to the sum of the scores of five lobes with a maximum score of 20 points.

CT Evaluation of Adiposity Parameters

CT scans were reviewed for hepatic steatosis, waist circumference, and visceral adipose tissue area.

On unenhanced CT, liver density less than 40 Hounsfield units (HU) is widely accepted as hepatic steatosis. For this study, we measured liver density from the right lobe, preferably from segment VIII, by positioning a region of interest (ROI) of approximately 10 cm², avoiding vessels, the biliary tree, and any focal lesions.

For visceral and subcutaneous adipose tissue (VAT and SAT) measurements, we used a semiautomatic software called BMI_CT (10). Measurements were made from a slice at the L2 corpus level. A manually drawn line separated the abdominal muscles and peritoneal cavity, and the software was employed to calculate SAT and VAT. These two areas were added together to calculate the total adipose tissue (TAT) area (Figure 2).

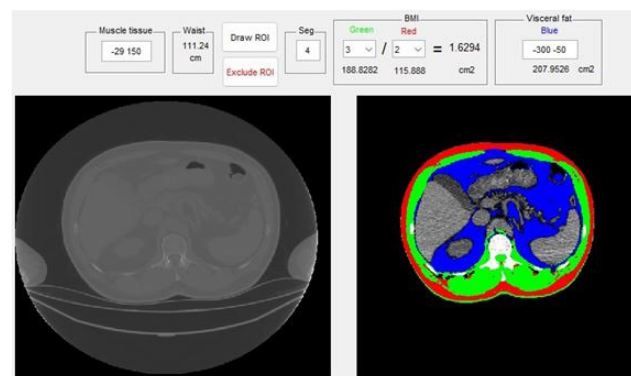


Figure 2. The process of semiautomatic quantification of body composition using the software. Subcutaneous adipose tissue is shown in red, visceral adipose tissue in blue, and muscle tissue in green

Statistical Analysis

IBM's SPSS 22.0 software (Chicago, IL) was performed for statistical analysis. Correlation heatmap plots were created using the Python 3.7.9 (Delaware, USA) software program. Shapiro Wilk, Mann-Whitney U Test, Independent Two-Sample t-test, Continuity Correction, and Fisher's Exact Tests, and Kruskal-Wallis H Test were employed in the analysis of the data set.

The mean±standard deviation was used to express continuous data that lined up to a normal distribution; the median (Q1-Q3) was used to represent those that did not. For categorical data, percentages (%) and frequencies were employed. Box-Plot (95% CI) was used to compare the median of TSS between "home treatment" and "hospital admission" groups. Pairwise comparison was applied for multiple sub-groups. The cut-off value was determined by applying receiver operating characteristic (ROC) analysis. Binary logistic regression with the enter method was applied

to investigate the factors affecting the follow-up status. The Hosmer-Lemeshow Test was used to model goodness of fit in regression analysis. The threshold for statistical significance was set at $p < 0.05$.

RESULTS

Ninety-eight patients participated in the study. Forty percent were male, and 60 percent were female. They ranged in age from 23 to 84, with a mean of 56.19 ± 15.88 .

Comparison of Home Treatment and Hospital Admission Groups

Table 1 compares the groups of patients treated at home and admitted to the hospital. Age was notably higher in the hospital admission group, although gender did not differ. Among biochemical markers, neutrophil, lymphocyte, and C-reactive protein (CRP) were higher in the latter group. D-dimer and ferritin levels were elevated in hospitalized patients, but these data could not be compared to the home treatment group due to their unavailability.

Among obesity parameters, patients in the hospital admission group had notably lower liver HU and significantly higher waist circumference ($p < 0.05$). VAT, SAT, or TAT areas did not significantly differ between the two groups.

Lung severity score was significantly higher in the hospital admission group ($p < 0.001$) (Figure 3). The ROC curves for the TSS were done, and the area under the curve (AUC) was calculated for the diagnostic effectiveness of TSS in detecting patients needed hospital admission. ROC analysis showed the AUC of TSS for deciding hospital admission was 0.800 (95%CI 0.715–0.885). The sensitivity and specificity of the TSS cutoff of 5.5 were 56.7% and 86.8%, respectively (Figure 4).

Binary logistic regression with the enter method was applied with age, lung severity score, and CRP parameters to decide if the patient requires hospitalization. It was significant and fit ($p < 0.001$ and $p = 0.523$, respectively).

To decide between outpatient management and hospitalization, status can be calculated according to the formula: Follow-up status = $-6.168 + 0.047 \cdot \text{age} + 0.591 \cdot \text{TSS} + 0.022 \cdot \text{CRP}$.

The classification table is shown in Table 2.

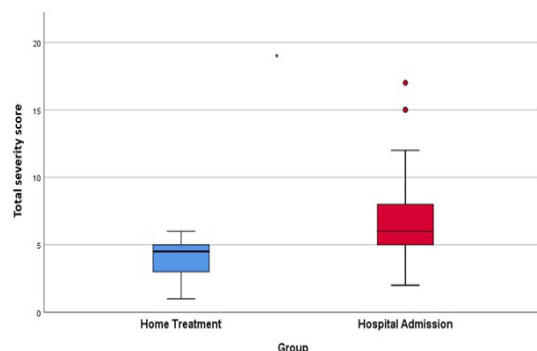


Figure 3. Box-plots for comparison of median differences of Total Severity Score (TSS) between “home treatment” and “hospital admission” groups, which represents a statistically significant difference between the two groups ($p < 0.001$), * represents statistically significant differences between groups ($p < 0.001$)

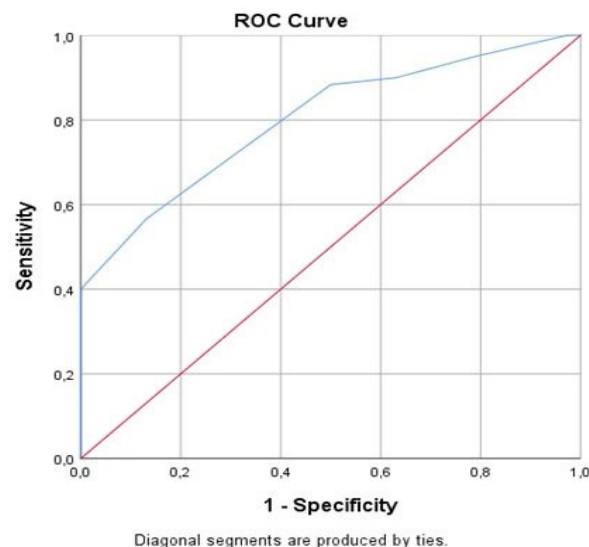


Figure 4. ROC curve for diagnostic performance of TSS in detection of patients who need hospital admission. ROC analysis showed the area under the curve (AUC) of TSS for deciding “hospital admission” was 0.800 (95%CI 0.715–0.885); The TSS cutoff of 5.5 had 56.7% sensitivity and 86.8% specificity

Comparison of COVID Ward Admission and ICU Admission Groups

The findings are shown in Table 3. Demographic features were not different among groups. TSS was significantly higher in the ICU admission group ($p = 0.005$) (Figure 5). Regarding biochemical markers, there were notable differences between the two groups in lymphocyte, CRP, d-dimer, and ferritin. Adiposity parameters did not differ among the two groups.

Comparison of ICU-Mortality and ICU-Survival Groups

The VAT/SAT ratio, higher in the ICU-mortality group, was the only metric that revealed a significant difference between these two groups (Table 4).

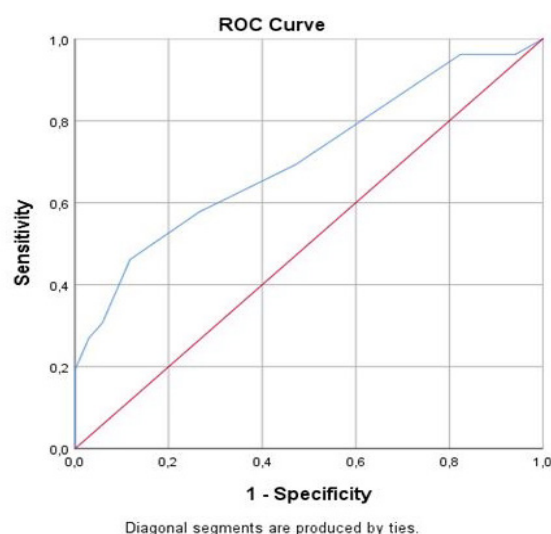


Figure 5. ROC curve for diagnostic performance of TSS in detection of patients who need ICU admission. ROC analysis showed the area under the curve (AUC) of TSS for deciding “ICU admission” was 0.708 (95%CI 0.572–0.843); The TSS cutoff of 7.5 had 46.2% sensitivity and 88.2% specificity

Table 1. Comparison of home treatment and hospital admission groups

Parameters	Participant group		p value
	Home treatment (n=38)	Hospital admission (n=60)	
Age (year)	51.0 (38.5-59.8)	63.0 (48.0-72.5)	0.002^b
VAT	101.8 (53.8-174.2)	142.3 (97.0-184.8)	0.072 ^b
SAT	159.9±78.8	182.2±90.2	0.215 ^a
TAT	283.0±128.9	327.4±114.9	0.079 ^a
VAT/SAT	0.60 (0.33-1.28)	0.82 (0.51-1.31)	0.180 ^b
Gender. (M/F) (M%)	14/24 (36.8)	25/35 (41.7)	0.634 ^c
Waist circumference	100.3±12.3	106.6±10.0	0.007^a
Liver HU	61.83 (56.95-65.46)	56.96 (49.63-62.65)	0.013^b
Total severity score	4.5 (3.0-5.0)	6.0 (5.0-8.0)	<0.001^b
Crazy paving (absent/present) (absent%)	30/8 (78.9)	37/23 (61.7)	0.117 ^c
Atoll sign (absent/present) (absent%)	37/1 (97.4)	55/5 (91.7)	0.400 ^d
Consolidation (absent/present) (absent%)	26/12 (68.4)	34/26 (56.7)	0.342 ^d
White blood count	6280.0 (4900.0-6280.0)	6430.0 (4845.0-8927.5)	0.856 ^b
Neutrophil	3900.0 (2430.0-4960.0)	4335.0 (3185.0-7467.5)	0.034^b
Lymphocyte	1740.0 (1250.0-2680.0)	1210.0 (960.0-1590.0)	<0.001^b
CRP	13.4 (5.2-24.0)*	86.2 (40.7-124.7)	<0.001^b

Continuous variables are presented as mean±standard deviation or median (Q1-Q3); categorical variables are presented as numbers (%); a: Independent Samples T Test was applied, b: Mann-Whitney U Test was applied, c: Continuity Correction Test was applied, d: Fisher's Exact Test was applied, *: Some participant data was missing

Table 2. Classification table for binary logistic regression

			Predicted		Percentage correct
			Group		
			1 (home treatment)	2 (hospital admission)	
Observed	Group	1 (home treatment)	26	9	74.3
		2 (hospital admission)	9	51	85.0
Overall percentage			74.3	85.0	81.1

Table 3. Comparison of COVID ward admission and ICU admission groups

Parameters	Participant group		p value
	COVID ward admission (n=34)	ICU admission (n=26)	
Age (year)	52.0 (45.5-67.0)	70.0 (56.5-78.5)	0.328 ^b
VAT	153.2±39.3	160.4±80.4	0.376 ^a
SAT	162.8±87.1	163.7±85.7	0.643 ^a
TAT	316.0±100.6	324.0±117.2	0.882 ^a
VAT/SAT	1.0 (0.6-1.8)	1.0 (0.5-2.4)	0.429 ^b
Gender (M/F) (M%)	13/21 (38.2)	12/14 (46.2)	0.725 ^c
Waist circumference	108.9 (104.5-114.9)	103.4 (96.5-109.8)	0.582 ^a
Liver HU	53.2±10.6	55.6±14.0	0.717 ^a
Total severity score	6.0 (4.0-7.0)	7.0 (5.0-10.0)	0.005^b
White blood count	6000.0 (5365.0-8065.0)	8500.0 (5677.5-13090.0)	0.110 ^b
Neutrophil	4350.0 (3600.0-5675.0)	6590.0 (3387.5-12095.0)	0.075 ^b
Lymphocyte	1590.0 (915.0-1770.0)	1080.0 (835.0-1257.5)	0.024^b
LDH	381.7±147.2	396.6±142.5	0.157 ^a
CRP	68.2±31.6	123.8±83.7	<0.001^a
D-dimer	700.0 (427.5-1202.0)	885.5 (587.8-2167.8)	0.001^b
Ferritin	332.9 (49.1-648.7)	360.6 (117.8-541.8)	0.034^b
Total cholesterol	167.7±72.3	144.3±39.4	0.508 ^a
LDL cholesterol	93.8±44.3	79.3±35.7	0.471 ^a
Triglyceride	173.1±80.4	170.5±69.0	0.823 ^a

Continuous variables are presented as mean±standard deviation or median (Q1-Q3); a: Independent Samples T Test was applied, b: Mann-Whitney U Test was applied, c: Continuity Correction Test was applied

Table 4. Comparison of ICU-mortality and ICU-survival groups			
Parameters	Participant group		p value
	ICU-mortality (n=10)	ICU-survival (n=16)	
Age (year)	70.5 (64.8-78.5)	66.5 (51.5-78.3)	0.262
VAT	166.0 (130.5-215.6)	144.1 (74.7-216.6)	0.220
SAT	60.3 (46.7-181.8)	189.8 (133.4-233.1)	0.182
TAT	283.0 ± 128.9	327.4 ± 114.9	0.698
VAT/SAT	2.6 (1.0-3.6)	0.6 (0.4-1.3)	0.036
BMICT	1.8 (0.7-2.5)	0.6 (0.5-0.9)	0.060
Gender (M/F) (M%)	7/3 (70.0)	5/11 (31.3)	0.105 ^c
Waist circumference	100.2 (92.6-107.1)	103.8 (99.2-112.0)	0.938
Liver HU	53.1 (40.6-56.9)	61.3 (53.9-68.1)	0.109
LDH	455.0 (302.8-528.0)	353.5 (270.0-481.5)	0.251
Total severity score	7.5 (5.0-8.5)	6.5 (5.3-13.8)	0.623
White blood count	8500.0 (4492.5-10510.0)	8965.0 (6140.0-14687.5)	0.551
Neutrophil	6590.0 (3177.5-8610.0)	7595.0 (3302.5-13557.5)	0.551
Lymphocyte	1115.0 (930.0-1822.5)	1030.0 (825.0-1217.5)	0.849
CRP	107.2 (97.6-239.0)	119.0 (41.6-140.4)	0.517
D-dimer	1410.5 (458.0-3505.3)	885.5 (615.5-1970.0)	0.776
Ferritin	291.0 (107.7-797.3)	389.2 (99.8-551.9)	0.698
Total cholesterol	125.0 (86.8-199.5)	148.0 (126.3-173.5)	0.972
LDL cholesterol	455.0 (302.8-528.0)	353.5 (270.0-481.5)	0.757
Triglyceride	127.0 (68.3-193.8)	199.5 (148.0-212.0)	0.330
Continuous variables are presented as mean ± standard deviation or median (Q1-Q3); a: Independent Samples T Test was applied, b: Mann-Whitney U Test was applied, c: Fisher's Exact Test was applied, *: Some participant data was missing			

DISCUSSION

Numerous studies have been conducted concerning the clinical, laboratory, and radiological methods and markers used to foresee the outcome of COVID-19 (11,12). The purpose of this study was to explore the impact of obesity markers and COVID-19 severity markers obtained from thorax CT and laboratory findings on the prognosis of COVID-19.

Many studies showed that older age significantly predicts severe COVID-19 and hospitalization (13,14). It is thought to result from weaker immune function combined with the underlying chronic diseases in older age. Similarly, our study found that patients in the hospital admission subgroup were notably older than those in the home treatment group. Although several studies suggest that advanced age is a significant predictor of COVID-19 mortality (15-17), our study found no significant age difference between the COVID ward and ICU admission subgroups, nor between ICU-survival and ICU-mortality subgroups.

Laboratory parameters have been reported as essential markers for monitoring COVID-19 pneumonia. Among the laboratory parameters frequently investigated were neutrophil and lymphocyte count, d-dimer as a coagulation biomarker, and inflammatory biomarkers such as CRP and ferritin.

Research indicates that individuals who develop severe COVID-19 have markedly decreased lymphocyte counts. Our findings also showed that patients who required hospitalization had lower lymphocyte counts.

Higher levels of CRP and ferritin were observed in severe COVID-19 patients and were indicative of poor prognosis (18-21). Our research showed an increase in CRP levels among hospitalized patients and an even greater increase among those admitted to the ICU. It is an acute inflammatory protein and is closely tied to severe illness. We observed elevated ferritin levels in patients who needed ICU admission. Severe COVID-19 patients have been found to have higher levels of ferritin due to a cytokine storm (22). This storm triggers the release of inflammatory cytokines, stimulating ferritin secretion by hepatocytes and macrophages (23).

In COVID-19 patients, endothelial dysfunction caused by the virus and activation of the coagulation cascade may lead to COVID-19-associated coagulopathy (7). Therefore, coagulation biomarkers were widely investigated as markers for COVID-19 severity.

As one of the initial coagulation biomarkers affected in COVID-19 patients, D-dimer has also revealed its potential as a prognostic factor for mortality upon admission (24). Our findings showed a significant correlation between elevated D-dimer levels and the need for ICU admission in hospitalized patients. D-dimer and ferritin levels could not be compared in the home treatment subgroup as they were not routinely evaluated in the emergency room.

Thorax CT scans are a reliable method for diagnosing and predicting the course of COVID-19 (25). The severity of COVID-19 infections has been evaluated using a variety of scoring systems (11,26).

Li et al. found that TSS could predict severe disease in COVID-19 patients (9). Our research revealed that TSS levels were notably elevated in hospitalized patients compared to those treated at home. We found that the TSS cutoff of 5.5 had 56.7% sensitivity and 86.8% specificity. Binary logistic regression was applied with age, TSS, and CRP parameters; the resulting formula had 74.3% sensitivity and 56.7% sensitivity in predicting hospitalization. We believe this formula could be easy to apply in emergency departments and help clinicians decide if the patients require hospitalization.

The TSS score was also higher in patients requiring ICU admission than those treated in COVID wards. The TSS cutoff of 7.5 had 56.7% sensitivity and 86.8% specificity for deciding ICU admission.

In our study, the waist circumference value was higher, and the liver HU value was lower in the hospitalized group compared to the home-treatment group. Further studies have revealed that hepatic steatosis can independently increase the likelihood of a worse prognosis in COVID-19 infection (27,28). It has been shown that circulating IL-6 levels are higher in patients with hepatic steatosis. This situation may impact the severe course of COVID-19 (29).

It is widely recognized that obesity is connected to cardiovascular diseases, stroke, certain types of cancer, and overall mortality. The distribution of fat tissue is just as important as the amount of fat in the body. Kuk et al. showed that visceral fat is an independent predictor of mortality (30). Another study by Zhang et al. revealed that abdominal adiposity independently predicts mortality risk, especially in non-obese women (31).

Several studies have linked obesity to a more severe course of COVID-19, particularly in young patients (1-3,32,33). The connection between visceral adiposity and the severity of COVID-19 has been widely investigated. The results of multiple studies indicate that increased VAT and VAT/SAT rates are linked to a more severe course of COVID-19 and subsequent ICU admissions (4-6).

For VAT and SAT measurements in our investigation, we preferred the L2 corpus level, as a slice 3 cm above L3 level had been suggested to more accurately reflect the quantity of visceral adipose tissue than other levels (34). Similarly, L1–L2 and L2–L3 levels were suggested to correlate more strongly with VAT volume compared to the L4–L5 level (35). However, there is no widely agreed-upon level in the literature for using CT to estimate the quantity of visceral adipose tissue and studies used several different levels for adipose tissue measurements. The initial segment where the lung parenchyma is completed (6), sections that pass from the L3 level (4), and the L3-L4 intervertebral disc level (5) are all used in studies looking at the link between COVID-19 and visceral obesity. The lack of impact of adiposity factors on prognosis in our study may be attributed to the varying levels at which the assessments were conducted. Likewise, our findings may differ from other studies based on the sample size of our subgroups.

Although there were no significant differences in TSS and laboratory parameters among the two subgroups of intensive care unit patients in our study, the mortality group had a noticeably higher VAT/SAT ratio ($p=0.036$). Our research suggests that the VAT/SAT ratio could be a potential indicator of mortality among severe COVID-19 patients who needs intensive care.

It has long been known that adipose tissue is an active endocrine organ and a source of inflammatory interleukin and cytokines and that increased adipose tissue has pro-inflammatory effects (16). Increasing amounts of adipose tissue lead to an increase in blood vessels and connective tissue cells, particularly macrophages, that secrete proinflammatory cytokines such as interleukin-6, which was found to be higher in patients with a fatal course of COVID-19 (36). In obese people, proinflammatory cytokine levels are higher in both fatty tissue and blood circulation, which may contribute to a chronic proinflammatory state, leading to a more severe course of the disease (35).

There are various limitations to our study. Our rather small sample size led to limited subgroup sizes. Hospital records were insufficient, and anthropometric measurements (weight, height or BMI) were inaccessible and couldn't be included in the study. Likewise, important medical history, including coexisting medical conditions such as hypertension and diabetes mellitus, which might have influenced the prognosis, could not be accessible. Since our study was retrospective, some laboratory findings were not available.

CONCLUSION

In this study, CT scans were effective in detecting COVID-19 infection, assessing the extent of lung involvement, and the severity of the disease. Additionally, they are highly beneficial in evaluating adiposity parameters such as waist circumference, hepatic steatosis and visceral and adipose tissue areas, which are identified as significant risk factors for severe illness in previous studies. Our findings indicate that hepatic steatosis and elevated waist circumference could act as predictors for hospitalization, whereas the elevated VAT/SAT ratio may be associated with increased mortality risk in patients admitted to the ICU. Combining laboratory results with findings obtained from CT scans regarding the severity of COVID-19 pneumonia and radiological adiposity parameters offers valuable insights that can assist in predicting the clinical progression of COVID-19 and guide clinical decision-making.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: The study received approval from Karamanoğlu Mehmetbey University's Institutional Ethics and Research Committee (approval number: 10-2022/07, approval date: 08.11.2022).

REFERENCES

- Alberca RW, Oliveira L de M, Branco ACCC, et al. Obesity as a risk factor for COVID-19: an overview. *Crit Rev Food Sci Nutr*. 2021;61:2262-76.
- Deng M, Qi Y, Deng L, et al. Obesity as a potential predictor of disease severity in young COVID-19 patients: a retrospective study. *Obesity*. 2020;28:1815-25.
- de Siqueira JVV, Almeida LG, Zica, BO et al. Impact of obesity on hospitalizations and mortality, due to COVID-19: a systematic review. *Obes Res Clin Pract*. 2020;14:398-403.
- Pediconi F, Rizzo V, Schiaffino S, et al. Visceral adipose tissue area predicts intensive care unit admission in COVID-19 patients. *Obes Res Clin Pract*. 2021;15:89-92.
- Favre G, Legueult K, Pradier C, et al. Visceral fat is associated to the severity of COVID-19. *Metabolism*. 2021;115:154440.
- Watanabe M, Caruso D, Tuccinardi D, et al. Visceral fat shows the strongest association with the need of intensive care in patients with COVID-19. *Metabolism*. 2020;111:154319.
- Battaglini D, Lopes-Pacheco M, Castro-Faria-Neto HC, et al. Laboratory biomarkers for diagnosis and prognosis in COVID-19. *Front Immunol*. 2022;13:857573.
- Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America Expert Consensus Statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA - Secondary Publication. *J Thorac Imaging*. 2020;35:219-27.
- Li K, Fang Y, Li W, et al. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). *Eur Radiol*. 2020;30:4407-16.
- Kim SS, Kim JH, Jeong WK, et al. Semiautomatic software for measurement of abdominal muscle and adipose areas using computed tomography: a STROBE-compliant article. *Medicine (Baltimore)*. 2019;98:e15867.
- Yang R, Li X, Liu H, et al. Chest ct severity score: an imaging tool for assessing severe COVID-19. *Radiol Cardiothorac Imaging*. 2020;2:e200047.
- Figliozzi S, Masci PG, Ahmadi N, et al. Predictors of adverse prognosis in COVID-19: a systematic review and meta-analysis. *Eur J Clin Invest*. 2020;50:e13362.
- Gallo Marin B, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: a literature review. *Rev Med Virol*. 2021;31:1-10.
- Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *J Infect*. 2020;80:e14-8.
- Palmieri L, Vanacore N, Donfrancesco C, et al. Clinical characteristics of hospitalized individuals dying with COVID-19 by age group in Italy. *J Gerontol A Biol Sci Med Sci*. 2020;75:1796-800.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*. 2020;395:1054-62. Erratum in: *Lancet*. 2020;395:1038.
- Leung C. Risk factors for predicting mortality in elderly patients with COVID-19: a review of clinical data in China. *Mech Ageing Dev*. 2020;188:111255.
- Kaushal K, Kaur H, Sarma P, et al. Serum ferritin as a predictive biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. *J Crit Care*. 2022;67:172-81.
- Cheng L, Li H, Li L, et al. Ferritin in the coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *J Clin Lab Anal*. 2020;34:e23618.
- Pepys MB. C-reactive protein predicts outcome in COVID-19: is it also a therapeutic target?. *Eur Heart J*. 2021;42:2280-3.
- Yitbarek GY, Walle Ayehu G, Asnakew S, et al. The role of C-reactive protein in predicting the severity of COVID-19 disease: a systematic review. *SAGE Open Med*. 2021;9:20503121211050755.
- Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. *Int J Infect Dis*. 2020;95:304-7.
- Torti FM, Torti SV. Regulation of ferritin genes and protein. *Blood*. 2002;99:3505-16.
- Poudel A, Poudel Y, Adhikari A, et al. D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19. *PLoS One*. 2021;16:e0256744.
- Rubin GD, Ryerson CJ, Haramati LB, et al. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the fleischner society. *Chest*. 2020;158:106-16.
- Francone M, lafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *Eur Radiol*. 2020;30:6808-17.
- Parlak S, Çıvgın E, Beşler M, Kayıpmaz A. The effect of hepatic steatosis on COVID-19 severity: chest computed tomography findings. *Saudi J Gastroenterol*. 2021;27:105-10.
- Palomar-Lever A, Barraza G, Galicia-Alba J, et al. Hepatic steatosis as an independent risk factor for severe disease in patients with COVID-19: a computed tomography study. *JGH Open*. 2020;4:1102-7.
- Wieckowska A, Papouchado BG, Li ZZ, et al. Increased hepatic and circulating interleukin-6 levels in human nonalcoholic steatohepatitis. *Am J Gastroenterol*. 2008;103:1372-9.
- Kuk JL, Katzmarzyk PT, Nichaman MZ, et al. Visceral fat is an independent predictor of all-cause mortality in men. *Obesity*. 2006;14:336-41.
- Zhang X, Shu XO, Gong Y, et al. Abdominal adiposity and mortality in Chinese women. *Arch Intern Med*. 2007;167:886-92.
- Iacobellis G, Malavazos AE, Ferreira T. COVID-19 rise in younger adults with obesity: visceral adiposity can predict the risk. *Obesity*. 2020;28:1795.
- Petrakis D, Margină D, Tsarouhas K, et al. Obesity a risk factor for increased COVID 19 prevalence, severity and lethality (Review). *Mol Med Rep*. 2020;22:9-19.
- Park HS, Park JY, Yu R. Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF- α , and IL-6. *Diabetes Res Clin Pract*. 2005;69:29-35.

35. Fain JN. Release of interleukins and other inflammatory cytokines by human adipose tissue is enhanced in obesity and primarily due to the nonfat cells. *Vitam Horm.* 2006;74:443-77.
36. Park HS, Park JY, Yu R. Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF- α , and IL-6. *Diabetes Res Clin Pract.* 2005;69:29-35.



Evaluation of Atherosclerosis and Arterial Stiffness with Angiogenic Growth Factors in Chronic Kidney Disease Patients

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Abstract

Aim: Cardiovascular (CV) complications are the most common cause of mortality in patients with chronic kidney disease (CKD). The study aimed to determine the relationship between angiotensin-2 (Ang-2) and vascular endothelial growth factor (VEGF) and atherosclerosis as determined by carotid artery intima-media thickness (CAT) and arterial stiffness (AS) as determined by brachial-ankle pulse wave velocity (bPWV) in pre-dialysis CKD patients.

Material and Method: The study included 126 (47.2%) male and 141 (52.8%) female pre-dialysis CKD patients. Presence of atherosclerosis was determined by CAT and presence of AS by bPWV. VEGF and Ang-2 serum levels were determined by enzyme-linked immunosorbent assays (ELISA).

Results: CAT, bPWV, and log10 Ang-2 values were significantly higher in patients compared to the healthy control group. Estimated glomerular filtration rate (eGFR), C-reactive protein (CRP), total cholesterol, triglycerides, CAT, and bPWV were higher and spot urine protein creatinine ratio was lower in patients with high mean log10 Ang-2 compared to the patients with low mean log10 Ang-2. There was a significant correlation between log10 Ang-2 and bPWV and CAT, and an inverse relationship with log10 VEGF.

Conclusion: Patients with CKD had increased development of atherosclerosis and AS, increased serum Ang-2 levels compared to healthy individuals. Ang-2 was significantly correlated with renal function and inversely correlated with proteinuria. Ang-2 was found to be correlated with inflammation and hyperlipidemia. A significant correlation was observed between Ang-2 and atherosclerosis and AS, and an inverse relationship was found with VEGF.

Keywords: Atherosclerosis, arterial stiffness, chronic kidney disease, angiotensin-2, vascular endothelial growth factor

INTRODUCTION

The risk of death due to cardiovascular (CV) diseases is quite high in those with chronic kidney disease (CKD). An early sign of atherosclerosis is an increase in arterial intima-media thickness. Carotid artery intima-media thickness (CAT) using ultrasonography is a non-invasive, inexpensive, and easily applicable method preferred for determining the presence of atherosclerosis (1). Increased CAT is thought to be an early sign of the development of atherosclerosis in cerebral, peripheral and coronary arterial vascular beds. Increased endothelial microparticles due to increased calcium-phosphate product as a result of hyperparathyroidism in CKD patients may cause changes in

the artery wall and cause atherosclerosis. Arterial stiffness (AS) is common in CKD patients. A study suggested that endothelial dysfunction, advanced age, and infections are the risk factors for AS in CKD patients (2). The brachial-ankle pulse wave velocity (bPWV) device was designed to record the pulse waves of the brachial and posterior tibial arteries automatically and simultaneously using an automated oscillometric method. Determination of AS in CKD patients with the bPWV device is easy to perform, reproducible, and yields similar results to other methods known as the gold standard (3).

Angiotensins provide vascular stabilization by binding to the endothelium-specific tyrosine kinase member receptor.

CITATION

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Angiopoietin-2 (Ang-2) is synthesized by endothelial Weibel-Palade bodies (WPB), binds to the endothelial receptor Tie-2, and plays an antagonistic role when endothelial cells are under stress. Vascular endothelial growth factors (VEGF) are effective in lymphangiogenesis, angiogenesis, and inflammation and synthesized from distal tubule and glomerular epithelial cells in the kidney. VEGF levels increase as Ang-2 increases. Ang-2 enables new vessel formation in the presence of VEGF. Ang-2 causes vascular regression and endothelial cell death in the absence of VEGF. VEGF and Ang-2 are thought to be compatible to form the microvasculature.

Matsunaga et al. suggested that vascular angiogenesis is an event that involves co-expression of both VEGF and Ang-2 (4). Lee et al. suggested that high Ang-2 and VEGF levels are associated with CV, including congestive heart failure and coronary artery disease (5). Lorbeer et al. suggested that relationship between CV mortality and Ang-2 (6). Chang et al. stated that high Ang-2 levels predict kidney failure in CKD patients (7).

Studies examining the angiogenic growth factors, atherosclerosis and AS in CKD patients are limited in number and the results are conflicting. Therefore, the present study aimed to investigate the relationship between the angiogenic growth factors Ang-2 and VEGF and atherosclerosis and AS in pre-dialysis CKD patients.

MATERIAL AND METHOD

Patient Selection

This prospective study was conducted with patients with CKD who applied to the nephrology outpatient clinic between January 2022 and January 2023.

Our study included 126 (47.2%) male and 141 (52.8%) female pre-dialysis CKD patients. The healthy control group consisted of 70 people who had no known disease or medication. Patients with no known history of pacemaker, coronary artery disease, or heart failure and over 18 years of age participated in the study. Exclusion criteria were: history of dialysis or kidney transplantation, history of active infection or malignancy within the last 3 months, previous angiographically proven coronary artery disease and therefore undergone surgical or mechanical revascularization, moderate to severe valvular insufficiency or valvular stenosis, known peripheral vascular disease, atrial fibrillation, atrial flutter, other tachyarrhythmias and bradyarrhythmias, severe left ventricular systolic dysfunction, congenital heart disease, respiratory system disease, systemic disease involving the aorta (such as Marfan, Ehler-Dahlnos). This study ethics committee numbered TABED 1-24-226 from Ankara City Hospital (date: 17/07/2024).

Clinical Measurements

Height-weight measurements, age, gender, medications, and comorbid diseases were determined. Body mass

index (BMI) was calculated. Patients who had previously used antihypertensive medication or had systolic blood pressure (SBP) ≥ 140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg were considered hypertensive. Fasting blood sugar ≥ 126 mg/dL and/or use of insulin or antidiabetic medication was considered diabetes mellitus (DM). The estimated glomerular filtration rate (eGFR) was calculated according to the formula by Levey et al. (8).

Laboratory Measurements

Serum creatinine, C- reactive protein (CRP), total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglyceride and low-density lipoprotein (LDL) levels were determined. Morning urine is preferred for urine laboratory testing. After the patient's urine is collected, it is sent to the laboratory. The laboratory measures the amount of protein and creatinine in the urine. Then, using these values, spot urine protein/creatinine ratio (SUPC) is calculated. VEGF and Ang-2 levels were measured using commercial enzyme-linked immunosorbent assay (ELISA) kits. Analytic range and sensitivity levels were 21-1497 pg/mL and <4 pg/mL for VEGF, 59.5-3980 pg/mL and 35.4 pg/mL for Ang-2.

Brachial-ankle pulse wave velocity

A noninvasive oscillometric aortic pressure measurement technique was used to measure pulse wave velocity (PWV) values in all patients. SphygmoCor (AtCor Medical Instruments) pulse wave analyzer was utilized as the measuring device. With the selected device, both left- and right-sided bPWV values were measured from cuffs both upper arms and ankles as previously described (9). The distances between the measurement sites of bPWV were automatically calculated according to the height of the patients. The length from the suprasternal notch to the brachial (Bb) and from the suprasternal notch to the ankle (Ba), and then the latency from the rise point of the brachial to the rise point (Bba) of each ankle waveform, were calculated. BPWV value was measured with the formula $(Ba-Bb)/Bba$.

Carotid artery intima-media thickness

Carotid artery intima-media thickness values were first measured in both internal carotid arteries with an ultrasonography device (Logiq P5 and linear probe). Three measurements were taken and the mean CAT was calculated as the average of the total measurements from both carotid arteries. In ultrasound B mode examination, the site between the echogenicity of the vascular cavity and the echogenicity of the media/adventitia layer of the vessel was visualized and measurements were taken from this site (10).

Statistical Analysis

IBM SPSS software was used in data analysis. Conformity to normal distribution was evaluated with the Kolmogorov-Smirnov test. Pearson chi-square test was

used to examine gender. Evaluation of laboratory data was made with the Mann Whitney U test, demographic finding, CAT and bPWV values. The correlation between log10 Ang-2 and log10 VEGF data, which do not show a normal distribution, and laboratory, CAT and bPWV data were analyzed with the Spearman rho correlation coefficient. Factors associated with Log10 Ang-2 and log10 VEGF were determined by logistic regression model. Frequency (percentage) was used for categorical data, and mean±standard deviation was used for quantitative data. The statistical significance level was determined as 0.05.

RESULTS

Patients' Characteristics

267 predialysis CKD patients were included. The average age of patients was 52.51±7.44 years.126 (47.2%) were male and 141 (52.8%) were female. A healthy control group of 70 people was created. Mean CAT was 0.67±0.16 mm, and bPWV was 8.79±1.87 m/sec. BMI (p=0.021), SBP, SUPC, CRP, total cholesterol, CAT, bPWV (all p<0.001), triglycerides (p=0.010), LDL-C (p=0.013), log10 Ang-2 (p=0.028) were higher in patients compared to healthy participants (Table 1).

Table 1. Clinical, demographic and laboratory values of the patient and healthy control group			
	Patients (n=267) Mean±S.D./n (%)	Healthy control group (n=70) Mean±S.D./n (%)	p
Age (years)	53.94±11.11	52.51±7.44	0.226*
Male/female	126 (47.2)/141 (52.8)	28 (40)/42 (60)	0.282**
BMI (kg/m²)	28.31±4.07	26.87±4.07	0.021*
Hypertensive nephrosclerosis	252 (94.4)		
Diabetic nephropathy	43 (16.1)		
SBP (mmHg)	135.32±22.83	118.67±11.02	<0.001*
ACEinh/ARB	31 (11.6)/109 (40.8)		
Calcium channel blockers	119 (44.6)		
Beta blockers	62 (23.2)		
Alpha blockers	10 (3.7)		
Diuretics	36 (13.5)		
Others	29 (10.9)		
Vitamin D/vitamin D analogue use	59 (22.1)		
Use of oral phosphate binder	2 (0.7)		
Stage 3 CKD	149 (55.8)		
Stage 4 CKD	93 (34.8)		
Pre-dialysis stage 5 CKD	25 (9.3)		
eGFR (mL/min/1.73 m²)	29.94±16.4	90.71±6.03	<0.001*
SUPC (g/day)	646.31±597.43	52.33±62.96	<0.001*
CRP (mg/dL)	4.4±3.55	2.43±2.68	<0.001*
Total cholesterol (mg/dL)	198.79±36.26	147.43±41.63	<0.001*
Triglyceride (mg/dL)	158±107.83	144.88±46.05	0.010*
LDL-C (mg/dL)	122.51±34.38	107.09±39.07	0.013*
HDL-C (mg/dL)	48.47±14.19	62.79±31.96	<0.001*
Log10 Ang-2 (pg/mL)	3.26±0.06	3.26±0.11	<0.028*
Log10 VEGF (pg/mL)	2.29±0.21	2.25±0.2	0.317*
CAT (mm)	0.67±0.16	0.6±0.55	<0.001*
bPWV (m/sec)	8.79±1.87	6.58±0.96	<0.001*
Data are presented as n (%), mean±SD; * Mann Whitney U test, **Pearson chi-square test; Abbreviations: BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, ACEinh: angiotensin converting enzyme inhibitor, ARB: angiotensin II receptor blocker, eGFR: estimated glomerular filtration rate, SUPC: spot urine protein creatinine ratio, CRP: C reactive protein, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, Ang-2: angiotensin 2, VEGF: vascular endothelial growth factor, CAT: carotid artery intima-media thickness, bPWV: Brachial-ankle pulse wave velocity			

Patient characteristics according to median angiogenic growth factor levels

The median log10 Ang-2 value was 3.26. eGFR, total cholesterol, bPWV (all p=0.001), CRP (p=0.003), triglycerides (p=0.020), LDL-C (p<0.001) and CAT (p=0.004) were significantly higher and SUPC (p<0.001) was significantly

lower in patients with log10 Ang-2>3.26 compared to those with log10 Ang-2≤3.26 (Table 2). The median log10 VEGF value was 2.3 pg/mL. SUPC (p<0.001) was significantly higher and eGFR, CRP, triglycerides, LDL-C, CAT, and bPWV (all p<0.001) were lower in patients with log10 VEGF>2.3 compared to those with log10 VEGF≤2.3 (Table 3).

Table 2. Patient characteristics according to median log10 Ang-2 levels			
	Log10 Ang-2 (pg/mL)≤3.26 (n=107)	Log10 Ang-2 (pg/mL)>3.26 (n=160)	p
eGFR (mL/min/1.73 m²)	22.35±10.91	33.34±19.44	0.001
SUPC (g/day)	1026.52±692.93	431.55±348.82	<0.001
CRP (mg/dL)	3.35±1.8	6.07±4.37	0.003
Total cholesterol (mg/dl)	186.02±38.63	210.49±33.27	0.001
Triglyceride (mg/dL)	125.98±33.52	145.53±39.47	0.020
LDL-C (mg/dL)	127.76±23.97	80.5±43.34	<0.001
CAT (mm)	0.62±0.1	0.69±0.21	0.004
bPWV (m/sec)	8.16±1.45	9.96±1.63	<0.001
Data are presented as n (%), mean±SD, Mann Whitney U test			

Table 3. Comparison of patient characteristics according to median log10 VEGF levels			
	Log10 VEGF (pg/mL) (n=102)	Log10 VEGF (pg/mL)>2.3 (n=165)	p
eGFR (mL/min/1.73 m²)	37.65±17.07	20.61±12.4	<0.001
SUPC (g/day)	500.1±747.89	877.77±410.53	<0.001
CRP (mg/dL)	6.12±4.14	3.16±2.05	<0.001
Total cholesterol (mg/dl)	201.52±49.46	197.08±24.89	<0.001
Triglyceride (mg/dL)	136.38±41.05	116.42±34.05	<0.001
LDL-C (mg/dL)	122.01±41.19	92.57±37.32	<0.001
CAT (mm)	0.75±0.07	0.58±0.18	<0.001
bPWV (m/sec)	9.42±2.11	8.75±1.19	<0.001
Data are presented as n (%), mean±SD, Mann Whitney U test			

Markers correlated with angiogenic growth factors

Log10 Ang-2 was significantly positively CAT (r=0.373, p<0.001) (Figure 1), and bPWV (r=0.274, p<0.001) (Figure

2). A significant positive correlation was between log10 VEGF and SUPC (r=0.134, p=0.043) and an inverse correlation between log10 VEGF and CAT (r=-0.555, p<0.001) (Figure 3), (Table 4).

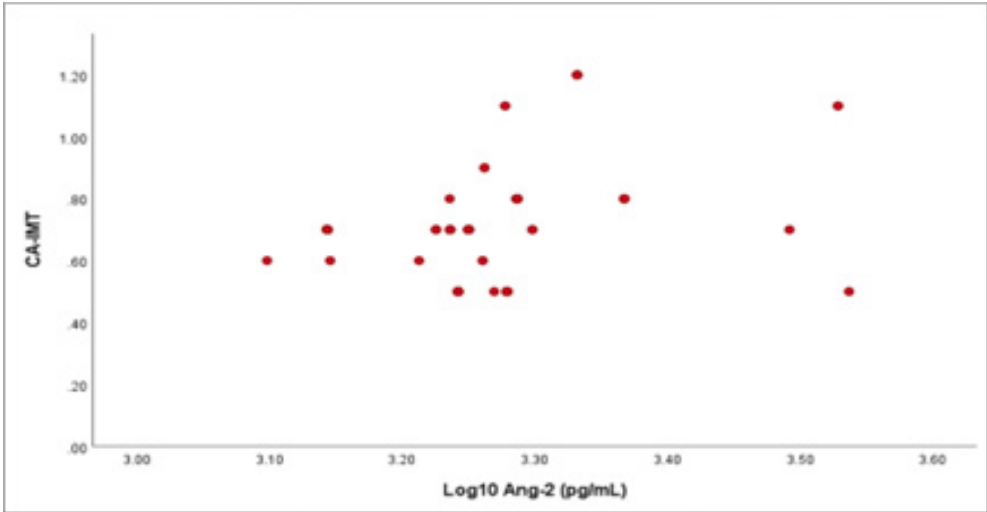


Figure 1. Relationship with log10 Ang-2 and CAT

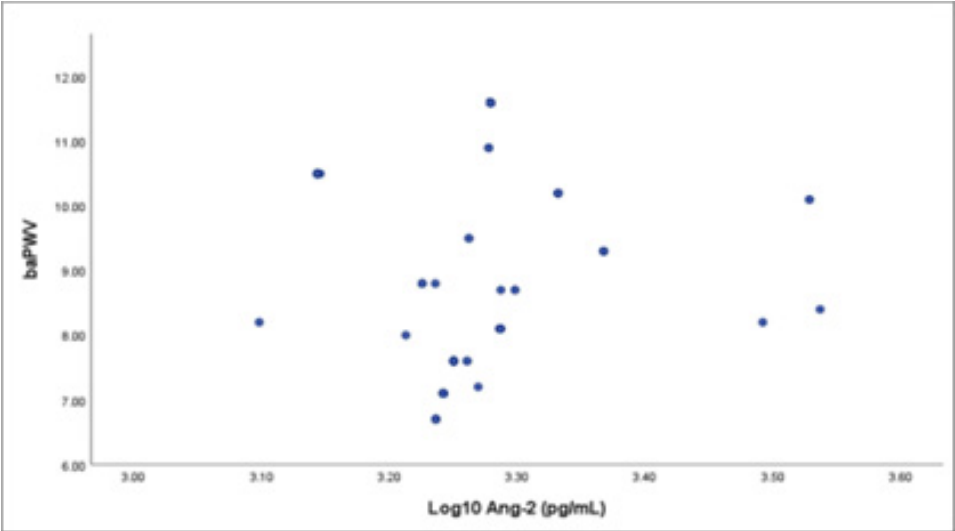


Figure 2. Relationship with log10 Ang-2 and bPWV

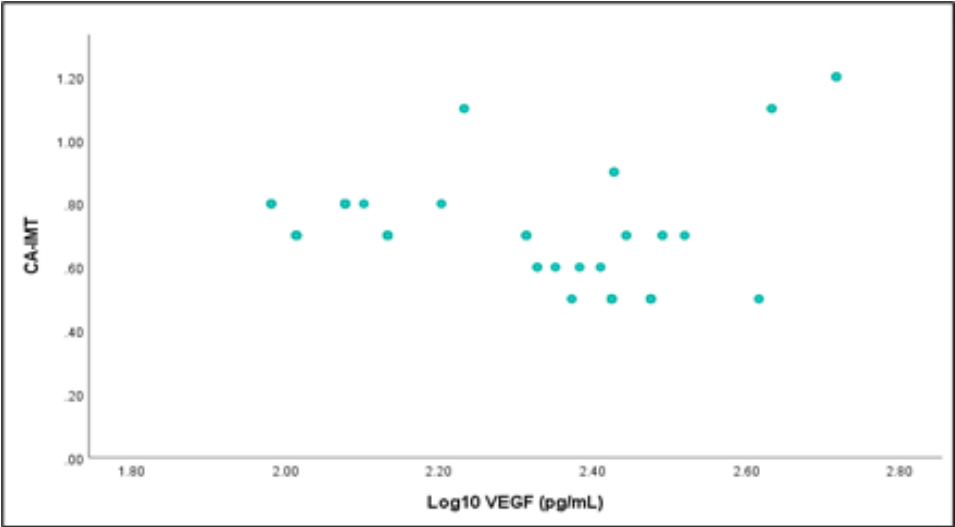


Figure 3. Relationship with log10 VEGF and CAT

Table 4. Factors associated with angiogenic growth factors in correlation analysis				
	Log10 Ang-2 (pg/mL)		Log10 VEGF (pg/mL)	
	r	p	r	p
eGFR (mL/min/1.73 m ²)	0.317	<0.001	-0.586	<0.001
SUPC (g/day)	-0.706	<0.001	0.134	0.043
CRP (mg/dL)	0.038	<0.001	-0.585	<0.001
Total cholesterol (mg/dl)	0.496	<0.001	-0.042	0.528
Triglyceride (mg/dL)	0.202	0.002	-0.238	<0.001
LDL-C (mg/dL)	0.695	<0.001	-0.083	0.212
CAT (mm)	0.373	<0.001	-0.555	<0.001
bPWV (m/sec)	0.274	<0.001	-0.554	<0.001

r: Spearman's rho correlation coefficient

In univariate logistic regression analysis, an increase in log10 Ang-2 (pg/mL) level was detected as the patients' eGFR value increased (OR=1.014, 95%CI 1.006–1.023).

In the model obtained by multivariate logistic regression analysis with the forward stepwise Wald method, a

1.073-fold increase in the log10 Ang-2 (pg/mL) level was detected with the increase in the eGFR value of the patients (OR=1.073, 95%CI 1.031–1.118). An increase in log10 Ang-2 (pg/mL) level was detected as the bPWV value of the patients increased (OR=1.673, 95%CI 1.131–2.476).

With the model created as a result of multivariate analysis, 81.2% of the cases were classified correctly.

In univariate logistic regression analysis, a 0.099-fold decrease in log10 VEGF (pg/mL). As the bPWV value of the patients increased, a 1.031-fold decrease was detected in log10 VEGF (pg/mL) levels (OR=1.031, 95%CI 1.003–1.061).

The increase in the bPWV value of the patients, a 0.386-fold decrease in the log10 VEGF (pg/mL) level was detected (OR=0.386, 95%CI 0.211–0.708) (Table 5). With the model created as a result of multivariate analysis, 96.5% of the cases are classified correctly.

Table 5. Factors associated with angiogenic growth factors in multivariate analysis								
	Univariate (Log10 Ang-2)		Multivariatefwald (Log10 Ang-2)		Univariate (Log10 VEGF)		Multivariatefwald (Log10 VEGF)	
	OR (95% GA)	p	OR (95% GA)	p	OR (95% GA)	p	OR (95% GA)	p
eGFR (mL/min/1.73 m²)	1.014 (1.006-1.023)	0.001	1.073 (1.031-1.118)	0.001	0.99 (0.982-0.998)	0.015		
SUPC (g/day)	0.999 (0.999-1)	<0.001	0.995 (0.993-0.997)	<0.001	1.001 (1-1.001)	<0.001		
CRP (mg/dL)	1.103 (1.052-1.156)	<0.001	1.482 (1.168-1.88)	0.001	1.127 (1.073-1.184)	<0.001	3.674 (2.198-6.141)	<0.001
Total cholesterol (mg/dl)	1.001 (1-1.003)	0.060				1.001 (1-1.002)	0.147	
Triglyceride (mg/dL)	1.002 (1-1.004)	0.047				1.001 (1-1.003)	0.113	
LDL-C (mg/dL)	1.005 (1.002-1.007)	<0.001	0.953 (0.934-0.973)	<0.001	1 (0.997-1.002)	0.689	0.705 (0.626-0.794)	<0.001
CAT (mm)	1.396 (0.95-2.052)	0.089			0.936 (0.639-1.371)	0.733	0 (0-0.005)	0.051
bPWV (m/sec)	1.036 (1.007-1.065)	0.016	1.673 (1.131-2.476)	0.010	1.031 (1.003-1.061)	0.032	0.386 (0.211-0.708)	0.002
OR: Odds ratio, CI: confidence interval, fwald: Forward Wald Method, Accuracy=0.978								

DISCUSSION

We observed that the progression of atherosclerosis and AS was increased in pre-dialysis chronic kidney patients compared to the healthy participants. Ang-2 was significantly correlated with renal function and inversely correlated with proteinuria. Ang-2 was significantly correlated with CRP and hyperlipidemia. A significant correlation was observed between Ang-2 and atherosclerosis and AS, and an inverse correlation was studied between VEGF and AS and atherosclerosis.

Hara et al. demonstrated that an imbalance between angiogenesis-related factors plays a role in the progression of CKD in their experimental study (11). Agyekum et al. reported that increased serum Ang-2 levels were observed in diabetics. In contrast to other studies, they argued that there was no difference in VEGF levels between diabetics and non-diabetics, and this might be attributed to the ethnic diversity in the comparative study including Caucasians and people of African origin (12). Nadar et al. Suggested that Ang-2 and VEGF levels increase in hypertensive CKD patients compared to normotensive individuals in the ASCOT study (13). Futrakul et al. suggested that decreased circulating VEGF levels and increased Ang-2 levels were observed in CKD patients with moderate to advanced renal dysfunction (14). In a study suggested that Ang-2 serum values increased in 61 hemodialysis and 24 peritoneal dialysis patients

compared to the healthy participants. They suggested that the increased Ang-2 levels might be attributed to increased WPB exocytosis in CKD patients related to decreased nitric oxide levels (15). In another study, It was reported that an increase in serum levels was observed due to a decrease in renal excretion of Ang-2 and an increase in its impaired synthesis from the kidneys (16). In our study, serum Ang-2 levels were found to be increased in CKD patients compared to healthy control group. This may be due to excessive WPB exocytosis in CKD patients in the presence of physical damage, endogenous chemicals, high dimethylarginine, as reported by Fiedler et al. (17). There was no difference in VEGF levels between patients and healthy control group. Tsai et al. Suggested that significant relationship between Ang-2 and renal progression in non-dialyzed CKD patients (18).

Lee et al. reported that high circulating levels of Ang-2 are correlated with CV diseases, including congestive heart failure and coronary artery disease (5). Chong et al. suggested that the relationship between elevated serum Ang-2 levels and increased CV events was more pronounced than Angiopoietin-1 (19). Molnar et al. reported that circulating Ang-2 predicted mortality in renal transplant recipients (20). In another study suggested that high level serum Ang-2 values were significantly correlated with major adverse CV events (21). This show us angiogenic growth

factors are associated with increased CV events. Therefore, we examined the correlation between VEGF and Ang-2 and atherosclerosis and AS in patients with pre-dialysis CKD.

Atherosclerotic plaques are present in up to 30% of CKD patients. In a study reported that CAT level was an indicator of the presence of atherosclerosis (22). Mayer et al. suggested that levels of angiogenic growth factors increase with increasing CKD stage and are associated with atherosclerosis (23). David et al. suggested that Ang-2 causes atherosclerosis through vascular microinflammation and endothelial activation in pre-dialysis stage 5 CKD patients (16). In our study, we identified a correlation between increased Ang-2 and atherosclerosis determined by CAT in CKD patients. An inverse correlation was observed between VEGF and atherosclerosis.

In addition to angiogenesis, Ang-2 is an important regulator in many pathophysiological processes including inflammation (24). Ang-2 is correlated with the proinflammatory response via P-selectin, E-selectin, and vascular cell adhesion molecule 1 (16). High Ang-2 serum levels can trigger the inflammatory gene expression and stimulates the endothelium to the inflammatory response. Circulating Ang-2 in patients with CKD was shown to be correlated with markers of systemic microinflammation (5). In our study, a significant correlation was observed between Ang-2 and CRP, which is considered as a marker of inflammation.

Upadhyay et al. reported increased AS development from early-stage renal failure (25). Morimoto et al. observed that AS progress increased as the stage of renal failure progressed in CKD patients (26). In our study, increased AS development was determined in pre-dialysis CKD patients compared to control group.

David et al. reported that increased Ang-2 levels were observed in 43 stage 4 pre-dialysis and 85 stage 5 dialysis (peritoneal dialysis, hemodialysis) patients. It was suggested that this difference could be attributed to the fact that the Ang/Tie axis causes different effects on coronary artery endothelium and peripheral artery endothelium. They reported that Ang-2 can be used as an indicator of mortality in stage 4-5 CKD patients independently of AS. The authors suggested that no relationship exists between Ang-2 and AS, which might be attributed to the fact that other factors play a role in patients undergoing dialysis that are different from those in pre-dialysis patients and that these factors may reduce the effect of Ang-2 on AS (27). Agyekum et al. reported increased AS development in diabetics and that it was correlated with increased Ang-2 (12). In our study, a relationship was found between Ang-2 and AS in pre-dialysis CKD patients. This could be due to the involvement of vascular smooth muscle cell transformation and local inflammation in the pathogenesis of AS as reported by Chang et al. (28).

CONCLUSION

We determined increased atherosclerosis, AS and serum Ang-2 levels were determined in pre-dialysis CKD patients compared to healthy individuals. Those with higher Ang-2

levels had higher renal function tests and less proteinuria. Those with higher VEGF levels had lower renal function tests and more proteinuria. Inflammation and hyperlipidemia were higher in high Ang-2 levels and lower in high VEGF levels. Atherosclerosis development was higher in high Ang-2 levels and lower in high VEGF levels. Ang-2 was significantly correlated with atherosclerosis and AS, whereas VEGF was inversely correlated. High Ang-2 serum grades in pre-dialysis CKD patients could be used as an indicator for development of adverse CV diseases. Further studies are needed to use VEGF and Ang-2 in clinical practice.

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REFERENCES

1. Bots ML, Hofman A, De Jong PT, Grobbee DE. Common carotid intima-media thickness as an indicator of atherosclerosis at other sites of the carotid artery. The Rotterdam Study. *Ann Epidemiol.* 1996;6:147-53.
2. Townsend RR, Wimmer NJ, Chirinos JA, et al. Aortic PWV in chronic kidney disease: a CRIC ancillary study. *Am J Hypertens.* 2010;23:282-9.
3. Yamashina A, Tomiyama H, Takeda K, et al. Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertens Res.* 2002;25:359-64.
4. Matsunaga T, Warltier DC, Tessmer J, et al. Expression of VEGF and angiopoietins-1 and -2 during ischemia-induced coronary angiogenesis. *Am J Physiol Heart Circ Physiol.* 2003;285:H352-8.
5. Lee KW, Lip GY, Blann AD. Plasma angiopoietin-1, angiopoietin-2, angiopoietin receptor tie-2, and vascular endothelial growth factor levels in acute coronary syndromes. *Circulation.* 2004;110:2355-60.
6. Lorbeer R, Baumeister SE, Dörr M, et al. Circulating angiopoietin-2, its soluble receptor Tie-2, and mortality in the general population. *Eur J Heart Fail.* 2013;15:1327-34.
7. Chang FC, Lai TS, Chiang CK, et al. Angiopoietin-2 is associated with albuminuria and microinflammation in chronic kidney disease. *PLoS One.* 2013;8:e54668.
8. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999;130:461-70.
9. Yokoyama H, Shoji T, Kimoto E, et al. Pulse wave velocity in lower-limb arteries among diabetic patients with peripheral arterial disease. *J Atheroscler Thromb.* 2003;10:253-8.
10. Homma S, Hirose N, Ishida H, et al. Carotid plaque and intima-media thickness assessed by b-mode ultrasonography in subjects ranging from young adults to centenarians. *Stroke.* 2001;32:830-5.

11. Hara A, Wada T, Furuichi K, et al. Blockade of VEGF accelerates proteinuria, via decrease in nephrin expression in rat crescentic glomerulonephritis. *Kidney Int.* 2006;69:1986-95. Erratum in: *Kidney Int.* 2006;70:1666.
12. Agyekum JA, Yeboah K. Angiopoietin-2 is associated with aortic stiffness in diabetes patients in Ghana: a case-control study. *Int J Vasc Med.* 2023;2023:3155982.
13. Nadar SK, Blann A, Beevers DG, Lip GY. Abnormal angiopoietins 1&2, angiopoietin receptor Tie-2 and vascular endothelial growth factor levels in hypertension: relationship to target organ damage (a sub-study of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)). *J Intern Med.* 2005;258:336-43.
14. Futrakul N, Butthep P, Futrakul P. Altered vascular homeostasis in chronic kidney disease. *Clin Hemorheol Microcirc.* 2008;38:201-7.
15. David S, Kümpers P, Hellpap J, et al. Angiopoietin 2 and cardiovascular disease in dialysis and kidney transplantation. *Am J Kidney Dis.* 2009;53:770-8.
16. David S, Kümpers P, Lukasz A, et al. Circulating angiopoietin-2 levels increase with progress of chronic kidney disease. *Nephrol Dial Transplant.* 2010;25:2571-6.
17. Fiedler U, Scharpfenecker M, Koidl S, et al. The Tie-2 ligand angiopoietin-2 is stored in and rapidly released upon stimulation from endothelial cell Weibel-Palade bodies. *Blood.* 2004;103:4150-6.
18. Tsai YC, Chiu YW, Tsai JC, et al. Association of angiopoietin-2 with renal outcome in chronic kidney disease. *PLoS One.* 2014;9:e108862.
19. Chong AY, Caine GJ, Freestone B, et al. Plasma angiopoietin-1, angiopoietin-2, and angiopoietin receptor tie-2 levels in congestive heart failure. *J Am Coll Cardiol.* 2004;43:423-8.
20. Molnar MZ, Kümpers P, Kielstein JT, et al. Circulating Angiopoietin-2 levels predict mortality in kidney transplant recipients: a 4-year prospective case-cohort study. *Transpl Int.* 2014;27:541-52.
21. Tsai YC, Lee CS, Chiu YW, et al. Angiopoietin-2 as a prognostic biomarker of major adverse cardiovascular events and all-cause mortality in chronic kidney disease. *PLoS One.* 2015;10:e0135181.
22. Poredos P. Intima-media thickness: indicator of cardiovascular risk and measure of the extent of atherosclerosis. *Vasc Med.* 2004;9:46-54.
23. Mayer G. Capillary rarefaction, hypoxia, VEGF and angiogenesis in chronic renal disease. *Nephrol Dial Transplant.* 2011;26:1132-7.
24. Fiedler U, Reiss Y, Scharpfenecker M, et al. Angiopoietin-2 sensitizes endothelial cells to TNF-alpha and has a crucial role in the induction of inflammation. *Nat Med.* 2006;12:235-9.
25. Upadhyay A, Hwang SJ, Mitchell GF, et al. Arterial stiffness in mild-to-moderate CKD. *J Am Soc Nephrol.* 2009;29:2044-53.
26. Morimoto S, Yurugi T, Aota Y, et al. Prognostic significance of ankle-brachial index, brachial-ankle pulse wave velocity, flow-mediated dilation, and nitroglycerin-mediated dilation in end-stage renal disease. *Am J Nephrol.* 2009;30:55-63.
27. David S, John SG, Jefferies HJ, et al. Angiopoietin-2 levels predict mortality in CKD patients. *Nephrol Dial Transplant.* 2012;27:1867-72.
28. Chang FC, Chiang WC, Tsai MH, et al. Angiopoietin-2-induced arterial stiffness in CKD. *J Am Soc Nephrol.* 2014;25:1198-209.



Bibliometric Analysis of Articles About the Use of MTA in Endodontics

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Abstract

Aim: The aim of this study was to perform a bibliometric and visualized analysis to identify and critically appraise articles on the use of Mineral Trioxide Aggregate (MTA) in endodontics.

Material and Method: A Web of Science (WoS) search was conducted on November 25, 2024, using the keywords 'root canal treatment' AND 'mineral trioxide aggregate' OR 'MTA' under the 'All Fields' option. Only articles of the 'Article' type were included in the study. The WoS category was limited to 'Dentistry Oral Surgery Medicine,' and the WoS index was filtered using 'Science Citation Index Expanded,' resulting in a total of 415 articles published between 1999 and 2024. The data of the studies were downloaded in 'BibTeX' format from WoS and analyzed using Biblioshiny software.

Results: It was found that 1398 authors contributed to the research in this field, 882 keywords were used, and 45 journal sources were referenced. A total of 415 articles were published with an annual growth rate of 14.09%. The majority of the articles were published in the Journal of Endodontics, with the United States being the leading country in terms of publication volume. The most frequently used keywords by authors in this field included 'mineral trioxide aggregate.'

Conclusion: The positive annual growth rate indicates an increasing interest in the field. The Journal of Endodontics holds a leading position in this domain. The United States ranks first in both publication and citation counts. This study expands the existing literature and offers new research topics to researchers, serving as an important reference for future studies related to MTA use in endodontics, especially in the national context.

Keywords: Bibliometrics, root canal treatment, mineral trioxide aggregate

INTRODUCTION

Mineral Trioxide Aggregate (MTA) was first introduced by Torabinejad in the 1990s and was approved by the U.S. Food and Drug Administration (FDA) for use in the United States in 1997 (1). MTA is a bioactive endodontic cement primarily composed of calcium and silica elements. To date, it has found applications in various treatments, including apexification, regenerative endodontics, perforation repair, vertical and horizontal root fractures, partial pulpotomy for Cvek pulpotomy, root canal treatment of deciduous teeth, and repair of resorptive defects (2). It is also used in the prophylactic partial pulpotomy treatment of dens invaginatus, as well as in sealing the affected junction areas of teeth with fusion and endodontic treatment needs (3). MTA, being a biocompatible material, has low

cytotoxicity. When extruded beyond the apex, it causes minimal inflammation. The formation of an odontoblastic layer induces the creation of a dentin bridge. By activating cementoblasts, it promotes tissue regeneration. It also stimulates the release of cytokines from pulpal fibroblasts, which in turn stimulates hard tissue formation and supports the rapid growth of cells. Although MTA is considered an indispensable biomaterial in endodontic procedures, it has certain disadvantages, such as a long setting time and the potential for tooth discoloration (4-6).

In 1969, Alan Pritchard coined the term "bibliometrics", applying arithmetic and applied statistics to the study of journals and books for scientific measurement analysis (7,8). Bibliometric analysis is an evaluation and analysis method that provides data on a publication's field of study, author

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and institution information, country of publication, citation count, inter-publication connections, and collaborations (9). These data networks offer both a visual and a general perspective on the examined topic (10). This evaluation not only highlights the connections between countries, institutions, and publications, but also offers the opportunity to analyze the current developments on a specific topic in a temporal cross-sectional manner (11). Since the discovery of MTA, the number of studies on MTA has increased. A comprehensive review of the current literature suggests that an extensive bibliometric analysis of MTA has not yet been conducted.

The aim of this bibliometric analysis is to identify progress and current trends in MTA from 1999 to November 2024, assessing the importance of publication and citation counts, countries, institutions, authors, journals and keywords. This analysis will provide clinicians and researchers with a comprehensive overview of the research status of MTA in the field of dentistry.

MATERIAL AND METHOD

Data Collection

Since the data used in this research are studies obtained from the Web of Science (WoS) database, it does not require ethics committee approval. On November 25, 2024, a WoS search was conducted using the keywords 'root canal treatment' AND 'mineral trioxide aggregate' OR 'MTA' in the 'All Fields' option.

Inclusion and Exclusion Criteria

Only publications written in English and classified as 'Articles' were included in the study. Conference proceedings, book chapters, review articles, and publications in languages other than English were excluded. Research articles obtained from the WoS search, after applying the aforementioned exclusion criteria and further limiting by the WoS category 'Dentistry Oral Surgery Medicine' and the WoS index 'Science Citation Index Expanded', resulted in 415 articles published between 1999 and 2024.

Data Analysis

The data from the studies that met the inclusion criteria were downloaded from WoS in 'BibTeX' format with 'Full Record' selected and analyzed using the Biblioshiny software, a part of the Bibliometrix package, on the RStudio platform (v 4.3.2; <https://posit.co/products/open-source/rstudio/>), which can be installed for free. The data scanning and analysis were performed by two researchers (Ö.K. and M.G.) to ensure the accuracy and reliability of the analysis. The analysis included parameters such as the number of articles, the number of authors, publishing journals, year of publication, citation number, author-country relationships, and keywords used.

RESULTS

A bibliometric analysis was conducted on articles published between 1999 and 2024 in the WoS database regarding the use of MTA in endodontics. The results show that research in this area was conducted by 1,398 authors, with 882

unique keywords used, and the articles were published in a total of 45 different journal sources. A total of 415 articles were published, with an annual growth rate of 14.09%. The highest peak in annual scientific productivity occurred in 2016, as depicted in Figure 1.

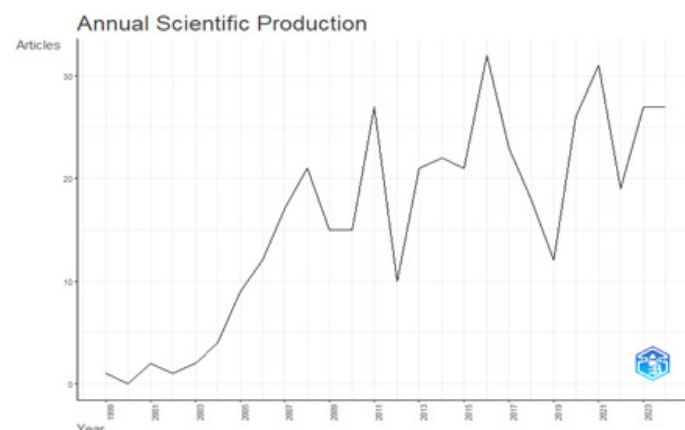


Figure 1. Annual scientific production

The majority of the articles were published in the Journal of Endodontics, followed by the International Endodontic Journal and Dental Traumatology. The ten most frequently used sources are shown in Figure 2.

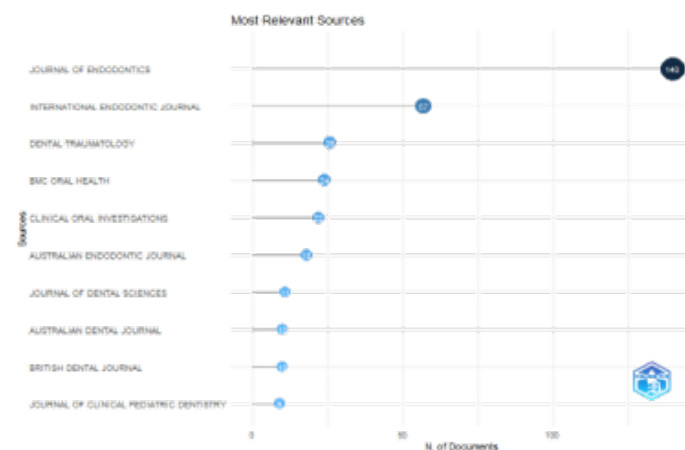


Figure 2. List of journals with the most frequent publications

The author with the most publications in the field of MTA use in endodontics was found to be Simos S., while the most affiliated institution was identified as Hacettepe University in Türkiye, as shown in Figure 3.

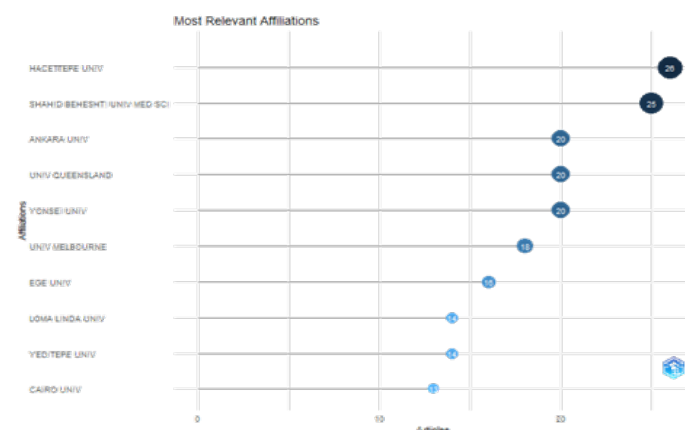


Figure 3. List of most affiliated institutions

The countries with the highest number of publications in this field, in order, are the United States, Brazil, Türkiye, China, and Iran. Our country ranks third globally in terms of the number of publications and citations related to the use of MTA in endodontics (Table 1). Figure 4 shows the collaboration between countries.

Table 1. Number of publications and citations by country		
	Number of publications	Number of citations
USA	191	3,677
Brazil	174	1,506
Türkiye	162	984
China	118	744
Iran	87	718

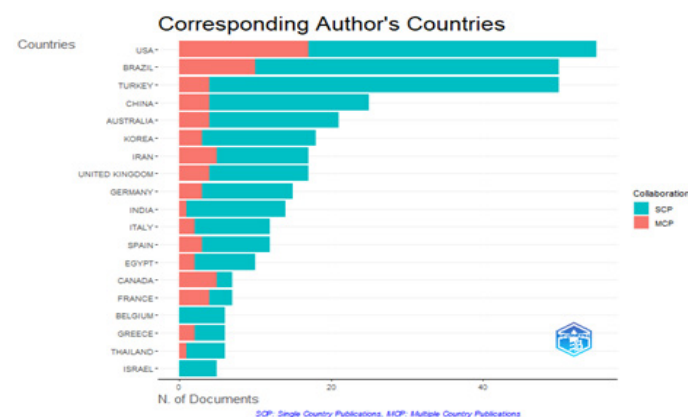


Figure 4. Inter-country collaborations (MCP: multi-country publications, SCP: single-country publications)

When examining the most frequently used keywords by authors in this field, "mineral trioxide aggregate" is followed by "tooth" and "teeth," with "calcium hydroxide" ranking third, as shown in Figure 5.

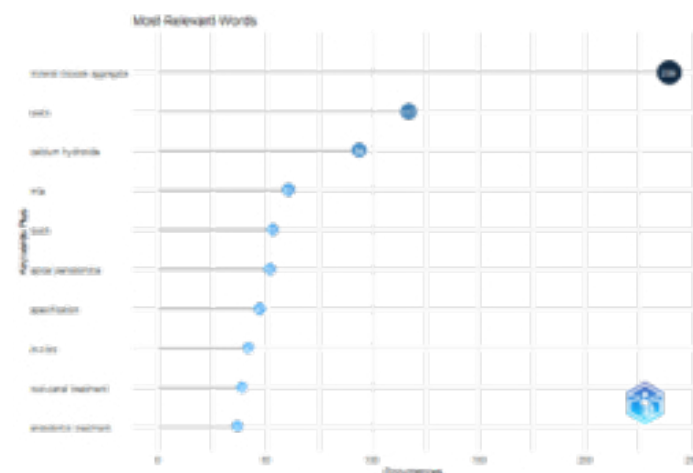


Figure 5. Most frequently used keywords by authors

DISCUSSION

This study presents a bibliometric analysis of research on the use of MTA in endodontics, based on an electronic literature review. The positive annual growth rate observed indicates a steadily increasing interest from researchers in this area.

In this study, the WoS database was chosen as the source for research data. Due to its extensive publication range, which includes articles dating back to 1945, WoS is a widely used database for citation analysis and provides more access to articles than other similar databases in the field of health sciences (12). One study has highlighted that citation counts may vary based on years and journals when searching across different databases, and databases that include theses and conference proceedings may lack sufficient technical precision. A journal's impact factor and indexing are critical parameters that reflect its quality (13). Therefore, only articles published in high-impact SCI-Expanded journals and written in English, the most valid language in the literature, were analyzed in this study.

MTA is a widely used material in endodontic procedures due to its biocompatibility and favourable physico-chemical characteristics (1,14). It has been used in dental treatments for over two decades, and reports suggest that it is playing an increasing role in root canal treatment (6). Research on the use of MTA in endodontics began in 1999, with a significant increase in the number of publications over time. As a result, 1,398 authors have contributed to this area, and 415 articles have been published with an annual growth rate of 14.09%. Furthermore, the increase in systematic analyses of MTA suggests growing interest from researchers in this discipline (15,16).

According to the results of our study, the United States is the country with the most publications and citations in this field. These findings are consistent with other bibliometric analyses, where the United States, with its vast financial resources, funding opportunities, and research facilities, tends to publish higher-impact journals more frequently (17,18). Moreover, the increasing number of scientific publications each year has led to a higher tendency for authors from other countries to cite U.S.-based articles (19,20).

Hacettepe University in Türkiye was identified as the institution with the most publications on MTA (21). Similar results have been reported in previous bibliometric analyses. This increase in publications may be attributed to the launch of the "TÜBİTAK International Scientific Publication Incentive Program" in 1993, which aimed to motivate researchers and improve the quality of publications (22). However, the effects of this incentive program became more evident in the early 2000s. In Iran, Shahid Beheshti University ranked second, receiving the highest citations for its published papers. Although MTA have a significant impact on clinical outcomes, the contributions of other renowned institutions in this field still appear to be lacking.

The total of citations to published articles is clearly related to the year of publication. The full impact of an article is usually recognized at least 20 years after publication (23,24). Accordingly, older research articles tend to be cited more than more recently published ones, regardless of their affect (25). The current study project an increasing citation tendency, consistent with previous studies. The most cited author is Dr. Simos S. from Newcastle University, UK.

Several bibliometric analyses have found that leading journals in a specific discipline account for a significant portion of all publications in that field (26,27). This bibliometric analysis reveals that a few leading journals contribute a large share of publications in the discipline of endodontics (28). The Journal of Endodontics and International Endodontic Journal were the leading journals with the highest publication numbers (140 and 57, respectively) and citation numbers (5083 and 1991, respectively).

Keywords are a crucial part of scientific papers. They not only assist in literature searches but also provide easy access to relevant research articles (29). Therefore, selecting appropriate keywords is essential to facilitate and define relevant searches (30). In this bibliometric analysis, the most frequently used keywords were Mineral Trioxide Aggregate (239 occurrences), Teeth (117 occurrences), Calcium Hydroxide (94 occurrences), and MTA (61 occurrences).

This study provides valuable insights into the distribution and emergence of knowledge related to MTA over time. It is worth noting that MTA research is well represented in the leading journals. These findings can be advantageous for future academics in identifying the best journals, areas of focus, and leading authors in the field has been well represented in the top journals.

CONCLUSION

In this study, a bibliometric analysis was conducted to examine the performance and trends of research articles on the use of MTA in endodontics. The positive annual growth rate indicates an increasing interest in this topic. The Journal of Endodontics is the leading journal in this field. The United States ranks first both in terms of publication volume and citation count. The most frequently used keyword is Mineral Trioxide Aggregate.

This study expands the current literature and provides a significant reference for future studies on the use of MTA in endodontics, particularly within the national context. It offers researchers new avenues for future research topics.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: Since the data used in this research are studies obtained from the Web of Science (WoS) database, it does not require ethics committee approval.

REFERENCES

1. Torabinejad M, Chivian N. Clinical applications of mineral trioxide aggregate. J Endod. 1999;25:197-205.
2. Camilleri J, Pitt Ford TR. Mineral trioxide aggregate: a review of the constituents and biological properties of the material. Int Endod J. 2006;39:747-54.
3. Cervino G, Laino L, D'Amico C, et al. Mineral trioxide aggregate applications in endodontics: a review. Eur J Dent. 2020;14:683-91.
4. Abboud KM, Abu-Seida AM, Hassanien EE, Tawfik HM. Biocompatibility of Neo MTA Plus® versus MTA Angelus as delayed furcation perforation repair materials in a dog model. BMC Oral Health. 2021;21:192.
5. Parirokh M, Torabinejad M, Dummer PMH. Mineral trioxide aggregate and other bioactive endodontic cements: an up date do verview – part I: vital pulp therapy. Int. Endod J. 2018;51:177-205.
6. Tawil PZ, Duggan DJ, Galicia JC. Mineral trioxide aggregate (MTA): its history, composition, and clinical applications. Compend Contin Educ Dent. 2015;36:247-64.
7. Tarazona-Alvarez B, Lucas-Dominguez R, Paredes-Gallardo V, et al. A bibliometric analysis of scientific production in the field of lingual orthodontics. Head Face Med. 2019;15:23. Erratum in: Head Face Med. 2019;15:24.
8. Caballé-Serrano J, Munar-Frau A, Delgado L, et al. Physico chemical characterization of barrier membranes for bone regeneration. J Mech Behav Biomed Mater. 2019;97:13-20.
9. Umeokafor N, Umar T, Evangelinos K. Bibliometric and scientometric analysis-based review of construction safety and health research in developing countries from 1990 to 2021. Safety Science. 2022;156:105897.
10. Liu HN, Yeung AWK, Leung WK. A bibliometric study of the top cited papers related to periodontal regeneration. J Oral Sci. 2021;63:201-8.
11. Mattos FF, Perazzo MF, Vargas-Ferreira F, et al. Top 100 most-cited papers in core dental public health journals: bibliometric analysis. Community Dent Oral Epidemiol. 2021;49:40-6.
12. Şahin TN, Özmen EE. Bibliometric analysis of permanent tooth avulsion articles in the Web of Science database. Türkiye Klinikleri J Dental Sci. 2024;30:588-94.
13. Ahmad P, Alam MK, Jakubovics N, et al. 100 years of the Journal of Dental Research: a bibliometric analysis. J Dent Res. 2019;98:1425-36.
14. Gandolfi MG, Taddei P, Tinti A, Prati C. Apatite forming ability (bioactivity) of ProRoot MTA. IntEndod J. 2010;43:917-29.
15. Hosoya N, Takigawa T, Horie T, et al. A review of the literature on the efficacy of mineral trioxide aggregate in conservative dentistry. Dent Mater J. 2019;38:693-700.
16. Mahgoub N, Alqadasi B, Aldhorae K, et al. Comparison between iRoot BP Plus (EndoSequence Root Repair Material) and mineral trioxide aggregate as pulp-cappingagents: a systematic review. J Int Soc Prev Community Dent. 2019;9:542-52.
17. Fardi A, Kodonas K, Gogos C, Economides N. Topcited articles in endodontic journals. J Endod. 2011;37:1183-90.
18. Ahmad SJS, Ahmed AR, Exadaktylos AK, et al. Systematic review on citation classics in minimally invasive gastrointestinal surgery. J Minim Access Surg. 2018;14:265-72.
19. Feijoo JF, Limeres J, Fernández-Varela M, et al. The 100 most cited articles in dentistry. Clin Oral Investig. 2014;18:699-706.
20. Hui J, Han Z, Geng G, et al. The 100 topcited articles in orthodontics from 1975 to 2011. Angle Orthod. 2012;83:491-9.

21. Tosun C. Bibliometric analysis of educational research in Turkey: 1981-2020 WoS articles. Hacettepe Univ J Educ. 2022;37:942-56.
22. Tonta Y. TÜBİTAK Türkiye adresli uluslararası bilimsel yayınları teşvik (UBYT) programının değerlendirilmesi. Ankara: TÜBİTAK ULAKBİM, 2017;21-22.
23. Arshad AI, Ahmad P, Dummer PMH, et al. Citation classics on dental caries: a systematic review. Eur J Dent. 2020;14:128-43.
24. Campbell FM. National bias: a comparison of citation practices by health professionals. Bull Med Libr Assoc. 1990;78:376-82.
25. Tonta Y. Contribution of Turkish researchers to the world's biomedical literature (1988–1997). Scientometrics. 2000;48:71-84.
26. Baltussen A, Kindler CH. Citation classics in anesthetic journals. Anesth Analg. 2004;98:443-51.
27. Ugolini D, Neri M, Cesario A, et al. Scientific production in cancer rehabilitation grows higher: a bibliometric analysis. Sup Care Cancer. 2012;20:1629-38.
28. Hennessey K, Afshar K, Macneily AE. The top 100 cited articles in urology. Can Urol Ass J. 2009;3:293-302.
29. Heboyen AG, Avetisyan AA, Margaryan MM. Clinical case of a rarely diagnosed tooth root internal resorption. N Armen Med J. 2018;12:87-92.
30. Heboyen AG, Avetisyan AA, Margaryan MM, et al. Rare clinical case of tooth root external resorption as a delayed post-traumatic complication. N Armen Med J. 2018;12:92-7.



The Use of Antibiotic-Impregnated Cement in the Surgical Treatment of Chronic Osteomyelitis in Children

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Abstract

Aim: Information in the literature related to paediatric chronic osteomyelitis is extremely limited as the disease can be prevented to a large extent in developed countries. The aim of this study was to evaluate the clinical and radiological results of patients treated with two-stage surgical debridement and antibiotic-impregnated cement because of chronic osteomyelitis, and to thereby contribute to the literature.

Material and Method: Two-stage surgical debridement and antibiotic-impregnated cement was performed because of chronic osteomyelitis in 8 patients (6 males, 2 females) with a mean age of 6 years (range, 2-11 years) between June 2018 and June 2022. Demographic data were recorded together with the time since the onset of symptoms, anatomic localisation, accompanying fractures, and laboratory parameters. Postoperatively, the patients were followed up in respect of infection recurrence, nephrotoxicity, and fracture healing with direct radiographs and laboratory tests.

Results: The mean follow-up period was 19 months (range, 12-30 months). The localisation of chronic osteomyelitis was determined to be the femur in 2 (25%) patients, the tibia in 3 (37%), the humerus in 2 (25%), and the radius in 1 (12%). In 3 (37%) patients with no history of trauma, the diagnosis made on first evaluation was osteomyelitis-related pathological fracture. No recurrence of infection was observed in any patient during the follow-up period after the final surgery. Full bone union was observed in the cases with accompanying fracture, and of these, deformity was determined in 2 and mild contracture in 1.

Conclusion: Paediatric chronic osteomyelitis can lead to severe problems of bone integrity, especially in cases which have been neglected or when presentation is delayed. Despite predictable complications, the application of antibiotic-impregnated cement may be effective in the context of providing infection eradication and bone union, which are the main treatment aims in this disease.

Keywords: Pediatric, chronic osteomyelitis, surgical treatment, antibiotic-impregnated cement

INTRODUCTION

Chronic osteomyelitis (CO) in the pediatric population is defined as a bone infection characterised by necrotic bone formation, lasting longer than 3 months. This prolonged form of osteomyelitis disease occurs due to neglect of or insufficient treatment of the acute and subacute forms of osteomyelitis caused by pyogenic organisms (1). The incidence data are limited in current literature related to this clinical condition, which is currently seen as a problem in under-developed countries. There are also insufficient

studies in the literature related to the surgical treatment of chronic osteomyelitis which leads to severe complications in children due to the protracted clinical course and frequent recurrences (2,3).

The aim of this study was to present the clinical and radiological results of patients treated in a tertiary-level healthcare centre in East Africa with two-stage surgical debridement and antibiotic-impregnated cement because of chronic osteomyelitis, and to thereby contribute to the literature.

CITATION

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MATERIAL AND METHOD

Patients

Ethics Committee approval was obtained for this descriptive, retrospective study (decision no: 846, dated: 07.09.2023). A total of 12 paediatric patients were applied with surgical debridement and antibiotic-impregnated cement for a diagnosis of chronic osteomyelitis between June 2018 and June 2022 in the Mogadishu Somalia Türkiye Recep Tayyip Erdoğan Training Research Hospital. The study included 8 of these patients (6 males, 2 females) with a mean age of 6 years (range, 2-11 years) who had sufficient clinical and radiological follow-up data. In addition to the demographic information of age and gender, a record was also made of the time since the onset of symptoms, anatomic localisation, accompanying fractures, and laboratory parameters. For the radiological evaluations in the diagnosis of the patients, anteroposterior and lateral radiographs of the involved extremity were obtained, and if necessary, magnetic resonance imaging (MRI) and computed tomography (CT) were performed.

Surgical Procedure

A two-stage surgical procedure was applied to the patients. In the first stage, following fluoroscopic checking of the focus in the involved extremity, a skin incision was made including the fistula tract when necessary, then the bone cortex was reached with debridement of the surrounding soft tissue. Corticotomy windows were opened at a size appropriate to the dimensions of the intramedullar necrotic bone tissue, and sequestered bone tissues were curetted. The debrided soft tissues and bone tissues were sent for pathological and microbiological examinations. After irrigation of the surgical area with physiological saline, antibiotic-impregnated cement was applied according to the width of the defective intramedullar canal and the surrounding soft tissue. To prepare the antibiotic-impregnated cement, 40mg liquid gentamicin was mixed with 40gr polymethylacrylate bone cement (4). In cases where there was no bone defect, an appropriate number of pellets with diameter of approximately half a centimetre obtained from this mixture were placed in the intrameduallar bone region and surrounding soft tissue area where debridement was made. Especially in cases with accompanying fracture and bone defect, the antibiotic-impregnated cement was applied in a single piece to function as a spacer according to the size of the bone defect (Figure 1). Also in these cases with accompanying fracture, fixation was applied with an additional external fixator or intramedullar Kirschner wire, then the first stage was terminated with primary closure of the wound sites. In cases where infection could be discounted with clinical and laboratory parameters during the follow-up, the second stage of surgery was performed by entering through the same incision lines and the antibiotic-impregnated cement pellets were removed

(Figure 2) and in cases with an accompanying fracture, fixation was renewed. In the second stage, grafting was not performed because no serious bone defects were observed. The time interval between the surgical stages was recorded.

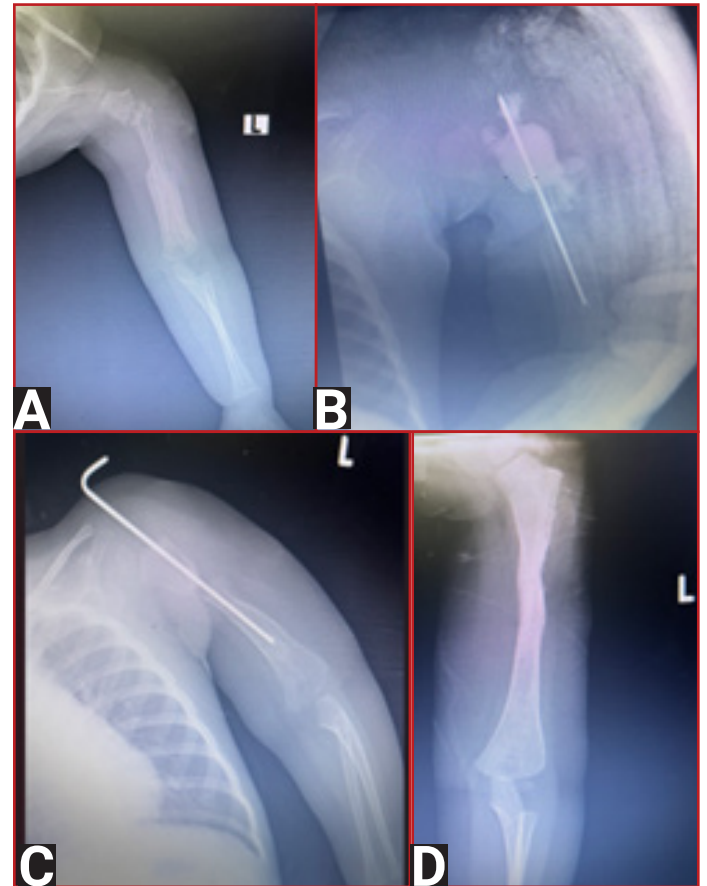


Figure 1. Case 7: (A) first diagnosis of a 2-year-old female with chronic osteomyelitis and accompanying pathological fracture in the left humerus, (B) first-stage application of antibiotic-impregnated cement spacer, (C) second-stage removal of the spacer and re-fixation, (D) direct radiographs at the final follow-up examination



Figure 2. Case 6: A 9-year-old male with chronic osteomyelitis in the right radius shaft and a history of distal radioulnar trauma; direct radiograph before the second stage and removal of the antibiotic-impregnated pellets

Follow-Up

After the surgery, intravenous broad-spectrum antibiotherapy was initiated for all the patients. The patients were followed up in the hospital for intravenous biotherapy of mean 13 days (range 6-25 days) according

to the micro-organism identified in the culture, and after discharge from hospital, oral treatment was continued for mean 4 weeks (range, 2-6 weeks). In the clinical follow-up, the patients were followed up in respect of infection recurrence, nephrotoxicity, and fracture healing with direct radiographs and laboratory tests.

RESULTS

Before presentation at the hospital, none of the patients had undergone surgery or received intravenous antibiotherapy treatment, and the duration of symptoms was mean 5.7 months (range, 4-8 months). In this period, patients had complaints of difficulty in using the

involved extremity, pain, sensitivity, swelling, and fever. Fistula formation was observed in 5 (62%) patients. The localisation of chronic osteomyelitis was determined to be the femur in 2 (25%) patients, the tibia in 3 (37%), the humerus in 2 (25%), and the radius in 1 (12%). According to the anamnesis obtained from the family, there was a history of trauma in 4 (50%) patients. In 1 (10%) of these patients, conservative treatment had been applied after an acute fracture. In 3 (37%) patients with no history of trauma, the diagnosis made on first evaluation was osteomyelitis-related pathological fracture. In all the patients, there were elevated values of white blood cells, C-reactive protein, and sedimentation rate (Table 1).

Table 1. Demographics and clinical characteristic of children at the time of initial examination						
Case	Age (years)	Duration of symptoms (months)	History	Location	Fracture	Laboratory data WBC (10 ³ /μl) / ESR (mm/h) / CRP (mg/l)
1	8	6	Trauma	Femur	No	13.800 / 73 / 89
2	6	8	Trauma	Tibia	Yes	11.560 / 60 / 54
3	2	5	-	Tibia	Yes	15.200 / 26 / 72
4	11	4	-	Humerus	No	8.080 / 72 / 55
5	5	7	-	Femur	Yes	12.750 / 58 / 48
6	9	6	Trauma	Radius	No	14.840 / 83 / 79
7	2	4	-	Humerus	Yes	10.250 / 55 / 74
8	5	6	Trauma	Tibia	No	15.330 / 98 / 92

CRP: C-reactive protein, ESR: eritocyte sedimentation rate, WBC: white blood cell

The data related to the treatment and follow up of the patients are presented in Table 2. The culture results were reported as no production in 3 (37%) patients and the identifiable organisms were Staphylococcus aureus (37%), Methicillin-

resistant Staphylococcus aureus (12%), and Streptococcus pyogenes (12%). No findings of tumour were determined in the pathological examinations of the patients and no nephrotoxicity was observed in any patient during the follow-up.

Table 2: Overview of treatment and follow-up						
Case	Causative organism	Antibiotics	Duration of IV antibiotics (days)	Duration of oral antibiotics (weeks)	Interval between stages (weeks)	Follow-up (months)
1	Staphylococcus aureus	Amoxicillin/clavulanic acid + teicoplanin	6	6	15	12
2	Negative	Teicoplanin + piperacillin/tazobactam	25	6	12	14
3	Negative	Amoxicillin/clavulanic acid + teicoplanin	20	4	20*	20
4	Staphylococcus aureus	Amoxicillin/clavulanic acid + teicoplanin	12	4	9	18
5	Negative	Amoxicillin/clavulanic acid + teicoplanin	8	4	16*	17
6	Staphylococcus aureus	clindamycin + rifampicin	14	2	15	16
7	MRSA	Vancomicin + meropenem	13	3	14*	28
8	Streptococcus pyogenes	Clindamycin + rifampicin	7	6	13	30

IV: intravenous, MRSA: Methicillin-resistant Staphylococcus aureus, *: re-operation between and/or after stages

The time interval between the surgical stages was mean 14 weeks (range, 9-20 weeks). Fixation of an accompanying fracture in the first stage was made with intramedullar

Kirschner wire in 3 patients (Cases 2, 3, and 7) and with an external fixator in 1 (Case 5). In these 4 cases, the cement was removed in the second-stage surgery, and fixation was

re-applied with intramedullar Kirschner wire. Additional debridement was performed once between the surgical stages in 1 patient (Case 2).

The mean follow-up period was 19 months (range, 12-30 months). No recurrence of infection was observed in any patient during the follow-up period after the final surgery. No limb length discrepancy or loss of range of movement in the adjacent joint was observed in any of the patients without accompanying fracture.

Full Bone

union was observed in the cases with accompanying fracture. In the final evaluations of these cases, tibia varum was determined in 1 patient (Case 2) (Figure 3), tibia valgum in 1 patient (Case 3), and mild contracture in the shoulder joint of 1 patient (Case 7).

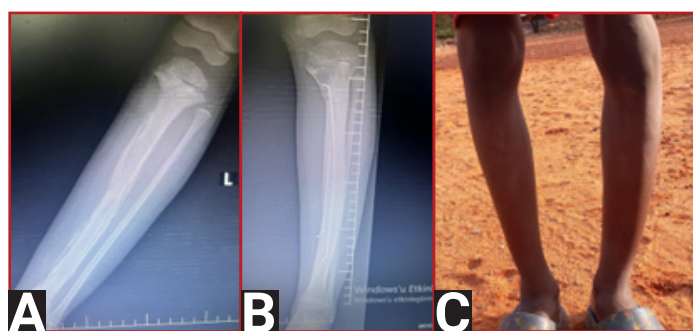


Figure 3. Case 2: A 6-year-old male with chronic osteomyelitis accompanied by fracture of the left tibia; (A) first evaluation, (B) after completion of treatment, (C) varus deformity seen on radiographs

DISCUSSION

There is extremely limited information in the literature related to paediatric chronic osteomyelitis (CO) and the surgical treatments of this. Current medical modalities which allow rapid diagnosis and treatment in early sites of acute inflammation that has developed through hematogenous spread or direct inoculation are extremely effective in preventing osteomyelitis becoming chronic (5). In contrast, the presence of CO continues to be a significant medical problem which must be dealt with in geographic regions with limited access to basic healthcare facilities. Although the incidence of osteomyelitis has been reported to be 80 per 100,000 in low-income countries, there are no data related to the extent of progression to the chronic stage (6). Moreover, in the sources where it is mentioned, CO is usually seen as a multifocal recurrent autoinflammatory entity or as a complication secondary to previous surgery, whereas all the current study cases were all untreated primary prolonged inflammation.

Although CO includes symptoms and findings similar to those of acute pyogenic osteomyelitis, such as fever, pain, swelling, and inability to use the affected extremity, continuation of the clinical condition throughout a 3-6-month period is important in respect of time-dependent definition in the differentiation from subacute

osteomyelitis. The condition forming the basis of time-dependent differentiation is the development of bone necrosis that can be seen without doubt radiologically (7). The cases in the current series had complaints ongoing for a period of up to approximately 6 months and had radiological findings that could be observed on direct radiographs. Moreover, the diagnosis was supported by MRI when necessary and by elevated values of white blood cells, C-reactive protein, and sedimentation rate.

Generally, aggressive debridement of necrotic bone and soft tissue with antibiotherapy form the basic treatment principle in all cases of CO (8). In the adult population, the application of antibiotic-impregnated cement to the surgical area after debridement is one of the frequently applied treatment methods (9). Studies showing the use of this method in paediatric cases are extremely limited in number. Paley (10) and Bar-On (11) reported that infection was safely eradicated using a two-stage surgical method with gentamicin-impregnated cement rods after intramedullar reaming. However, the patients in those series were relatively older children. In the current study patients, the intramedullar canal width was narrow because of their young age, so to avoid creating an iatrogenic fracture, the method of intramedullar reaming was not preferred. In another study, Andreacchio et al. (12) applied tobramycin-impregnated calcium sulphate to 12 skeletally immature CO patients. However, it is not possible to provide spacer support with the properties of these calcium sulphate beads in patients with accompanying fracture and bone defect. Furthermore, to be able to open a serous drainage route from the incision area after the application of bio-absorbable bone substitutes such as calcium sulphate can constitute a risk in respect of wound healing (13,14).

The basic aim of applying local antibiotherapy through cement or bio-absorbable bone substitutes is to avoid the toxicity that can be created by the doses of systemic drugs required to provide the desired level of antibiotic concentration in the surgical field. In contrast to the many studies reporting the safety of local application of antibiotics, there are also data in the literature showing that administration of ≥ 4 gr vancomycin or >1 gr aminoglycoside can create toxicity (15-17). As not all the prepared antibiotic-impregnated cement was used in the current cases, it is not possible to state the net amount of antibiotic applied locally. However, no notable findings of nephrotoxicity were encountered in any patient during the follow-up period.

In the microbiological examinations, no agent could be determined in 3 patients (Cases 2, 3, 5), while the predominance of methicillin-sensitive *Staphylococcus Aureus* observed in the other cases was consistent with the literature (18). Although the duration of intravenous antibiotherapy in the current series was relatively shorter than that of similar studies (11,12) because of the hospital and cost conditions observed, it was considered

appropriate to continue with oral treatment after discharge for patients with a decrease of >50% in C-reactive protein levels after the first stage of surgery and no wound site complications (19). Additional debridement was only performed on one patient (Case 2) as sufficient clinical and laboratory improvement was not seen, and the duration of intravenous antibiotherapy in this patient was relatively longer.

Paediatric osteomyelitis is important both in terms of treatment difficulties and orthopaedic complications. The most important of these are subperiosteal abscess in which the surrounding soft tissue is also affected, avascular necrosis, deformities, limb length discrepancy, and bone defects formed after pathological fractures (20). The current study can be considered of great importance as it included cases with a pathological fracture in the basis of CO, for which the main reason is undoubtedly the delayed presentation of the patients and the lack of or insufficiency of basic treatment facilities during that period.

Although full bone union was able to be obtained in all the patients with no recurrence of infection, all the patients who had varying degrees of deformity and contracture during the follow-up period were seen to be the children with an accompanying primary or pathological fracture.

There were some limitations to this study, primarily that the low number of cases prevented statistical evaluations. The study subject of the two-stage antibiotic-impregnated cement technique was performed based on the preference of the surgeon, and no data were available of an alternative technique for the purposes of comparison. Complications that could be observed as a result of the treatment were included in the follow-up period, and for complications which may be observed in the long-term, a longer follow-up period is needed.

CONCLUSION

Paediatric CO occurring because of insufficient treatment of acute osteomyelitis in cases that have been neglected or that present late can lead to severe problems of bone integrity. Despite predictable complications, the application of antibiotic-impregnated cement may be effective in the context of providing infection eradication and full bone union, which are the main treatment aims in this disease.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: This study was carried out with the scope of the approval and information of Mogadishu Somalia Türkiye Recep Tayyip Erdoğan Training Research Clinical Research Ethics Committee (Date and Decision No: 07.09.2023 and 846).

REFERENCES

1. Dich VQ, Nelson JD, Haltalin KC. Osteomyelitis in infants and children. A review of 163 cases. Am J Dis Child. 1975;129:1273-8.
2. Gornitzky AL, Kim AE, O'Donnell JM, Swarup I. Diagnosis and management of osteomyelitis in children: a critical analysis review. JBJS Rev. 2020;8:e1900202.
3. Howard-Jones AR, Isaacs D. Systematic review of systemic antibiotic treatment for children with chronic and sub-acute pyogenic osteomyelitis. J Paediatr Child Health. 2010;46:736-41.
4. Hsieh PH, Tai CL, Lee PC, Chang YH. Liquid gentamicin and vancomycin in bone cement: a potentially more cost-effective regimen. J Arthroplasty. 2009;24:125-30.
5. Arnold JC, Bradley JS. Osteoarticular infections in children. Infect Dis Clin North Am. 2015;29:557-74.
6. Jaramillo D, Dormans JP, Delgado J, et al. Hematogenous osteomyelitis in infants and children: imaging of a changing disease. Radiology. 2017;283:629-43.
7. Howard JL, Buckley R, McCormack R, et al. Complications following management of displaced intra-articular calcaneal fractures: a prospective randomized trial comparing open reduction internal fixation with nonoperative management. J Orthop Trauma. 2003;17:241-9.
8. Hollmig ST, Copley LA, Browne RH, et al. Deep venous thrombosis associated with osteomyelitis in children. J Bone Joint Surg Am. 2007;89:1517-23.
9. Canavese F, Corradin M, Khan A, et al. Successful treatment of chronic osteomyelitis in children with debridement, antibiotic-laden cement spacer and bone graft substitute. Eur J Orthop Surg Traumatol. 2017;27:221-8.
10. Paley D, Herzenberg JE. Intramedullary infections treated with antibiotic cement rods: preliminary results in nine cases. J Orthop Trauma. 2002;16:723-9.
11. Bar-On E, Weigl DM, Bor N, et al. Chronic osteomyelitis in children: treatment by intramedullary reaming and antibiotic-impregnated cement rods. J Pediatr Orthop. 2010;30:508-13.
12. Andreacchio A, Alberghina F, Paonessa M, et al. Tobramycin-impregnated calcium sulfate pellets for the treatment of chronic osteomyelitis in children and adolescents. J Pediatr Orthop B. 2019;28:189-95.
13. Marais LC, Ferreira N. Bone transport through an induced membrane in the management of tibial bone defects resulting from chronic osteomyelitis. Strategies Trauma Limb Reconstr. 2015;10:27-33.
14. Ferguson JY, Dudareva M, Riley ND, et al. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis: a series of 195 cases. Bone Joint J. 2014;96-B:829-36.
15. Jung J, Schmid NV, Kelm J, et al. Complications after spacer implantation in the treatment of hip joint infections. Int J Med Sci. 2009;6:265-73.
16. Menge TJ, Koethe JR, Jenkins CA, et al. Acute kidney injury after placement of an antibiotic-impregnated cement spacer during revision total knee arthroplasty. J Arthroplasty. 2012;27:1221-7.

17. Luu A, Syed F, Raman G, et al. Two-stage arthroplasty for prosthetic joint infection: a systematic review of acute kidney injury, systemic toxicity and infection control. *J Arthroplasty*. 2013;28:1490-8.
18. Yeo A, Ramachandran M. Acute haematogenous osteomyelitis in children. *BMJ*. 2014;348:g66. Erratum in: *BMJ*. 2014;348:1326.
19. Congedi S, Minotti C, Giaquinto C, et al. Acute infectious osteomyelitis in children: new treatment strategies for an old enemy. *World J Pediatr*. 2020;16:446-55.
20. Saavedra-Lozano J, Mejías A, Ahmad N, et al. Changing trends in acute osteomyelitis in children: impact of methicillin-resistant *Staphylococcus aureus* infections. *J Pediatr Orthop*. 2008;28:569-75.



Perioperative Anesthesia Management and Mortality Predictors in Pediatric Patients Undergoing Craniotomy for Cranial Tumors

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Abstract

Aim: Studies investigating the effects of perioperative anesthesia management on outcomes in patients undergoing craniotomy for pediatric intracranial tumors are limited in the literature. Our aim in this study was to investigate the effects of perioperative anesthesia management on mortality. Secondly, other mortality predictors were investigated.

Material and Method: A total of 165 patients aged <18 years who underwent craniotomy due to intracranial tumor in our hospital were included in the retrospective study between 01/2018 and 09/2024. Patients were divided into two groups according to the intraoperative anesthetic agents used. There were 58 patients in the sevoflurane group and 107 patients in the remifentanyl and propofol groups. The primary endpoint was in-hospital mortality.

Results: In the sevoflurane group, the mean age (2.5 [3] vs. 7 [8], $p<0.001$) and body weight (15 [13] vs. 25 [8], $p<0.001$) of the patients were lower. Sevoflurane was the preferred anesthetic agent instead of remifentanyl in the younger age group. Therefore, the perioperative vital signs of the patients also differed at a statistically significant level ($p<0.05$ for each). In the univariable logistic regression analyses; weight (OR=0.866, 95% CI=0.771-0.971, $p=0.014$), blood transfusion (OR=13.143, 95% CI=1.624-106.333, $p=0.016$), need for inotropes (OR=19.125, 95% CI=2.378-153.835, $p=0.006$), and comorbid diseases (OR=4.681, 95% CI=1.080-20.297, $p=0.039$), were parameters associated with mortality.

Conclusion: Our study found no link between perioperative anesthesia management and in-hospital mortality in pediatric patients who underwent craniotomy for intracranial tumors. However, low body weight, comorbidities, intraoperative blood transfusion, and inotropic support were associated with in-hospital mortality. Our study may help clinicians assess perioperative risk for patients who planned craniotomy.

Keywords: Pediatric anesthesia, craniotomy, mortality

INTRODUCTION

The most frequent solid tumor in children is a brain tumor. The incidence rate of all primary brain and central nervous system cancers in children (ages 0–19) is 4.71 per 100,000 person-years, according to the US Central Brain Tumor Registry (1). Surgery is the mainstay of treatment for children's brain tumors. In addition to removing as many tumors as feasible to increase survival and reduce the tumor burden for other treatment modalities, surgery aims to diagnose the tissue accurately. Relieving symptoms, improving quality of life, increasing lifespan, and occasionally even curing the tumor are all possible advantages of tumor excision.

Compared to adult neurooncological surgical procedures, pediatric neurological tumor operations have a higher risk due to several factors, such as a higher frequency of big tumors, complicated midline tumors, and posterior fossa tumors. Various variables, such as the large heterogeneity in tumor kind and site, the small number of patients, and the absence of widely accepted reporting guidelines, exacerbate this in pediatric neurooncological surgery. Furthermore, other significant variables affect results that are not always connected to the quality of surgery, such as differences in the patient's state at diagnosis, the location and severity of the illness at presentation, and any delays in diagnosis. There aren't many extensive series in the

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pediatric neurosurgical literature that discuss morbidity outcomes in pediatric neurooncological surgery, and they all employ rather different metrics. There is no published systematic study on the subject, nor is there a metric that is widely accepted for measuring surgical morbidity in pediatric neurooncology.

Pediatric patients undergoing craniotomy for tumor resection present unique challenges in perioperative anesthesia management due to their physiological and anatomical differences compared to adults. Hemodynamic instability, often caused by significant blood loss during surgery, is a critical concern, as children have a smaller blood volume and are more susceptible to rapid decompensation. Additionally, positioning during craniotomy, such as the prone or sitting position, can lead to ventilation difficulties, including impaired oxygenation and increased risk of airway obstruction. These factors necessitate meticulous monitoring and tailored anesthetic strategies to ensure hemodynamic stability and adequate ventilation. Anesthesiologists must also consider the potential for postoperative complications, such as cerebral edema or seizures, which further complicate perioperative care (2).

Although 30-day mortality rates in pediatric tumor surgery generally range from 0.5% to 5%, these rates may vary depending on various factors such as the type of surgery, the hospital's level of experience, the patient's age, the size of the tumor, the histopathological type of the tumor, and the health status of the patients (3-6).

There are no sufficient studies investigating perioperative anesthesia management and its relationship with mortality. Our aim in this study was to investigate the effect of perioperative anesthesia management on in-hospital mortality in pediatric patients who underwent craniotomy for intracranial tumors. Our second aim was to investigate other mortality predictors.

MATERIAL AND METHOD

All patients under the age of 18 who underwent craniotomy due to intracranial tumor at Dicle University Faculty of Medicine Hospital between 01.01.2018 and 30.09.2024 were retrospectively included in our study. Only individuals treated with a surgical technique compatible with tumor biopsy or craniotomy were included in the sample, and spinal cord tumors were excluded. All parameters such as age, sex, ASA classification, preoperative laboratory parameters, operation duration, anesthesia duration, perioperative vital signs, perioperative blood transfusion, or inotropic needs of the patients were obtained from hospital records. We defined mortality as in-hospital mortality. Patients with a history of previous surgery (3), those with serious systemic disease (such as advanced heart disease, liver failure, and other systemic diseases) (5), patients with active infection (4), those who received chemotherapy or radiotherapy before surgery (6), and patients with missing data (22) were excluded. The entire population was divided into two groups according to perioperative anesthesia management. There were 58 patients in the sevoflurane group and 107 patients

in the remifentanyl and propofol combination remifentanyl group. The patient flow chart is schematized in Figure 1. Ethical approval was obtained from the ethics committee of Dicle University Faculty of Medicine for the study (295-16/10/2024). Our study was conducted in accordance with the principles of the Helsinki Declaration.

Perioperative Anesthesia Management

All patients were evaluated according to the American Society of Anesthesiologists (ASA) classification. In this retrospective study, patients who had undergone a uniform perioperative anesthetic approach were selected to ensure comparability in assessing mortality factors. Every patient had a preoperative evaluation that comprised a comorbidity assessment, imaging investigation, and neurological examination. All surgeries were carried out under general anesthesia, and the attending anesthesiologist chose between inhalation and intravenous anesthesia induction based on whether the patient had signs of intracranial hypertension. Following endotracheal intubation, general anesthesia was maintained with an intravenous infusion of either sevoflurane (Sevoflurane Liquid 100%, Queensborough) at a concentration <1 MAC or propofol (Propofol, Fresenius Kabi, Sweden) (6–12 mg/kg/h) and remifentanyl (0.02–0.2 μ g/kg/min). Comorbid diseases were defined as cardiovascular, respiratory, hematological, endocrinological, metabolic, neurological, congenital diseases, and others. The goal of both regimens was to minimize intracranial pressure while maintaining stable hemodynamics and cerebral perfusion pressure. Electrocardiography, invasive arterial pressure, end-tidal CO_2 , pulse oximetry, and temperature were all monitored during the procedure. Mannitol or hypertonic saline was used as necessary to control intracranial pressure, and fluids were carefully given to avoid cerebral edema. Transfusions were given and blood loss was tracked. To maintain appropriate hematocrit levels, blood loss was tracked and transfusions were given in accordance with institutional procedures. For postoperative follow-up, every patient was sent to the intensive care unit. Postoperative hemoglobin and hematocrit measurements, length of hospital stays, length of intensive care unit stay, and whether the patients were intubated or extubated were all documented during the postoperative phase.

Statistical Analysis

The data was analyzed using SPSS version 26.0 for Windows (Armonk, NY, USA: IBM Corporation). The normal distribution of continuous data was assessed using histograms and the Kolmogorov-Smirnov and Shapiro-Wilks tests. The mean $\pm$ standard deviation (SD) was used to represent normally distributed continuous data, whereas the median (interquartile range [IQR]) was used to represent non-normally distributed continuous variables. When comparing continuous variables with a normal distribution across two groups, the student t-test was employed; for continuous variables that were not normally distributed, the Mann-Whitney U test was employed. Categorical variables were shown as percentages, and the chi-square test or Fisher-

Freeman-Halton test was used for comparison between groups. Mortality factors were identified using univariable logistic regression analysis. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

A total of 165 patients under the age of 18 were included in the study. There were 58 patients in the sevoflurane group and 107 patients in the remifentanyl group. 49.7% (82) of the population were female.

In the sevoflurane group, the mean age (2.5 [3] vs. 7 [8], $p<0.001$) and body weight (15 [13] vs. 25 [8], $p<0.001$) of the patients were lower. Sevoflurane was the preferred anesthetic agent instead of remifentanyl in the younger age group. Therefore, the preoperative, intraoperative and postoperative vital signs (mean arterial pressure and heart

rate) of the patients also differed at a statistically significant level ($p<0.05$ for each). No significant difference was observed between the groups in terms of gender, duration of anesthesia, duration of intensive care follow-up, tumor size, rate of emergency surgery, perioperative oxygen saturation, blood transfusion, comorbid disease, and in-hospital mortality ($p>0.05$ for each). In the sevoflurane group, preoperative hemoglobin, urea, and creatinine values were lower, and white blood cell and potassium levels were higher ($p<0.05$ for each).

Inotropic agent requirement (4 [6.9] vs. 0 [0], $p=0.006$) was lower, and rate of intubated removal from the operating room to intensive care (31 [53.4] vs. 84 [78.5], $p<0.001$) was higher in the sevoflurane group. While ASA 2-3 rates were higher in the sevoflurane group, ASA 1-4 rates were lower ($p=0.038$) (Table 1).

Table 1. Baseline characteristics of the total population

Parameters	Sevoflurane group (n=58)	Remifentanyl and propofol group (n=107)	Total (n=168)	p-value
Age (month) (IQR)	2.5 (3)	7 (8)	5 (8)	<0.001
Weight (kg) (IQR)	15 (13)	25 (8)	20 (19)	<0.001
Female gender, n (%)	23 (39.7)	59 (55.1)	82 (49.7)	0.058
Preoperative SaO ₂ (%)	97.8±2.4	98.3±1.3	98.1±1.8	0.165
Intraoperative SaO ₂ (%)	99±1.9	99.3±0.8	99.2±1.2	0.234
Postoperative SaO ₂ (%)	98.2±2.3	98.8±1	98.6±1.6	0.056
Preoperative heart rate (bpm)	118.6±19.4	107.2±17.5	111.2±18.9	<0.001
Intraoperative heart rate (bpm)	117.4±20.1	99.6±16.3	105.9±19.6	<0.001
Postoperative heart rate (bpm)	117.9±29.9	100±20.6	106.3±24.9	<0.001
Preoperative MAP (mmHg)	66.8±11.1	76.5±10.1	73.1±11.4	<0.001
Intraoperative MAP (mmHg)	63.5±8.8	72.5±9.5	69.3±10.2	<0.001
Postoperative MAP (mmHg)	62.1±8.5	72±9.1	68.6±10.1	<0.001
Anesthesia time (min)	373±217	542±218	483±231	0.344
ICU hospitalization time (month)(IQR)	14.5 (21)	16 (19)	16 (20)	0.743
Tumor size (mm)	44.2±14.9	41.4±14.7	41.8 (14.7)	0.598
In-hospital mortality, n (%)	2 (3.4)	8 (7.5)	10 (6.1)	0.300
ASA, n (%)				0.038
1	4 (6.9)	25 (23.6)	29 (17.7)	
2	39 (67.2)	50 (50)	92 (56.1)	
3	14 (24.1)	24 (22.6)	38 (23.2)	
4	1 (1.7)	4 (3.8)	5 (3)	
Blood transfusion, n (%)	28 (48.3)	44 (41.1)	72 (43.6)	0.376
Emergency operation, n (%)	19 (32.8)	29 (27.1)	48 (29.1)	0.445
Comorbid disease, n (%)	3 (5.2)	13 (12.1)	16 (9.7)	0.148
Need for inotropes, n (%)	4 (6.9)	0 (0)	4 (2.4)	0.006
Unable to extubate in the operation room, n (%)	31 (53.4)	84 (78.5)	115 (69.7)	<0.001
Preoperative laboratory parameters				
Hemoglobin (mg/dL)	11.4±1.2	12.1±1.5	11.8±1.4	0.003
White blood cell (mg/dl)	12.2±6.2	9.7±4.6	10.7±5.4	0.023
Urea (mg/dl)	20.4±8.9	24.3±9	22.9±9.1	0.015
Creatinine (mg/dl)	0.37±0.13	0.42±0.13	0.39±0.13	0.020
Sodium (mol/L)	135.4±3.9	136.4±2.9	136.1±3.3	0.057
Potassium (mmol/L)	4.4±0.5	4.2±0.5	4.3±0.5	0.011
Clora (mmol/L)	104.6±4.2	104±3.2	104.2±3.6	0.343
Aspartate transaminase (IU/L)-IQR	31 (14)	27 (13)	29 (14)	0.159
Alanine transaminase (IU/L)-IQR	14 (9)	15 (6)	15 (8)	0.703
Lactate (mmol/L)-IQR	3 (3)	1 (2)	1.5 (3)	0.058

MAP: mean arterial pressure, ICU: intensive care unit, ASA: American Society of Anesthesiologists

Logistic Regression Analyses

Univariable logistic regression analyses were performed to determine mortality predictors. The univariable logistic regression analysis included variables that differed statistically between groups and parameters whose relationship with mortality is discussed in the literature. In the univariable logistic regression analysis; weight (OR=0.866, 95% CI=0.771-0.971, p=0.014), blood transfusion (OR=13.143, 95% CI=1.624-106.333, p=0.016), need for inotropes (OR=19.125, 95% CI=2.378-153.835, p=0.006), and comorbid disease (OR=4.681, 95% CI=1.080-20.297,

p=0.039), were parameters associated with mortality.

No statistically significant relationship was observed between age (OR=0.811, 95% CI=0.655-1.004, p=0.054), anesthesia duration (OR=1.002, 95% CI=0.999-1.004, p=0.173), intubated removal from operating room (OR=1.794, 95% CI=0.367-8.768, p=0.470), ICU hospitalization time (OR=0.980, 95% CI=0.933-1.029, p=0.412), tumor size (OR=1.044, 95% CI=0.968-1.125, p=0.265), GFAP positivity (OR=3.164, 95% CI=0.906-12.062, p=0.070), vimentin positivity (OR=3.160, 95% CI=0.835-11.968, p=0.090) and mortality (Table 2).

Table 2. Logistic regression analysis for mortality predictors		
Parameters	OR (95% CI)	p-value
Age	0.811 (0.655-1.004)	0.054
Weight	0.866 (0.771-0.972)	0.014
Anesthesia time	1.002 (0.999-1.004)	0.173
Unable to extubate in the operating room	1.794 (0.367-8.768)	0.470
ICU hospitalization time	0.980 (0.933-1.029)	0.412
Tumor size	1.044 (0.968-1.125)	0.265
Blood transfusion	13.143 (1.624-106.333)	0.016
Need for inotropes	19.125 (2.378-153.835)	0.006
GFAP positivity	3.164 (0.906-12.062)	0.070
Vimentin positivity	3.160 (0.835-11.968)	0.090
Comorbid disease	4.681 (1.080-20.297)	0.039

DISCUSSION

In this study, we investigated the effect of perioperative anesthesia management on mortality. In addition, we investigated other predictors of mortality in our patient group. In our study, the number of patients who died during postoperative in-hospital follow-up was 10 and therefore multivariable logistic regression analyses could not be performed. According to the results of our study, we think that perioperative anesthesia management has no significant effect on mortality. According to our study, the predictors of mortality were; comorbid disease, low weight, blood transfusion, and need for inotropes.

Hemodynamic stability and cerebral perfusion optimization are the main goals of perioperative anesthesia management for patients undergoing pediatric intracranial tumor surgery. Children are more vulnerable to hypoxia and hypotension because of their elevated cerebral metabolic oxygen rate (6). While muscle relaxants and analgesics are chosen depending on the patients' pharmacological reaction, inhalational anesthetic, and balanced anesthesia procedures are typically recommended (7,8). Positioning and blood loss reduction strategies are not widely used. Although anesthetic management does not directly impact survival rates, our study revealed that it had no obvious effect on mortality, highlighting the significance of management in attaining the best possible surgical results.

Previous studies have shown significant relationships between young age groups and short-term mortality.

Children less than one year at diagnosis had a considerably greater short-term death rate (OR 6.7) than children between the ages of one and twenty-one, according to a study by Hankinson TC et al (3). A study by O'Kane et al. found a similar outcome, with a statistically significant 30-day mortality rate of 7.1% for children under the age of two and 2.0% for those between the ages of two and fourteen (2). In our study, mortality was investigated without separating patients according to age group, and no significant relationship was found between age and in-hospital mortality. We attribute this to the small size of our total patient population. The total number of patients who died in our population was only ten. We think that this rate may change with a higher number of patients who develop mortality.

Although there was no significant relationship between age and mortality in our study, we found that weight, which showed a significant positive correlation with age, was associated with mortality. According to a study by Liu et al., the risk of postoperative mortality and BMI have a nonlinear association (9). They demonstrated that in male patients (>18 years old) having a craniotomy for brain tumors, a low preoperative weight (BMI<18.5 kg/m²) increased the chance of postoperative mortality. Many previous studies have discussed the obesity paradox in cancer patients. In these studies, patients were classified according to BMI and it was shown that underweight and overweight patients were at risk for mortality (10-12). In our study, BMI was not used, but the body weight of the patients was taken into account. In the pediatric age group,

percentile curves are used instead of BMI. In our study, we associate the relationship between body weight and mortality with lower body weight in young children.

The effect of blood transfusion on mortality in pediatric intracranial tumor surgeries is a critical area of research, as transfusions can influence postoperative outcomes significantly. Studies indicate that while blood transfusions are often necessary, they are associated with increased risks of complications, including infections (13) and longer hospital stays (14), which can ultimately affect mortality rates. In our study, we determined the relationship between blood transfusion and overall mortality, although it was not an independent predictor.

Because the use of inotropic agents can vary greatly depending on the patient's health and the surgical context, the impact of these drugs on mortality in pediatric brain tumor procedures is complex and has not been adequately studied. Although inotropes are frequently used to treat hemodynamic instability, some studies have associated them with higher mortality rates (15-17). Although a relationship was observed between inotropic need and mortality in our study, we believe that this result should be investigated further, as only four patients in total required inotropic support.

Numerous studies demonstrating the influence of comorbid diseases on surgical outcomes have demonstrated the substantial correlation between comorbidity and mortality in pediatric patients having tumor surgery (18-20). Comorbidities can raise the risk of death and worsen treatment-related side effects. Similar to previous studies, comorbid diseases were associated with mortality in our study too.

Limitations

As in many studies, our study has many limitations. The most notable limitation is the small number of patients, which prevents us from performing detailed statistical analysis. Since our study was designed retrospectively, bias cannot be eliminated. We do not have data on the cause of death in patients who died; all-cause deaths were investigated in the study. In addition, we did not have data on factors that could affect mortality, such as the surgical technique used and operator experience. These deficiencies may have affected the results of the study. Although the mortality rates in our study are similar to previous studies, they are not generalizable because they included patients who underwent surgery at a single center. Univariable logistic regression was used, but multivariable analysis was not performed. This is an important limitation of our larger study because univariable analysis does not account for interdependencies among variables. We do not have data on the patient's preoperative chemotherapy or radiotherapy treatments. Preoperative neoadjuvant treatments may have affected the results because they reduce the tumor diameter and decrease blood flow. Another limitation of our study is the lack of data on tumor histology types. Tumor histology

types may potentially alter the results regarding total mortality. In our study, we do not have data on the extent of surgical resection, which would be expected to alter outcomes related to mortality and hospitalization. This may have affected the results of the study.

CONCLUSION

In our study, we found that perioperative anesthesia management was not associated with in-hospital mortality in patients undergoing craniotomy for pediatric intracranial tumors. In addition, we found that factors such as low body weight, comorbid diseases, need for intraoperative blood transfusion, and need for intraoperative inotropic support were associated with in-hospital mortality. Our study may guide clinicians in perioperative risk assessment in patients scheduled for craniotomy due to intracranial tumors.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: Ethical approval was obtained from the ethics committee of Dicle University Faculty of Medicine for the study (295-16/10/2024). Our study was conducted in accordance with the principles of the Helsinki Declaration.

REFERENCES

1. Thakkar JP, McCarthy BJ, Villano JL. Age-specific cancer incidence rates increase through the oldest age groups. *Am J Med Sci.* 2014;348:65-70.
2. Sümpelmann R, Becke K, Crean P. Pediatric anesthesia practice in Europe: a survey of the European Society for Paediatric Anaesthesiology. *Pediatric Anesthesia.* 2017;27:811-9.
3. O'Kane R, Mathew R, Kenny T, et al. United Kingdom 30-day mortality rates after surgery for pediatric central nervous system tumors. *J Neurosurg Pediatr.* 2013;12:227-34.
4. Hankinson TC, Dudley RW, Torok MR, et al. Short-term mortality following surgical procedures for the diagnosis of pediatric brain tumors: outcome analysis in 5533 children from SEER, 2004-2011. *J Neurosurg Pediatr.* 2016;17:289-97.
5. Sletvold TP, Boland S, Schipmann S, Mahesparan R. Quality indicators for evaluating the 30-day postoperative outcome in pediatric brain tumor surgery: a 10-year single-center study and systematic review of the literature. *J Neurosurg Pediatr.* 2023;31:109-23.
6. Sherrod BA, Rocque BG. Morbidity associated with 30-day surgical site infection following nonshunt pediatric neurosurgery. *J Neurosurg Pediatr.* 2017;19:421-7.
7. Palaniswamy SR, Beniwal M, Venkataramaiah S, Srinivas D. Perioperative management of pediatric giant supratentorial tumors: challenges and management strategies. *J Pediatr Neurosci.* 2019;14:211-7.
8. Rath GP, Dash HH. Anaesthesia for neurosurgical procedures in paediatric patients. *Indian J Anaesth.* 2012;56:502-10.

9. Liu Y, Hu H, Han Y, et al. Body mass index has a nonlinear association with postoperative 30-day mortality in patients undergoing craniotomy for tumors in men: an analysis of data from the ACS NSQIP database. *Front Endocrinol (Lausanne)*. 2022;13:868968.
10. He J, Jia L, Zhang Y, et al. Obesity paradox for postoperative mortality in young Chinese patients undergoing craniotomy for brain tumor resection. *J Neurosurg Anesthesiol*. 2023. doi: 10.1097/ANA.0000000000000932.
11. Tsang NM, Pai PC, Chuang CC, et al. Overweight and obesity predict better overall survival rates in cancer patients with distant metastases. *Cancer Med*. 2016;5:665-75.
12. Reichle K, Peter RS, Concin H, Nagel G. Associations of pre-diagnostic body mass index with overall and cancer-specific mortality in a large Austrian cohort. *Cancer Causes Control*. 2015;26:1643-52.
13. Acker SN, Nolan MM, Prendergast C, et al. Blood transfusion is associated with adverse outcomes in pediatric solid tumor oncology patients following tumor resection. *J Pediatr Hematol Oncol*. 2023;45:137-42.
14. Wang T, Luo L, Huang H, et al. Perioperative blood transfusion is associated with worse clinical outcomes in resected lung cancer. *Ann Thorac Surg*. 2014;97:1827-37.
15. Davidson J, Tong S, Hancock H, et al. Prospective validation of the vasoactive-inotropic score and correlation to short-term outcomes in neonates and infants after cardiothoracic surgery. *Intensive Care Med*. 2012;38:1184-90.
16. Favia I, Vitale V, Ricci Z. The vasoactive-inotropic score and levosimendan: time for LVIS?. *J Cardiothorac Vasc Anesth*. 2013;27:e15-6.
17. Gaies MG, Jeffries HE, Niebler RA, et al. Vasoactive-inotropic score is associated with outcome after infant cardiac surgery: an analysis from the Pediatric Cardiac Critical Care Consortium and Virtual PICU System Registries. *Pediatr Crit Care Med*. 2014;15:529-37.
18. Torres-Espíndola LM, Demetrio-Ríos J, Carmona-Aparicio L, et al. Comorbidity Index as a predictor of mortality in pediatric patients with solid tumors. *Front Pediatr*. 2019;7:48.
19. STARSurg Collaborative; EuroSurg Collaborative. Association between multimorbidity and postoperative mortality in patients undergoing major surgery: a prospective study in 29 countries across Europe. *Anaesthesia*. 2024;79:945-56.
20. Hernández-Regino LM, De Jesús Castillejos-López M, Aquino-Gálvez A, et al. Clinical characteristics and mortality predictors of patients with cancer hospitalized by COVID-19 in a pediatric third-level referral center. *Front Pediatr*. 2022;10:960334.



Artificial Intelligence as a Partner in Ankylosing Spondylitis Care: Evaluating ChatGPT's Role and Performance

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Abstract

Aim: Artificial Intelligence may have significant potential to assist clinicians in decision-making and diagnosis, especially in units dependent on up-to-date guidelines such as rheumatology. This study aims to evaluate the effectiveness of ChatGPT in providing clinicians with evidence-based information about ankylosing spondylitis (AS).

Material and Method: Frequently asked questions (FAQs) about AS were developed by reviewing commonly accessed patient-oriented websites, social media platforms, and official hospital pages. Questions were designed based on scientific guidelines, particularly the American College of Rheumatology (ACR) and Assessment of SpondyloArthritis international Society (ASAS)-European League Against Rheumatism (EULAR) axial spondyloarthritis guidelines. ChatGPT's responses were evaluated on a 1-to-4 scale. Each question was posed twice to assess reproducibility, with consistency defined by identical scores across both attempts.

Results: ChatGPT demonstrated an overall accuracy of 81.9% in its responses to 72 FAQs. The highest accuracy (91.7%) was observed in responses related to the prevention of AS. Of the 36 questions based on ACR and ASAS-EULAR guidelines, ChatGPT provided accurate answers for 22 (61.1%), with three responses receiving the lowest grade (4). Reproducibility of ChatGPT's responses was 88.8% across all FAQs and 83.3% for guideline-specific questions.

Conclusion: This study highlights the potential of ChatGPT as a supportive tool for patient education and clinician reference, particularly for general FAQs. However, accuracy for questions derived from ACR and ASAS-EULAR guidelines was lower (61.1%), emphasizing the need for clinician oversight.

Keywords: Artificial intelligence, ankylosing spondylitis, ChatGPT, guideline

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic, systemic, inflammatory rheumatic complication that impacts the axial spine and sacroiliac joints (1). If left untreated, new bone formation in the axial skeleton and entheses can occur, leading to the fusion of the spine (2). AS patients have many challenges due to the inherent nature of the illness and its many physical and mental complications leading to a reduced quality of life and a significant financial burden for patients, their families and the communities.

The high rate of comorbidities in AS may stem from overlapping risk factors, ongoing systemic inflammation,

or particular treatments, such as long-term use of non-steroidal anti-inflammatory drugs or corticosteroids. The co-occurrence of other medical conditions in AS patients is related to negative impacts such as reduced quality of life, higher healthcare expenses, increased mortality rates, and increased disease activity (3,4). AS typically manifests in the third decade of life or earlier, with rare presentations occurring after the age of 45. The global prevalence of AS is estimated to range from 0.1% to 1.4% (5).

In recent years, online sources have played a crucial role in enhancing public health awareness, with many patients turning to platforms like YouTube, Twitter, Instagram, and tools like generative pre-trained transformers (such as

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ChatGPT) for information on health issues (6). The rapid advancement of artificial intelligence (AI) models brings substantial ethical challenges, especially concerning the risks of misuse. Key concerns include vulnerabilities, limited transparency in AI algorithms, the risk of inaccuracies or fabricated information in AI-generated content, and the need for high levels of security and precision—particularly in sensitive fields like medical diagnostics, where outcomes can directly impact lives (7).

ChatGPT, an AI application developed by OpenAI, is capable of understanding and generating natural language. The potential applications of ChatGPT have been extensively explored, with recent research focusing on its effectiveness and reliability in healthcare settings (8). Previous studies have examined the accuracy of ChatGPT's responses to various diseases (9-11). However, late diagnosis and treatment of AS, which is common in the society especially in young adult ages when productivity is high, increases the healthcare burden. However, it is known that it negatively affects returns to work.

For this reason, it is important to increase the knowledge of both the public and healthcare professionals about this disease in today's world where computer and artificial intelligence systems are used extensively. No artificial intelligence-based information research on AS has been found in the literature. It is important to note that ChatGPT includes a disclaimer emphasizing that its outputs do not replace medical advice. This study appraises the reliability, accuracy, and reproducibility of ChatGPT's responses regarding AS, thereby providing insights into its potential role in augmenting patient and clinician education.

MATERIAL AND METHOD

AS-related frequently asked questions (FAQs) were developed by reviewing websites commonly accessed by patients, along with official hospital sites. Preference was given to sources linked to credible and authoritative organizations, such as federal health agencies, prominent medical institutions, academic research bodies, and well-known AS advocacy groups. Additionally, inquiries posed by patients on social media platforms such as Instagram, YouTube and Facebook along with their accompanying comments, were leveraged in the development of the question list.

These scientifically based questions were crafted to align with the American College of Rheumatology (ACR) and Assessment of SpondyloArthritis international Society (ASAS)-European League Against Rheumatism (EULAR) guidelines for axial spondyloarthritis, and all questions were compiled into a separate questionnaire. Questions that were unrealistic, repetitive, contained advertisements, had grammatical errors, or required personal responses were excluded from the study. The FAQs were classified into five distinct categories: 11 questions addressed general information, 10 focused on risk factors, 13 covered non-pharmacological treatments, 26 pertained to pharmacological treatments, and 12 explored prevention strategies. The full list of the 72 questions used in the study, categorized by topic, is presented in Table 1. A total of 36 questions, based on the ACR and ASAS-EULAR axial spondyloarthritis guidelines, were included. The specific ACR and ASAS-EULAR guideline recommendations used for response evaluation are summarized in Table 2.

Table 1. Frequently asked questions about ankylosing spondylitis
General
1) What is ankylosing spondylitis, and how does it affect the body?
2) Who is at risk for the development of ankylosing spondylitis and in which age group is it more common?
3) What are the signs and symptoms of ankylosing spondylitis, and what signs and symptoms does it cause if it is left untreated?
4) What are the early warning signs of ankylosing spondylitis and inflammatory back pain?
5) How is ankylosing spondylitis diagnosed, which auxiliary tests are mainly used in the diagnosis?
6) Is it inherited through genetics, is there a racial origin?
7) Which parts of the body are most commonly affected by the disease and how it can affect life?
8) What medical treatments and medications are available for the management of ankylosing spondylitis and the slowing of disease progression?
9) How important is early detection and treatment in preventing the progression of ankylosing spondylitis?
10) What kind of exercise program and physical activity should be used in people with ankylosing spondylitis to improve the symptoms associated with the disease?
11) Which vitamin and mineral supplements are preferred to help manage ankylosing spondylitis?
Risk factors
1) Is age a significant risk factor for ankylosing spondylitis? Is there a particular age range for the onset of the disease?
2) What is the role of gender in the development of ankylosing spondylitis, and how do men and women differ in their experience of the condition?
3) Is there an increased risk of developing ankylosing spondylitis due to genetics, autoimmune disease, or family history?
4) What is the impact of race and ethnicity on the risk of developing ankylosing spondylitis? Is there a correlation between living in a specific geographical area and the likelihood of ankylosing spondylitis?
5) Which lifestyle factors, including smoking and excessive alcohol consumption, contribute to the risk of ankylosing spondylitis?
6) What is the link between the gut microbiome and the development of ankylosing spondylitis, and how is this linked to gastrointestinal health?
7) Is there a correlation between stress-related hormonal changes and the development of ankylosing spondylitis?
8) What is the impact of pregnancy and postnatal hormonal changes on the development of ankylosing spondylitis, and how do hormonal imbalances affect the risk?
9) What is the relationship between immune system dysfunctions and the development of ankylosing spondylitis?
10) Is there a specific test that identifies a risk factor for the disease?

Table 1. Frequently asked questions about ankylosing spondylitis**Non-pharmacological treatments**

- 1) What non-pharmacological approaches are available for managing ankylosing spondylitis, and how do they compare in effectiveness to medications?
- 2) What is the role of physical activity in the management of ankylosing spondylitis and what types of exercise are recommended?
- 3) Are there any specific lifestyle changes or non-pharmacological interventions that ankylosing spondylitis patients can adopt to reduce their disease activity?
- 4) Can stress management techniques, such as yoga and tai chi, positively impact disease progression?
- 5) What is the significance of abstaining from smoking and limiting alcohol consumption in relation to the progression of ankylosing spondylitis disease activity?
- 6) How can the risk of disease activity in ankylosing spondylitis be reduced by maintaining a healthy body weight?
- 7) How does the implementation of physical therapy programs in ankylosing spondylitis affect disease activity, and why?
- 8) What are the benefits of providing posture and posture training to patients in relation to the disease?
- 9) Are there any benefits of heat applications (hot towels, hot shower) or cold applications (ice packs) on pain and inflammation?
- 10) Does swimming and aquatic exercise have any benefits in disease management?

Pharmacological treatments

- 1) What is the first line of treatment for ankylosing spondylitis?
- 2) What are non-steroidal anti-inflammatory drugs, and how do they work to treat ankylosing spondylitis? What are some common non-steroidal anti-inflammatory drugs, medications used for ankylosing spondylitis treatment?
- 3) How are non-steroidal anti-inflammatory drugs taken, and what are the dosing schedules?
- 4) What are the potential side effects and risks associated with non-steroidal anti-inflammatory drugs use?
- 5) How long is non-steroidal anti-inflammatory drugs treatment typically recommended, and is there a maximum duration of use?
- 6) What is the role of corticosteroids in the treatment of ankylosing spondylitis? Is their use a long-term treatment?
- 7) What are the potential side effects and risks associated with corticosteroids drugs use?
- 8) What are tumor necrosis factor inhibitors drugs and how do they help to treat ankylosing spondylitis?
- 9) Is the anti-TNF drug group composed of corticosteroid drugs?
- 10) What are the biological drugs used in ankylosing spondylitis?
- 11) What drugs are IL-17 inhibitors? What are their mechanisms of action?
- 12) How are anti-TNF drugs taken, and what are the dosing schedules?
- 13) How are IL-17 inhibitors drugs taken, and what are the dosing schedules?
- 14) When are anti-TNF drugs and IL-17 inhibitors started as a treatment option?
- 15) What are the potential benefits and risks associated with anti-TNF drugs treatment?
- 16) What are the potential benefits and risks associated with IL-17 inhibitors drugs treatment?
- 17) How long is anti-TNF drugs treatment typically recommended, and is there a maximum duration of use?
- 18) How long is IL-17 inhibitors drugs treatment typically recommended, and is there a maximum duration of use?
- 19) What are conventional synthetic antirheumatic drugs and how does it work to treat ankylosing spondylitis?
- 20) How are conventional synthetic antirheumatic drugs taken, and what are the dosing schedules?
- 21) What are the potential side effects and risks associated with DMARDs use?
- 22) How long is conventional synthetic antirheumatic drugs treatment typically recommended, and is there a maximum duration of use?
- 23) What is methotrexate and what group of medicines does it belong to? How is it used?
- 24) Is anti-TNF therapies an immunosuppressant?
- 25) What is the meaning of primary non-responsiveness to an anti-TNF? Which drug group should be used as an alternative?
- 26) What is the meaning of secondary non-responsiveness to an anti-TNF? Which drug group should be considered for switching?

Prevention

- 1) Is there any way to prevent ankylosing spondylitis? What are the steps that can be taken to help control the disease?
- 2) Is it possible that regular physical activity may help alleviate symptoms associated with ankylosing spondylitis?
- 3) What lifestyle changes could be considered by patients with ankylosing spondylitis to potentially reduce their disease activity?
- 4) Is stress an aggravating factor in ankylosing spondylitis? What are the methods for dealing with stress?
- 5) What effect does smoking cessation have on controlling the symptoms or reducing the effects of the disease?
- 6) Which changes in daily life can help us to reduce and control the symptoms of the disease?
- 7) In which way does the implementation of physiotherapy programs in ankylosing spondylitis affect disease activity?
- 8) What is the impact of the control of the posture on the disease?
- 9) Is it important for people with ankylosing spondylitis symptoms to take the medication prescribed by their doctor regularly? Can consistently use of medication effectively manage symptoms and impede disease progression?
- 10) What are the positive effects of swimming and water-based exercise programs on the symptoms of the disease?
- 11) Do psychosocial interventions have a positive impact on disease outcomes?
- 12) Can disease activity be managed through a balanced and healthy diet? What is the impact of gluten or dairy products on disease symptoms?
- 13) Can regular education and counselling on ankylosing spondylitis increase treatment adherence?

Table 2. Guideline recommendations

1. Which is the first treatment option for adults with active ankylosing spondylitis?
2. Which non-steroidal anti-inflammatory drugs are preferred for treatment?
3. What is the recommended treatment option for adults with active ankylosing spondylitis that persists despite treatment with NSAIDs?
4. What is the preferred drug for patients with severe peripheral arthritis or in the absence of TNFi?
5. Is there a particular TNFi that is preferred?
6. Is treatment with TNFi conditionally recommended for adults with active AS despite treatment with NSAIDs, compared to treatment with secukinumab or ixekizumab?
7. What treatment is conditionally recommended for adults with active AS despite NSAID therapy and contraindications to TNFi?
8. For adults with active AS who don't respond to the first TNFi used, is switching to a different TNFi or treating with secukinumab or ixekizumab conditionally recommended?
9. For adults with active AS who have not responded to the first TNFi treatment, is treatment with another TNFi conditionally recommended?
10. What is the local parenteral treatment option for adults with isolated active sacroiliitis despite treatment with NSAIDs?
11. What should be the duration of treatment with NSAIDs for adults with stable AS?
12. In adults with active enthesitis despite treatment with NSAIDs, treatment with locally administered parenteral glucocorticoids is conditionally recommended over no treatment with local glucocorticoids. Which tendon sites should be avoided?
13. What are the recommended intervals for monitoring confirmed AS disease activity?
14. Which laboratory tests should be monitored regularly for assessment of disease activity?
15. What scoring criteria are used to decide how to treat active non-radiographic axial SpA in adults?
16. When using biological medication in adults with uncertain axial SpA activity, which radiological method is conditionally recommended for evaluating disease activity?
17. Are radiological methods used to confirm inactivity in adults with stable nonradiographic axial SpA?
18. Should adults with axial SpA who are active or radiographically unstable on any treatment require repeated spine radiographs at a scheduled interval as a standard approach?
19. Which drugs should be considered first in patients with peripheral arthritis involvement?
20. How do we determine that patients are unresponsive to the impact of NSAIDs?
21. Should lower doses of methotrexate be recommended for adults receiving TNFi therapy?
22. What are the options for treatment in the first, second and third lines?
23. What treatment is used for a patient with isolated sacroiliitis and enthesitis?
24. Which agent is used to treat recurrent uveitis or inflammatory bowel disease in patients?
25. What should be done if a patient has a high degree of kyphosis, hip arthritis and a spinal fusion?
26. If a patient has achieved stability while taking one or a combination of drugs as part of their treatment, how should their medication be managed?
27. What medications reduce the risk of worsening symptoms in adults with inflammatory bowel disease?
28. Should dual energy X-ray absorptiometry (DXA) scanning be used to screen for osteopenia/osteoporosis?
29. Is it necessary to have an echocardiogram to screen for heart valve disease?
30. Is physical therapy recommended for people with ankylosing spondylitis?
31. Is there a physical therapy intervention that is preferred to another?
32. Are there any exercises recommended to improve posture and balance control?
33. What lifestyle changes should be recommended to patients in order to manage ankylosing spondylitis?
34. Which foods should be recommended for patients to consume in order to manage ankylosing spondylitis?
35. What kind of exercises should be recommended to patients in order to manage ankylosing spondylitis?
36. For which muscle groups should exercise programs be applied for patients?

The answers were evaluated by two clinician physicians (physiatrists) with seven years of clinical and academic experience in AS. It was evaluated by two different clinicians and the same clinician's answers were accepted as correct. Clinicians were consulted when there were different opinions. The evaluator rated each ChatGPT response on a scale from 1 to 4: a score of 1 indicated fully correct information, 2 indicated correct but incomplete information, 3 indicated partially correct information with some inaccuracies, and 4 indicated entirely incorrect information. A response was considered accurate if an

experienced physiotherapist deemed it complete without needing further input. For questions based on ACR and ASAS-EULAR axial spondyloarthritis guidelines, guideline-specific information was used as a benchmark to assess the accuracy of ChatGPT's responses.

To assess the reproducibility of ChatGPT's responses on AS, each question was asked in written form twice on separate days. Consistent responses—those receiving the same score on both occasions—were considered repeatable. If ChatGPT's answers fell into different score

categories or varied in detail, they were viewed as lacking reproducibility. Ethics committee approval was not needed for this study, as no patient data was used.

Statistical Analysis

The statistical analysis was performed using Excel Version 22 (Microsoft, Redmond, WA, USA). The scores assigned to each answer were reported as percentages. The questions were divided into two main groups: general FAQs and those formulated based on ACR and ASAS-EULAR guidelines. Scores assigned to each response were calculated and presented as percentages, thereby providing a clear overview of ChatGPT's performance across different question categories.

RESULTS

Analyzing the flowchart of the study, which shows the reasons for excluding some questions related to AS, 85 of the 157 questions evaluated were excluded from the study because they were not able to meet the criteria.

These included 25 repetitive questions, 19 grammatically inadequate questions, 27 questions with subjective responses and 13 questions concerning personal health. The remaining 72 questions were included in the study. ChatGPT achieved an accuracy rate of 81.9% across 72 FAQs, correctly answering 59 questions. In total, eight responses (11.1%) were rated as grade 2, and five responses (7.0%) as grade 3, with no responses falling into grade 4. The most accurate responses were observed in the categories of prevention (91.7%) and general information (90.9%). In contrast, responses pertaining to non-pharmacological treatments demonstrated the lowest level of accuracy with a recorded rate of 69.2%. Additionally, a mere 22 out of the 36 questions (61.1%) based on the ACR and ASAS-EULAR guidelines were answered correctly, with three responses (8.3%) categorized as grade 4. The evaluation of responses to AS-related FAQs, as well as the grading of answers to questions aligned with ACR and ASAS-EULAR guidelines, is documented in Table 3 and illustrated in Figure 1.

Table 3. Evaluation of responses to ankylosing spondylitis-related questions categorized by question type				
	Grade 1	Grade 2	Grade 3	Grade 4
All questions (n=72)	59 (81.9%)	8 (11.1%)	5 (7.0%)	
General information (n=11)	10 (90.9%)	1 (9.1%)	-	-
Risk factors (n=10)	8 (80.0%)	1 (10.0%)	1 (10.0%)	-
Non-pharmacological treatments (n=13)	9 (69.2%)	2 (15.4%)	2 (15.4%)	-
Pharmacological treatments (n=26)	21 (80.7%)	3 (11.5%)	2 (7.8%)	-
Prevention (n=12)	11 (91.7%)	1 (8.3%)	-	-
ACR/ASAS-EULAR Guideline (n=36)	22 (61.1%)	7 (19.4%)	4 (11.1%)	3 (8.3%)

ACR: American College of Rheumatology, ASAS: Assessment of SpondyloArthritis International Society, EULAR: European League Against Rheumatism

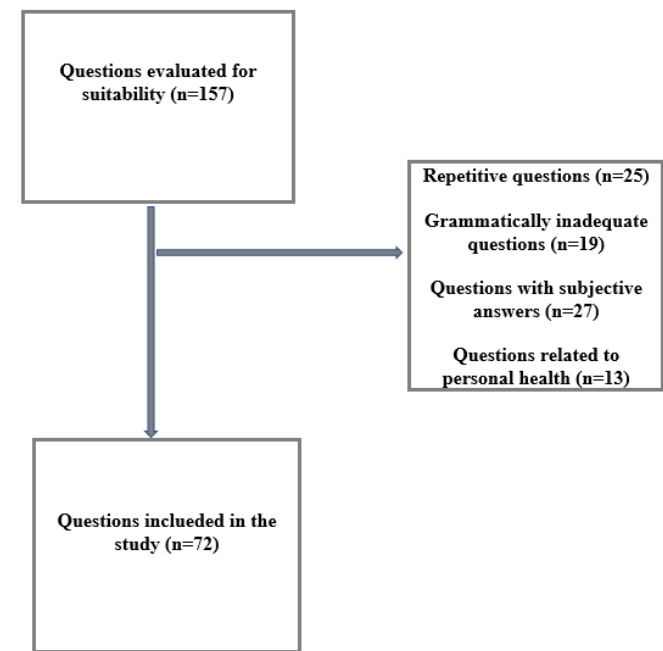


Figure 1. Flow chart of the study

ChatGPT's reproducibility rate across 72 FAQs was 88.8%, while its reproducibility for responses based on

ACR guidelines was 83.3%. The highest repeatability was observed in responses related to AS prevention (92.8%) and general information (90.9%) (Table 4). A full list of the 72 frequently asked questions used in this study is provided in Table 3.

Table 4. The consistency rate of answers provided for repeated questions	
	Reproducibility, n (%)
All questions (n=72)	64 (88.8%)
General information (n=11)	10 (90.9%)
Risk factors (n=10)	9 (90.0%)
Non-pharmacological treatments (n=13)	11 (84.6%)
Pharmacological treatments (n=26)	23 (88.4%)
Prevention (n=12)	11 (91.6%)
ACR Guideline (n=36)	30 (83.3%)

ACR: American College of Rheumatology

DISCUSSION

Machine learning has evolved with the ever-expanding development of artificial neural networks that resemble human neurons, with inputs and outputs affected by biases and weights. AI technology is becoming an increasingly important part of our daily lives. Its potential

is being exploited more and more in the field of healthcare. Although there are benefits to be gained from AI, there are also many concerns about its use in health care (8,9,12). Key knowledge gaps regarding ChatGPT's role in medical research and clinical practice include its accuracy in providing reliable health information, ethical and legal considerations, the interpretability of AI-driven decisions, potential biases, integration into healthcare systems, professional AI literacy, patient perspectives, and privacy concern (11,13).

The study aimed to assess awareness of ChatGPT about AS, a disease that affects approximately 1 to 1.5 percent of the global population. The study discovered that ChatGPT was capable of providing accurate answers to 81.9% of the most frequently asked questions about AS. In addition, the highest accuracy rate of responses of ChatGPT belonged to the questions regarding the prevention of AS questions. Conversely, ChatGPT yielded accurate responses in only 61.1% of the inquiries formulated in accordance with AS guideline specifications. This finding underscores a deficiency in the platform's capacity to manage intricate, evidence-based clinical recommendations.

The reliability and accuracy of online health sources are often questionable, and various research studies have shown that online material contains information which might be inaccurate and not complete. In their study, Alsyoud et al. examined the contents of online web sources concerning prostate cancer. The researchers found that inaccurate information was encountered 30 times more frequently than legitimate and reliable information (14). Also, Yeo et al. referred questions on cirrhosis and hepatocellular carcinoma to ChatGPT, which yielded a 76.9% success rate in providing accurate responses. However, the model was unable to ascertain decision making boundaries and the duration of treatment (15). Lastly, Moraht et al. entered a sample of 50 questions about medicines into ChatGPT. Only 13 out of 50 answers (26%) were correct (16). In contrast, Ozgor and Simavi analysed ChatGPT's performance in answering endometriosis questions and concluded that ChatGPT answered endometriosis questions satisfactorily, correctly answering over 90% of questions (17). Also, Cinar analysed ChatGPT's performance in answering questions about osteoporosis. The author found that ChatGPT provided appropriate responses to inquiries regarding osteoporosis and accurately responded to over 80% of the FAQ (10).

Finally, Dyckhoff-Shen et al. The accuracy of ChatGPT's responses to ten essential questions on brain abscess diagnosis and treatment was assessed against the guidelines issued by the European Society for Clinical Microbiology and Infectious Diseases. Without any data manipulation, 70% of the answers closely aligned with the guideline recommendations (18). The results of the study showed that more than four out of five responses to ChatGPT on the subject of AS provided accurate and entirely truthful data. In contrast to numerous alternative online sources, ChatGPT utilizes a multitude of references

when formulating responses to inquiries, thereby ensuring the precision and caliber of its outputs.

Guidelines are valuable resources that synthesize findings from numerous meta-analyses and clinical trials; they are scientifically rigorous and provide recommendations for everyday practice. In contrast, inquiries about where to locate evidence-based scientific literature can be more difficult to address (19). Antaki et al. conducted a study in which ChatGPT was utilized to respond to the examination questions posed by first-year ophthalmology residents. The results indicated that ChatGPT correctly answered 55.8% of the questions, which was comparable to the performance of the residents (20). Research by Caglar et al. (9) revealed that ChatGPT demonstrated an accuracy rate of 93.6% in responses to inquiries based on pediatric urology guidelines. Nonetheless, the present study found that the rate of accuracy for ChatGPT responses to inquiries aligned with ACR guidelines stood at 61.1%, a figure that falls short when benchmarked against the accuracy rate of the FAQ concerning AS.

One intriguing question is whether computers may eventually replace a clinician. The emergence of ChatGPT last year further increased interest in this area. Research has indicated that AI can achieve performance levels comparable to or exceeding those of humans on licensing exams, including the United States Medical Licensing Examination (USMLE), as well as specialist recruitment assessments like the UK's Multi-Specialty Recruitment Assessment (21,22). According to Gilson et al., ChatGPT was able to correctly answer 60% of the questions in medical school exams (13).

As seen in our study, artificial intelligence; gave less accurate answers to complex questions about AS diagnosis and treatment recommended by the guidelines. Additionally, in real life, patients' presentations are often atypical, so many people consider medicine to be an art as well as a science (23).

Limitations

It is important to note that this study has some limitations, such as only covering a certain period and not including all contents about AS uploaded to the internet. Furthermore, the observed variability in outputs due to minor variations in wording underscores the necessity for expeditious standardization. Moreover, it is important to recognize that the study was carried out exclusively in English. It is evident that English maintains its preeminence in academic and social online environments. It is essential to highlight that this study did not assess the clarity of ChatGPT's responses. Nevertheless, future research could examine how intelligible ChatGPT's answers are to individuals with different educational backgrounds.

CONCLUSION

The findings of the current study revealed for the first time that ChatGPT offered satisfactory responses to over 81% of FAQs related to AS. However, the accuracy of its

answers to questions based on the ACR and ASAS-EULAR axial spondyloarthritis guidelines dropped to 61.1%. While it exhibits potential as an educational resource, clinicians must critically interpret its outputs, ensuring accuracy and contextual relevance.

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REFERENCES

1. Sieper J, Poddubnyy D. Axial spondyloarthritis. *Lancet*. 2017;390:73-84.
2. Navarro-Compán V, Sepriano A, El-Zorkany B, van der Heijde D. Axial spondyloarthritis. *Ann Rheum Dis*. 2021;80:1511-21.
3. Zhao SS, Robertson S, Reich T, et al. Prevalence and impact of comorbidities in axial spondyloarthritis: systematic review and meta-analysis. *Rheumatology (Oxford)*. 2020;59:iv47-57.
4. López-Medina C, Molto A. Comorbidity management in spondyloarthritis. *RMD Open*. 2020;6:e001135.
5. Akkoc N. Are spondyloarthropathies as common as rheumatoid arthritis worldwide? A review. *Curr Rheumatol Rep*. 2008;10:371-8.
6. Yuksel B, Cakmak K. Healthcare information on YouTube: pregnancy and COVID-19. *Int J Gynaecol Obstet*. 2020;150:189-93.
7. Chandwar K, Prasanna Misra D. What does artificial intelligence mean in rheumatology?. *Arch Rheumatol*. 2024;39:1-9.
8. Zhou Z. Evaluation of ChatGPT's capabilities in medical report generation. *Cureus*. 2023;15:e37589.
9. Caglar U, Yildiz O, Meric A, et al. Evaluating the performance of ChatGPT in answering questions related to pediatric urology. *J Pediatr Urol*. 2024;20:26.e1-5.
10. Cinar C. Analyzing the performance of ChatGPT about osteoporosis. *Cureus*. 2023;15:e45890.
11. Tulandi T. Disclosure of artificial intelligence/ChatGPT-generated manuscripts. *J Obstet Gynaecol Can*. 2023;45:543-4.
12. Gilson A, Safranek CW, Huang T, et al. How does ChatGPT perform on the United States Medical Licensing Examination (USMLE)? The implications of large language models for medical education and knowledge assessment. *JMIR Med Educ*. 2023;9:e45312. Erratum in: *JMIR Med Educ*. 2024;10:e57594.
13. Ong CWM, Blackburn HD, Migliori GB. GPT-4, artificial intelligence and implications for publishing. *Int J Tuberc Lung Dis*. 2023;27:425-6.
14. Alsyouf M, Stokes P, Hur D, et al. 'Fake News' in urology: evaluating the accuracy of articles shared on social media in genitourinary malignancies. *BJU Int*. 2019;124:701-6.
15. Yeo YH, Samaan JS, Ng WH, et al. Assessing the performance of ChatGPT in answering questions regarding cirrhosis and hepatocellular carcinoma. *Clin Mol Hepatol*. 2023;29:721-32.
16. Morath B, Chiriac U, Jaszowski E, et al. Performance and risks of ChatGPT used in drug information: an exploratory real-world analysis. *Eur J Hosp Pharm*. 2024;31:491-7.
17. Ozgor BY, Simavi MA. Accuracy and reproducibility of ChatGPT's free version answers about endometriosis. *Int J Gynaecol Obstet*. 2024;165:691-5.
18. Dyckhoff-Shen S, Koedel U, Brouwer MC, et al. ChatGPT fails challenging the recent ESCMID brain abscess guideline. *J Neurol*. 2024;271:2086-101.
19. Zhou Z, Wang X, Li X, Liao L. Is ChatGPT an evidence-based doctor?. *Eur Urol*. 2023;84:355-6.
20. Antaki F, Touma S, Milad D, et al. Evaluating the performance of ChatGPT in ophthalmology: An analysis of its successes and shortcomings. *Ophthalmol Sci*. 2023;3:100324.
21. Kung TH, Cheatham M, Medenilla A, et al. Performance of ChatGPT on USMLE: potential for AI-assisted medical education using large language models. *PLOS Digit Health*. 2023;2:e0000198.
22. Tsoutsanis P, Tsoutsanis A. Evaluation of large language model performance on the Multi-Specialty Recruitment Assessment (MSRA) exam. *Comput Biol Med*. 2024;168:107794.
23. Panda SC. Medicine: science or art?. *Mens Sana Monogr*. 2006;4:127-38.



The Relationship Between Antipsychotic Use and Functionality in Patients with Bipolar Disorder: A Naturalistic Observational Study

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Abstract

Aim: The aim of this study is to investigate the impact of antipsychotic use on functioning and medication adherence in patients with bipolar disorder (BD) in remission.

Material and Method: The study included 142 patients with BD who were diagnosed with remission according to DSM-5 criteria. The patients were administered various scales, including the Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HAM-D), Brief Psychiatric Rating Scale (BPRS), Bipolar Disorder Functioning Scale, and Morisky Medication Adherence Scale. Study participants had a HAM-D score of less than 7, a YMRS score of less than 4, and no manic, depressive, or hypomanic symptoms in the past 6 months.

Results: 50.7% of study participants were female. The results showed that those not taking antipsychotics were more likely to live with someone, while those taking antipsychotics were more likely to be alone and have lower incomes. No important difference was found when patients and controls were examined in terms of gender, employment status or disease-related parameters. Antipsychotic users had higher scores in emotional functioning, whereas non-users had higher scores in family and friendships, social activities, and general functioning. Medication adherence correlated positively with social relationships but negatively with emotional, intellectual, and sexual functioning. Female gender and antipsychotic use were identified as significant predictors of overall functioning.

Conclusion: This study highlights that while antipsychotics are beneficial during the acute phase of BD, their long-term impact on functioning during remission should not be ignored. The results demonstrate the importance of an individualized treatment strategy that balances symptom management with quality of life and regularly reassesses the need for antipsychotic treatment in long-term care.

Keywords: Antipsychotic, bipolar disorder, functioning, medication adherence, treatment

INTRODUCTION

Bipolar disorder (BD) is a chronic illness that occurs with manic, depressive and mixed episodes. It commonly begins with a depressive period at a young age and is almost always diagnosed after a manic or mixed episode. It is identified by repetitive periods of illness during which the person may continue to live with subthreshold symptoms or in a euthymic state (1). Recurrent episodes seen in BD cause disability by negatively affecting the person's functionality over time. BD is ranked tenth by the World Health Organization among illnesses that impair functioning (1). The lifetime prevalence of BD has

been reported to be approximately 1%. More recent data report that bipolar spectrum disorder affects 6% of the population (2).

Initially, therapy for BD focuses on stabilizing the patient's condition in the acute phase (3). Once acute stabilization is achieved, treatment goals aim to prevent relapses, reduce subthreshold symptoms and improve work and social functioning. However even after receiving treatment, patients frequently still experience functional and quality of life impairments (4). Impaired functioning increases the likelihood of disability and death in patients with BD. For this reason, functional

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impairments can become the main issues in BD and must be addressed in the treatment process (5).

After the first manic or mixed episode of BD, many patients require long-term prophylactic treatment to avoid future flare-ups. In spite of recent pharmacological advances, treatment adherence remains a critical factor in determining treatment outcomes. Nonadherence rates to long-term pharmacotherapy for BD have been reported to range from 20% to 66%, with an average nonadherence rate of 41% (6-8). Nonadherence to therapy is a common cause of relapse and leads to negative outcomes such as increased outpatient visits, rehospitalizations, decreased social functioning, and suicide (9-12). Moreover, nonadherence to treatment increases the utilization and costs of health services (13). However, it is known that there are various reasons for nonadherence to treatment, such as side effects. Therefore, it is critical to examine the link between antipsychotics used in the treatment of BD and treatment adherence. Studies examining the relationship between mood stabilizers and antipsychotic treatment on functioning and medication adherence in BD are limited (14,15). Early intervention with antipsychotics, especially during the acute phase, may help improve functioning, but the long-term impact of these medications on compliance and functioning is still unclear (16). In this context, we investigate the effects of antipsychotics used to treat BD on functionality and compliance (17).

As a result of all this data, the current research focuses on the effects of antipsychotics on functionality and medication compliance in BD. It aims to evaluate the differences in disease severity, functionality level, and medication compliance with the use of antipsychotics in BD in outpatients in remission.

MATERIAL AND METHOD

This cross-sectional study was led by the Department of Psychiatry at Ankara Etlik City Hospital.

Participant: This research was planned with patients diagnosed with BD who were followed up in the psychiatry department of Ankara Etlik City Hospital. All participants were clinically interviewed by two experienced clinicians before being enrolled in the study. This study included individuals diagnosed with BD according to the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5). The participants were individuals who applied to the polyclinic as outpatients, were between the ages of 18-65, and were at least primary school graduates. The volunteers who participated in the study were those who had a HAM-D score <7 and a YMRS score <4 and who had not shown manic, depressive or hypomanic symptoms in the last 6 months. The individuals included in the study had been followed up in our hospital's psychiatry clinic for the last 1 year. Exclusion criteria of the study were delirium, dementia, amnesic disorders,

mental retardation or other organic mental disorders, autism spectrum disorders, alcohol or substance dependence, schizophreniform and other psychotic disorders, pregnancy or puerperium in female patients, unregulated systemic or metabolic diseases. Patients with a past history of these conditions who are currently stable and well-controlled were not excluded. This approach was adopted to minimize confounding effects on functionality and medication adherence, thereby ensuring that the observed outcomes are more directly attributable to the effects of antipsychotic treatment in bipolar disorder. 142 patients were included in this research. 108 of those included in the research were using antipsychotics and 34 were not using antipsychotics.

Procedure: This study was carried out by acquiring consent paperwork from patients who applied to Ankara Etlik City Hospital Psychiatry Outpatient Clinic and had been identified with BD consistent with the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) between January 2025 and February 2025. The BD diagnosis was established using the Structured Clinical Interview for DSM-5 (SCID-5). Patients who agreed to take part in the observation were given a shape that included sociodemographic information (which include a period of illness, wide variety of hospitalizations, wide variety of suicide attempts) through the clinicians. Young Mania Rating Scale (YMRS), Brief Psychiatric Rating Scale (BPRS) and Hamilton Depression Rating Scale (HAM-D) were administered by the clinician to determine whether the patients' symptoms were in exacerbation or remission. The Bipolar Disorder Functioning Questionnaire (BDFQ) and Morisky Medication Adherence Scale (MMAS) were completed by the participants. Participants who completed the study were included in the statistical analysis and divided into two groups based on their antipsychotic use.

This study was conducted in accordance with the Declaration of Helsinki and has been approved by the ethics committee (Ankara Etlik City Hospital Ethics Committee, 30/10/2024, AEŞH-BADEK-2024-1065).

Measurements Tools

Sociodemographic Data Form: The sociodemographic data form consists of semi-structured questions asking basic demographic information and clinical variables such as age, marital status, education level, occupation, history of psychiatric illness, medical history, family history of psychiatric illness, family history of medical illness, years since diagnosis, medications taken, non-psychiatric medications taken, number of depressive episodes, number of manic episodes, number of hospitalizations.

Hamilton Depression Rating Scale (HAM-D): Developed by Hamilton to assess the severity of depression. This scale rates 17 depressive symptoms on a 3- or

5-point scale. As a result of the assessment, 16-25 is considered as mild, 26-40 as moderate, and 40 or more as severe depressive syndrome (18). A validity and reliability study in Türkiye was conducted by Akdemir et al. conducted (19).

Young Mania Rating Scale (YMRS): Developed by Young et al. scale. It is used to measure the severity of manic episodes. The scale consists of 11 items, seven of which are 5-point Likert-type items and the remaining four are 9-point Likert-type items. The lowest achievable value on the scale is 0 and the highest is 44. The validity and reliability of the Turkish version were examined by Karadağ et al. (20,21).

Brief Psychiatric Rating Scale (BPRS): A scale developed by Overall and Gorham is used to measure symptoms of severe psychosis and some depression (22). It consists of 18 items and is a 7-point Likert-type scale. In the original version, the point distribution is represented on a scale from 0 to 6, with values from 15 to 30 indicating milder syndromes and values above 30 indicating severe syndromes. The lowest value is 0 and the highest value is 108. There is no cut-off value. This scale is used for comparative studies. The validity and reliability of this scale in Türkiye was verified by Soykan (23).

Bipolar Disorder Functioning Questionnaire (BDFQ): This is a 52-item self-report scale that measures the level of functioning of bipolar disorder patients during the symptomatic interictal or recovery phase. This scale was developed by Aydemir et al. (24). It includes 11 subscales: emotional functioning, cognitive functioning, sexual functioning, sense of stigma, social withdrawal, family relationships, relationships with friends, participation in social activities, daily activities and hobbies, spontaneous and potential use, and work/occupation. No limit values are set, so its use in comparative studies is recommended.

Morisky Medication Adherence Scale (MMAS): This is a scale developed by D.E. Morisky developed a self-management scale to measure medication adherence (25). This scale consists of four closed questions with two options. The questions are answered with yes/no. Answering "no" to all questions is considered high adherence, answering "yes" to one or two questions is considered moderate, and answering "yes" to three or four questions is considered low adherence. The scale is easy to complete. A Turkish validity and reliability study was conducted by Bahar et al. (26).

Statistical Analysis

In presenting the data, mean $\pm$ standard deviation (SD) was used for continuous variables, and percentages and frequencies were used for categorical variables. Demographic and clinical characteristics between the antipsychotic and non-antipsychotic groups were

analyzed using chi-squared tests for categorical variables and Student's t-tests when parametric assumptions were met for continuous variables. If parametric assumptions were not met, Mann-Whitney U-tests were used. Normality was assessed using the Shapiro-Wilk test. The relationship between two continuous variables was assessed using Pearson correlation tests. In addition, linear regression analysis was used to determine significant variables associated with the total functioning score at the final assessment. All statistical calculations were performed using Statistical Package for Social Sciences (SPSS) 22.0. All p-values were calculated two-sided, and a p-value less than 0.05 was considered significant.

RESULTS

The study involved 142 volunteers, with a mean age ranging from 18 to 65 years. Of these, 50.7% (n=72) were women. A comparison of the sociodemographic and clinical data of the study groups is presented in Table 1. When comparing the two groups, a significantly higher proportion of married individuals was observed in the non-antipsychotic user group ($p=0.008$), while the unmarried rate was higher among antipsychotic users. Regarding economic status, it was found that individuals using antipsychotics had lower incomes ($p=0.023$). No statistically significant differences between the groups in terms of gender, employment status, smoking rate, duration of illness, number of hospitalizations, number of manic episodes, or the use of mood stabilizers ($p>0.05$).

A comparison of BDFQ, MMAS, YMRS, HAM-D and BPRS of the study groups is presented in Table 2. The emotional functioning scores of antipsychotic users were found to be significantly higher than those of non-users ($p=0.003$). However, the non-antipsychotic group demonstrated superior scores in areas such as domestic and friendship relationships, social withdrawal, participation in social activities, daily activities, hobbies, and overall functioning. This distinction was statistically significant for all measures ($p=0.001$, 0.003 , 0.004 , 0.010 , 0.022 and $p<0.001$ respectively).

Correlations between MMAS scores and BDFQ subtypes are shown in Table 3. In line with the basic statistical analyses, a significant relationship was found between the variables and the BDFQ Total Score as a result of the multiple linear regression analysis conducted to reveal the predictive value of gender and antipsychotic use, which were thought to have an effect on the BDFQ Total Score (Adjusted $R^2=0.106$, $F(6,135)=3.772$, $p=0.002$). The results indicated that both female gender ($p=0.030$) and antipsychotic use ($p<0.001$) were significant predictors of the BDFQ Total Score. The linear regression model is shown in Table 4.

Table 1. Comparison of sociodemographic characteristics of the participants according to antipsychotic use						
Variable		Antipsychotic use		Statistic	df	p value
		Yes (n=108)	No (n=34)			
Age; year, mean±SD		38.72±11.68	42.29±11.18	t=1.520	140	0.119
Gender; n (%)	Female	55 (50.9)	17 (50)	$\chi^2=0.009$	1	0.925
	Male	53 (49.1)	17 (50)			
Marital status; n (%)	Single	47 (43.5)	5 (14.7)	$\chi^2=9.623$	2	0.008**
	Married	55 (50.9)	25 (73.5)			
	Divorced/widow	6 (5.6)	4 (11.8)			
Working status; n (%)	Working	31 (28.7)	13 (32.2)	$\chi^2=1.009$	1	0.295
	Not-working	77 (71.3)	15 (61.8)			
Education year; year, mean±SD		10.49±3.39	10.73±4.28	t=0.343	140	0.732
Economic status; n (%)	High	18 (16.7)	10 (29.4)	$\chi^2=8.044$	2	0.023*
	Middle	23 (21.3)	12 (35.3)			
	Low	63 (58.3)	12 (35.3)			
Smoking; yes, n (%)		54 (50)	17 (50)	$\chi^2=0.000$	1	1.000
Mental illness in the family; yes, n (%)		70 (64.8)	18 (52.9)	$\chi^2=1.547$	1	0.214
Physical illness in the family; yes, n (%)		35 (32.4)	13 (38.2)	$\chi^2=0.393$	1	0.531
Duration of illness; year, mean±SD		13.33±7.64	14.50±9.21	t=0.738	140	0.462
Number of hospitalizations; n, mean±SD		2.19 ±2.45	2.20 ±2.64	t=0.023	140	0.981
Number of depressive episodes; n, mean±SD		4.01 ±3.10	4.58 ±3.56	t=0.900	140	0.370
Number of manic episodes; n, mean±SD		4.54 ±2.84	3.52±2.40	t=1.885	140	0.061
Mood stabilizer use; yes, n (%)		94 (87.0)	30 (88.2)	$\chi^2=0.034$	1	0.855
Type of mood stabilizer; yes, n (%)	None	14 (13.0)	4 (11.8)	$\chi^2=1.451$	3	0.694
	Lithium	53 (49.1)	14 (41.2)			
	Valproate	40 (37.0)	15 (44.1)			
	Carbamazepine	1 (0.9)	1 (2.9)			
Dual mood stabilizer; yes, n (%)		9 (8.3)	1 (2.9)	$\chi^2=1.149$	1	0.284
Type of Antipsychotic; yes, n (%)	Quetiapine	65 (60.2)		$\chi^2=0.812$	1	0.368
	Olanzapine	22 (20.4)				
	Aripiprazole	11 (10.2)				
	Paliperidone	2 (1.9)				
	Risperidone	8 (7.4)				
Double Antipsychotic; yes, n (%)		12 (11.1)				
Antidepressant use; yes, n (%)		10 (9.3)	5 (14.7)			

*: p values≤0.05, **: p values≤0.01

Table 2. Comparison of Bipolar Disorder Functioning Questionnaire, Morisky Medication-Taking Adherence Scale, Young Mania Rating Scale, Hamilton-Depression Rating Scale, Brief Psychiatric Rating Scale according to antipsychotic use					
Variable	Antipsychotic use		Statistic	df	p value
	Yes (n=108)	No (n=34)			
Bipolar Disorder Functioning Questionnaire					
Emotional functioning	3.88±1.16	3.26±0.66	z=1271		0.003*
Intellectual functioning	5.90±2.16	5.29±1.48	z=1622		0.286
Sexual functioning	7.38±3.10	7.08±3.51	t=-0.462	140	0.645
Feelings of stigmatization	8.0±1.80	7.85±2.06	t=-0.400	140	0.690
Social withdrawal	6.96±1.54	7.91±1.02	t=3.349	140	0.001**
Household relations	16.38±2.88	16.02±2.30	t=3.045	140	0.003*
Relations with friends	11.57±2.20	12.79±1.85	t=2.926	140	0.004*
Participation to social activities	12.75±3.11	14.38±3.27	t=2.620	140	0.010*
Daily activities and hobbies	13.44±2.38	14.55±2.61	t=2.320	140	0.022*
Taking initiative and self sufficiency	6.20±1.19	6.26±1.18	t=0.261	140	0.795
Occupation	6.63±1.35	6.61±1.01	t=-0.084	140	0.933
Total	99.06±7.19	104.05±8.27	t=3.404	140	<0.001**
Morisky Medication Adherence Scale	7.102±1.06	6.88±1.14	t=-1.027	140	0.306
Young Mania Rating Scale	0.58±1.03	0.73±1.21	t=0.716	140	0.475
Hamilton-Depression Rating Scale	2.66±1.73	2.50±1.60	t=-0.497	140	0.620
Brief Psychiatric Rating Scale	2.47±2.13	1.76±1.59	t=-1.781	140	0.077
*: p values≤0.05, **: p values≤0.01					

*: p values≤0.05, **: p values≤0.01

Table 3. Morisky Medication Adherence Scale Scores correlations with Bipolar Disorder Functioning Scale subtypes		
Bipolar Disorder Functioning Questionnaire	Morisky Medication Adherence Scale	
	r	p
Emotional functioning	-0.155	0.109
Intellectual functioning	-0.376	<0.001
Sexual functioning	-0.229	0.017
Feelings of stigmatization	0.155	0.109
Social withdrawal	0.302	0.001
Household relations	0.285	0.003
Relations with friends	0.318	0.001
Participation to social activities	0.098	0.315
Daily activities and hobbies	-0.095	0.328
Taking initiative and self sufficiency	-0.039	0.692
Occupation	-0.046	0.639
Total	0.066	0.497

Table 4. Linear regression model created to determine predictors of Bipolar Disorder Functioning Scale							
Predictor	Estimate	SE	95% confidence interval		t	p	Standard estimate
			Lower	Upper			
Age	-0.036	0.058	-0.151	0.079	-0.618	0.538	-0.054
Gender (female–male)	2.819	1.284	0.279	5.359	2.195	0.030	0.364
Antipsychotic use (yes–no)	-5.337	1.484	-8.271	-2.403	-3.597	<0.001	-0.690
Brief Psychiatric Rating Scale	-0.153	0.318	-0.781	0.475	-0.482	0.631	-0.040
Education year	-0.261	0.193	-0.643	0.121	-1.350	0.179	-0.122
Morisky Medication Adherence Scale	1.063	0.598	-0.120	2.247	1.777	0.078	0.149

DISCUSSION

This study was conducted to analyze the results of antipsychotic use on functioning and medication adherence in BD. The most important result of the study was that those not using antipsychotics had higher scores in domestic and friend relationships, social withdrawal, social activity participation, daily activities, hobbies, and overall functioning and in the total functionality area, and their emotional functionality was lower. In addition, antipsychotic use and female gender were found to be independent predictors of total functionality in BD. It is hypothesized that the findings of this study will lead to a more comprehensive evaluation of antipsychotic use in BD patients and may prompt a revision of current antipsychotic treatment practices.

By focusing on these targeted aims, the study fills a critical gap by demonstrating that among patients in remission, antipsychotic use is linked to a complex functional profile characterized by improved emotional regulation yet significant deficits in social interactions, domestic activities, and overall functioning. Notably, non-antipsychotic users scored higher in several of these domains, suggesting that the benefits of antipsychotic therapy may be accompanied by unintended adverse effects on other aspects of daily life. Our results are consistent with reports in the literature (27). There may be several reasons for these results. Bipolar patients prescribed antipsychotics may represent a relatively more severe spectrum of illness than those who are not on antipsychotic treatment. Research suggests that

high symptom severity in BD may influence the decision to add an antipsychotic to the treatment regimen (28). In the study conducted by Tıǧlı Filizer and colleagues, participants were classified into three groups according to their medication regimen: individuals taking mood stabilizers, those on a combination of mood stabilizers and antipsychotics and those prescribed three or more medications. Results from the comparison among these three groups indicated that patients who were only using mood stabilizers demonstrated high levels of functionality compared to those on three or more medications (27). They also showed that the use of a combination treatment, including antipsychotics, had statistically significant negative effects on aspects such as decision-making independence, social interactions, and leisure activities (27). Previous studies have highlighted that persistent subthreshold depressive symptoms can also negatively impact various functional domains, including work performance, social interactions, and cognitive functioning (29). In contrast, Yen et al. evaluated the quality of life in bipolar disorder patients compared to individuals with schizophrenia and healthy controls, examining the effects of second-generation antipsychotics. They found that the quality of life in bipolar patients, across domains such as physical, psychological, social relationships, and environment, was more similar to that of schizophrenia patients and lower than that of healthy controls. This finding suggests that while pharmacological treatment is essential for managing symptoms, its impact on overall quality of life may be limited (30). Considering these inconsistencies, the data presented, and the complexity

of the situation at hand, more in depth analysis is required to determine if the observed results are linked to the impact of medications or indicative of a serious illness with an unfavorable prognosis.

One of the findings of this study indicates that over half of the patients with BD were unemployed, underscoring the substantial impact of the condition on morbidity and its role in determining the severity of the illness. Furthermore, evidence suggests that patients with BD who experience a higher number of depressive episodes are more likely to encounter long-term unemployment compared to those without such factors (31). A similar result is also observed in functionality studies conducted in the elderly population. Elderly patients with BD showed significantly greater impairments in functioning as compared to the control group, particularly in areas of autonomy, occupational functioning, cognitive abilities, financial management, and interpersonal relationships (32). Moreover, the accumulation of episodes over the years predicts future relapses and may consequently be associated with poor outcomes (33).

Looking at studies examining the relationship between medication adherence and functioning, one study suggests that improved medication adherence can result in better mood episode control, which is crucial for bipolar illness stability (34). However, the effect of adherence on capability may be influenced by numerous factors, which include the severity of the disorder, the presence of comorbid conditions, and the facet results of medications (27). Various psychotropic medications and the side effects of antipsychotic treatments have been reported to have a negative impact on functioning (35). In our study, we observed that as medication adherence increased, both intellectual and sexual functioning decreased. This suggests that the negative effects of antipsychotics on functioning become more pronounced with higher adherence, possibly due to their side effects. It is important to note, however, that this relationship may also be influenced by confounding factors such as age, metabolic effects, and concomitant medications, as well as side effects like sedation, weight gain, and metabolic disturbances. Although our baseline comparisons (see Table 1) showed no statistically significant differences between groups regarding age and concomitant medication usage, the possibility of residual confounding cannot be completely ruled out. Second-generation antipsychotics, particularly risperidone, can lead to hyperprolactinemia by causing hypothalamic-pituitary dysregulation, which may induce sexual dysfunction by causing decreased libido, erectile dysfunction, and other sexual problems (36). Due to the nature of BD, which necessitates long-term pharmacotherapy, patients may experience a variety of side effects, including metabolic syndrome and weight gain, particularly with second-generation antipsychotics (37). Studies have shown that overactivation of the amygdala is present in patients

with BD (38). During normal sexual response, amygdala activity decreases as sexual pleasure increases; however, this hyperactivation, which is frequently seen in BD, may lead to decreased sexual satisfaction (39). In a study involving 80 BD patients in remission and 80 healthy controls, it was reported that the patients exhibited poorer functioning than controls in areas such as intellectual and sexual functioning, perceived stigma, introversion, family relationships, friendships, and engagement in community activities (27). Poor sexual functioning in BD may be related both to some pathophysiological mechanisms related to BD and to the symptoms of the disorder.

Individuals with BD often experience intense mood swings, which can lead to difficulties in managing emotions. A number of studies have shown that the use of antipsychotics in BD is effective in stabilizing mood (40). Effective mood stabilization can lead to enhanced emotional regulation, reduced dysregulation, and improved overall emotional functioning.

However, because this is a cross-sectional study, patients treated with mood stabilizers alone may have a milder course of illness or less severe episodes than those treated with a combination of mood stabilizers and second-generation antipsychotics. Due to these limitations, we cannot rule out the possibility that medication load, disease progression, and other uncontrolled variables may have influenced our results. Therefore, when interpreting the study findings, it should be considered that differences in functioning may stem from factors other than treatment modalities. Moreover, the cross-sectional design and lack of a follow-up period limit our ability to report on the long-term effects of symptoms and treatment, underscoring the need for longitudinal studies to generalize the results. The strengths of this study include sufficient sample size and similar characteristics across all subgroups, as our sample consisted solely of patients with, bipolar I disorder, which is relatively homogeneous. Long-term follow-up studies are necessary to further evaluate the relationship between clinical characteristics and functional ability.

CONCLUSION

In BD, impairments across multiple functional domains are present even during remission. Although patients can achieve remission, they often do not relapse and tend to recover to premorbid levels of psychosocial functioning. However, second-generation antipsychotics used in treatment have adverse effects in addition to residual symptoms. While the benefits of antipsychotics in the acute phase of BD are undeniable, their effects on overall functioning in patients in remission should also be considered. During long-term treatment, antipsychotic regimens should be periodically reevaluated; treatments that are no longer needed should be gradually reduced or discontinued, and the potential side effects and costs of continued psychotropic therapy should be carefully assessed.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: This study was conducted in accordance with the Declaration of Helsinki and has been approved by the ethics committee (Ankara Etlik City Hospital Ethics Committee, 30/10/2024, AEŞH-BADEK-2024-1065).

REFERENCES

- Sachs GS, Thase ME, Otto MW, et al. Rationale, design, and methods of the systematic treatment enhancement program for bipolar disorder (STEP-BD). *Biol Psychiatry*. 2003;53:1028-42.
- Kessler RC, Akiskal HS, Angst J, et al. Validity of the assessment of bipolar spectrum disorders in the WHO CIDI 3.0. *J Affect Disord*. 2006;96:259-69.
- Karanti A, Kardell M, Lundberg U, Landén M. Changes in mood stabilizer prescription patterns in bipolar disorder. *J Affect Disord*. 2016;195:50-6.
- Gokcay H, Solmaz M. The association between mood stabilizers, sleep quality, and functioning in patients with remitted bipolar disorder. *J Clin Psychopharmacol*. 2024;44:258-62.
- Keskin N, Tamam L, Ozpoyraz N. Assessment of sleep quality in bipolar euthymic patients. *Compr Psychiatry*. 2018;80:116-25.
- Berk L, Hallam KT, Colom F, et al. Enhancing medication adherence in patients with bipolar disorder. *Hum Psychopharmacol*. 2010;25:1-16. Erratum in: *Hum Psychopharmacol*. 2010;25:192.
- Lingam R, Scott J. Treatment non-adherence in affective disorders. *Acta Psychiatr Scand*. 2002;105:164-72.
- Vieta E. Improving treatment adherence in bipolar disorder through psychoeducation. *J Clin Psychiatry*. 2005;66:24-9.
- Lama S, Lakshmi KV, Shyangwa PM, Parajuli P. Level of compliance and factors associated with non-compliance to treatment among the mentally ill patients. *Health Renaiss*. 2012;10:113-7.
- Sajatovic M, Davies M, Hrouda DR. Enhancement of treatment adherence among patients with bipolar disorder. *Psychiatr Serv*. 2004;55:264-9.
- Sajatovic M, Ignacio RV, West JA, et al. Predictors of nonadherence among individuals with bipolar disorder receiving treatment in a community mental health clinic. *Compr Psychiatry*. 2009;50:100-7.
- Baldessarini RJ, Tondo L, Hennen J. Effects of lithium treatment and its discontinuation on suicidal behavior in bipolar manic-depressive disorders. *J Clin Psychiatry*. 1999;60:77-116.
- Eaddy M, Grogg A, Locklear J. Assessment of compliance with antipsychotic treatment and resource utilization in a medicaid population. *Clin Ther*. 2005;27:263-72.
- Levin JB, Aebi ME, Tatsuoka C, et al. Adherence to psychotropic and nonpsychotropic medication among patients with bipolar disorder and general medical conditions. *Psychiatr Serv Wash DC*. 2016;67:342-5.
- Bauer M, Glenn T, Alda M, et al. Association between adherence with an atypical antipsychotic and with other psychiatric drugs in patients with bipolar disorder. *Pharmacopsychiatry*. 2021;54:75-80.
- Bonnin CM, Torrent C, Vieta E, Martínez-Arán A. Restoring functioning in bipolar disorder: functional remediation. *Harv Rev Psychiatry*. 2014;22:326-30.
- Gruber J, Harvey AG, Wang PW, et al. Sleep functioning in relation to mood, function, and quality of life at entry to the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *J Affect Disord*. 2009;114:41-9.
- Nutt DJ. The Hamilton Depression Scale- Accelerator or break on antidepressant drug discovery?. *J Neurol Neurosurg Psychiatry*. 2014;85:119-20.
- Akdemir A, Örsel S, Dağ İ, et al. Hamilton depresyon derecelendirme ölçeğinin (HDDÖ) geçerliliği-güvenilirliği ve klinikte kullanımı. 3P Psikiyatri Psikoloji Psikofarmakoloji Dergisi. 1996;4:251-9.
- Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry*. 1978;133:429-35.
- Karadağ F, Oral T, Yalçın FA, Erten E. Reliability and validity of Turkish translation of Young Mania Rating Scale. *Türk Psikiyatri Derg*. 2002;13:107-14.
- Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychological Reports*. 1962;10:799-812.
- Soykan Kahraman Ç. Institutional differences and case typicality as related to diagnosis symptom severity prognosis and treatment. Master thesis. Middle East Technical University. Ankara, 1990.
- Aydemir O, Eren I, Savaş H, et al. Development of a questionnaire to assess inter-episode functioning in bipolar disorder: Bipolar Disorder Functioning Questionnaire. *Türk Psikiyatri Derg*. 2007;18:344-52.
- Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24:67-74.
- Bahar G, Savas H, Nal A, et al. Reliability and validity of the Morisky Medication Adherence Scale for bipolar mood disorder. *Alpha Psychiatry*. 2014;15:141-9.
- Tiğli Filizer A, Cerit C, Tüzün B, Aker AT. Social aspect of functioning deteriorates more than individual aspect in patients with remitted bipolar disorder. *Noro Psikiyatr Ars*. 2016;53:158-62.
- Ringen PA, Reponen EJ, Vedal TSJ, et al. Predictors for antipsychotic dosage change in the first year of treatment in schizophrenia spectrum and bipolar disorders. *Front Psychiatry*. 2019;10:649.
- Aguglia A, Fusar-Poli L, Natale A, et al. Factors associated with medication adherence to long-acting injectable antipsychotics: results from the STAR network depot study. *Pharmacopsychiatry*. 2022;55:281-9.
- Yen CF, Cheng CP, Huang CF, et al. Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission. *Bipolar Disord*. 2008;10:617-24.

31. Zimmerman M, Galione JN, Chelminski I, et al. Sustained unemployment in psychiatric outpatients with bipolar disorder: frequency and association with demographic variables and comorbid disorders. *Bipolar Disord.* 2010;12:720-6.
32. Comes M, Rosa A, Reinares M, et al. Functional impairment in older adults with bipolar disorder. *J Nerv Ment Dis.* 2017;205:443-7. Erratum in: *J Nerv Ment Dis.* 2019;207:522.
33. Rosa AR, Reinares M, Franco C, et al. Clinical predictors of functional outcome of bipolar patients in remission. *Bipolar Disord.* 2009;11:401-9.
34. Berger A, Edelsberg J, Sanders KN, et al. Medication adherence and utilization in patients with schizophrenia or bipolar disorder receiving aripiprazole, quetiapine, or ziprasidone at hospital discharge: a retrospective cohort study. *BMC Psychiatry.* 2012;12:99.
35. Sanchez-Moreno J, Martinez-Aran A, Tabarés-Seisdedos R, et al. Functioning and disability in bipolar disorder: an extensive review. *Psychother Psychosom.* 2009;78:285-97.
36. Cichon GJ, Qadri SF. Risperidone-induced sexual dysfunction case report. *Cureus.* 2023;15:e35357.
37. Vancampfort D, Stubbs B, Mitchell AJ, et al. Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. *World Psychiatry Off J World Psychiatr Assoc WPA.* 2015;14:339-47.
38. Phillips ML, Swartz HA. A critical appraisal of neuroimaging studies of bipolar disorder: toward a new conceptualization of underlying neural circuitry and a road map for future research. *Am J Psychiatry.* 2014;171:829-43.
39. Rowland DL. Neurobiology of sexual response in men and women. *CNS Spectr.* 2006;11:6-12.
40. Luca M, Prossimo G, Messina V, et al. Epidemiology and treatment of mood disorders in a day hospital setting from 1996 to 2007: an Italian study. *Neuropsychiatr Dis Treat.* 2013;9:169-76.



Effects of Stroke Severity on Treatment Initiated in the Emergency Department

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Abstract

Aim: Stroke severity depends on the treatments administered from the moment the patient enters the emergency department and the success of patient management. In our study, we aimed to evaluate the effect of National Institutes of Health Stroke Scale (NIHSS) scoring on intervention time and the relationship of qualitative measures with clinical outcome in patients in our stroke center.

Material and Method: The files of patients who underwent iv TPA and/or mechanical thrombectomy in the emergency department who were followed up at the stroke center between 2022 and 2023 were retrospectively reviewed. Patients were divided into 4 groups as NIHSS score 0-5, 5-10, 10-20, ≥ 21 ; 3 groups as modified Rankin Scale (MRS) score 0-2, 3-5 and 6. Mean, standard deviation, median minimum, maximum, frequency and ratio values were used in the descriptive statistics of the data. ANOVA (Tukey test), Kruskal-Wallis, Mann-Whitney u test were used in the analysis of quantitative independent data; chi-square test was used in the analysis of qualitative independent data, and Fischer test was used when chi-square test conditions were not met.

Results: Symptom puncture, symptom recanalization, puncture recanalization, door imaging, door TPA, door puncture times did not differ significantly ($p>0.05$) between stroke severity groups. The first-pass recanalization rate was significantly ($p<0.05$) higher in the MRS III-IV-V group than in the MRS 0-I-II group, while the first-pass recanalization rate did not differ significantly ($p>0.05$) between the MRS VI group and the MRS 0-I-II, MRS III-IV-V groups. In the group with bleeding at 24 hours, TICI stage was significantly ($p<0.05$) lower, 3rd month MRS score was significantly ($p<0.05$) higher, and tan score was significantly ($p<0.05$) lower than the group without bleeding at 24 hours.

Conclusion: Although there is no correlation between stroke severity and emergency department quality-metrics times, recanalization success has an effect on good outcome. In stroke, the coordination and experience of all components of the neurology and emergency medicine clinics should be good in terms of diagnosis and timing.

Keywords: Thrombectomy, stroke, iv Tpa, emergency service

INTRODUCTION

Stroke is the leading cause of disability and one of the most prevalent causes of mortality globally (1). Initially, intravenous tissue plasminogen activator (iv tPA) was recommended as the primary treatment option, as per the first published guidelines. However, recent research has demonstrated the effectiveness of mechanical thrombectomy for large vessel occlusions. Notably, mechanical thrombectomy is now included in the guidelines for acute ischemic stroke (AIS) patients presenting within the first six hours, specifically for those with occlusions in the M1 segment of the internal carotid artery (ICA) or the middle cerebral artery (MCA) (2-5). Furthermore,

findings from the DAWN and DEFUSE-3 studies have led to an extension of the treatment window for mechanical thrombectomy to 24 hours for AIS patients (6,7).

AIS constitutes a neurological emergency that necessitates prompt and interventional treatment. Given that the initial presentation occurs in the emergency department, the provision of rapid and effective treatment is critically important (5). In both our country and globally, the process of establishing a diagnosis and making a treatment decision should ideally be completed within 45 minutes of presentation. Should thrombolytic therapy and/or mechanical thrombectomy (MT) be deemed necessary, it is imperative that the door-to-needle time remains under 60

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minutes (8). However, factors such as overcrowding in the emergency department, along with delays in the diagnosis and treatment of acute stroke patients, contribute to an extended length of stay in the emergency department (9).

Numerous factors can influence the efficacy and timeliness of treatment in the emergency department, including patient volume, waiting times for triage and ward admission, and disorganized emergency entries resulting from irregular operational procedures. Consequently, the severity of the condition and the physician's ability to identify an acute stroke case that necessitates prompt intervention, appropriate triage, and effective patient management are critical for achieving favorable clinical outcomes. The National Institutes of Health Stroke Scale (NIHSS) is a standardized scoring system that assesses the severity of a patient's neurological deficits on a scale from 0 to 42. This scoring system is instrumental in determining the appropriateness of iv tPA and/or MT in emergency situations. Therefore, the objective of our study was to investigate whether the NIHSS score influences the timing of intervention in patients receiving iv tPA in conjunction with MT or MT alone. Additionally, we aimed to evaluate the clinical outcomes and the incidence of intracerebral hemorrhage among patients treated at our stroke center using qualitative measures.

MATERIAL AND METHOD

This study received approval from the Clinical Studies Ethics Committee of University of Health Sciences Haseki Training And Research Hospital (Decision No: 261-2023) and was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

The medical records of patients who were monitored at the stroke center from 2022 to 2023, underwent MT, and received iv tPA in the emergency department were subjected to a retrospective review. Demographic information, medical history, medication usage, baseline neurologic examination results, time of hospital admission, angiography data, imaging times, and neurologic examination findings at 24 hours and 3 months were extracted from patient records. The demographic data and door duration for the patients are presented in Table 1. Additionally, we aimed to assess the clinical outcomes and intracerebral hemorrhage status of patients at our stroke center using qualitative criteria. The qualitative criteria employed included symptom puncture, symptom recanalization, puncture recanalization, door imaging, door iv tPA administration, and door puncture times.

Patient Selection

The study included patients with occlusion of the P1 segment of the basilar artery (BA), posterior cerebral artery (PCA), ICA (tandem, T, L), or M1 segment of the MCA, as determined by computed tomography (CT) of the brain, provided that there was no evidence of bleeding. Eligible participants had an Alberta Stroke Program Early Computed Tomography (ASPECT) score greater than 6. Patients with ASPECT scores below 6 were not included in the study because it was thought that this would affect bleeding rates. Since our study was classified according to

the NIHSS score, NIHSS limitation was not considered in the inclusion criteria. Additionally, participants had a pre-stroke modified Rankin Scale (MRS) score of 0-1, a symptom-to-door time of less than 4.5 hours, or a symptom-to-door time ranging from 4.5 to 16 hours. There were no ischemic lesions observed on magnetic resonance imaging (MRI) in the FLAIR sequence, and all patients underwent MT. Patients with an ASPECT score of less than 6 or those with bleeding on brain CT were excluded from the study.

Patients were categorized into three groups based on their NIHSS scores, MRS scores, and the presence or absence of intracranial hemorrhage. The NIHSS scores were further subdivided into four categories: 0-5, 5-10, 10-20, and ≥ 21 . The MRS scores were classified into three groups: 0-2, 3-5, and 6. Additionally, patients were divided into two groups based on the presence or absence of intracranial hemorrhage at the 24-hour mark.

Endovascular Treatment

Upon presentation at the emergency department, patients were evaluated by a neurologist. All patients underwent non-contrast brain CT and computed tomography angiography (CTA). Those without contraindications who presented within the first 4.5 hours after the onset of symptoms, as well as those admitted within 16 hours without ischemic lesions evident on magnetic resonance imaging (MRI) FLAIR sequences, were administered alteplase at a dosage of 0.9 mg/kg in the emergency department before being transferred to the angiography unit for MT.

Clinical evaluation scales were employed to assess early ischemic changes on cranial CT using the ASPECT scoring system (10). The modified Tan scoring system was utilized to determine the collateral score on CTA (11). The level of recanalization was assessed according to the modified Treatment in Cerebral Ischemia (mTICI) classification (12). Specifically, mTICI 0 was characterized by the absence of flow, mTICI 1 indicated filling of the distal MCA without blood supply to the cortical branches, mTICI 2a represented filling of less than half of the MCA irrigation area, mTICI 2b denoted filling of more than half of the MCA irrigation area, mTICI 2c indicated filling of the entire MCA irrigation area but at a slower rate than the normal side, and mTICI 3 signified complete recanalization. Following the initial thrombectomy attempt, mTICI 2c-3 recanalization was classified as first-pass recanalization. Intracerebral hemorrhages observed on brain CT at 24 hours post-MT were evaluated according to the criteria established by the European Cooperative Acute Stroke Study (ECASS III). Hemorrhages that resulted in an increase of ≥ 4 points in the NIHSS score at admission were classified as symptomatic intracerebral hemorrhage (ICH). The disability status at 90 days was assessed using the MR.

Statistical Analysis

Statistical analysis was conducted utilizing various descriptive statistics, including mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was assessed using the Kolmogorov-Smirnov test and the Shapiro-Wilk test. For the analysis of quantitative independent data, ANOVA

(with Tukey's post-hoc test), the Kruskal-Wallis test, and the Mann-Whitney U test were employed. The Chi-square test was utilized for the analysis of qualitative independent data, while Fisher's exact test was applied when the conditions for the Chi-square test were not satisfied. The statistical analyses were performed using SPSS version 28.0.

RESULTS

The mean age of the patients in this study was 69.5 years (standard deviation: 16.7; range: 21.0-96.0). Among the total of 132 patients, 76 (55%) were male and 62 (45%) were female. A total of 57 patients (47%) were identified as smokers, 87 patients (63%) had a diagnosis of hypertension, 75 patients (54%) had atrial fibrillation, 54 patients (39%) had coronary artery disease, 29 patients (21%) had diabetes, and 37 patients (27%) were classified as obese. Additionally, 26 patients (19%) had a prior history of stroke. Thirteen patients (11%) were receiving warfarin,

while 23 patients (17%) were on newer generation oral anticoagulants.

The mean admission ASPECT score was 9.3 (standard deviation: 0.9; range: 6.0-10.0), and 59 patients (43%) received iv tPA. Among the 138 patients who underwent thrombectomy, the mean time from symptom onset to puncture was 247.9 minutes (standard deviation: 166.6), the mean time from symptom onset to recanalization was 303.1 minutes (standard deviation: 171.8), and the mean time from puncture to recanalization was 53.3 minutes (standard deviation: 17.9). The mean door-to-imaging time was 18.8 minutes (standard deviation: 16.6), the mean door-to-TPA time was 48.7 minutes (standard deviation: 20.7), and the mean door-to-puncture time was 55.4 minutes (standard deviation: 17.0). Furthermore, successful reperfusion, defined as TICl scores of 2B, 2C, or 3, was achieved in 118 out of 130 patients (85%) (see Table 1).

Table 1. Demographic data and door durations			
		Min-Max	Median
Age		21.0-96.0	75.0
Sex	Woman		76 (55)
	Man		62 (45)
Cigarette smoking	(-)		81 (59)
	(+)		57 (41)
Comorbid disease			
Hypertension			87 (63)
Atrial fibrillation			75 (54)
Coronary artery disease			54 (39)
Diabetes mellitus			29 (21)
Obesity			37 (27)
Stroke history	(-)		112 (81)
	(+)		26 (19)
Large vessel occlusion	(-)		0 (0)
	(+)		138 (100)
Warfarin use	(-)		123 (89)
	(+)		15 (11)
NOAC use	(-)		115 (83)
	(+)		23 (17)
IV TPA	(-)		79 (57)
	(+)		59 (43)
Admission ASPECT		6.0-10.0	10.0
Symptom puncture time		30.0-730.0	202.5
Symptom recanalization time		90.0-810.0	252.5
Puncture recanalization time		10.0-125.0	50.0
Door imaging time		5.0-120.0	15.0
Door TPA time		20.0-110.0	45.0
Door puncture time		15.0-90.0	56.0
TICl score	0		13 (10)
	2A		7 (5)
	2B		35 (25)
	2C		22 (16)
	3		61 (44)

SD: standard deviation, ASPECT: Alberta Stroke Programme Early CT score, NOAC: new oral anticoagulant, IV TPA: intravenous tissue plasminogen activator, TICl: treatment in cerebral ischemia

The mean NIHSS admission score was 10.4±3.3, while the NIHSS score at the 24th hour was 6.2±5.0. The MRS score at three months was recorded as 2.2±2.1. First-pass recanalization was successfully achieved in 57 out of 138 patients, representing 41.4% of the cohort. The incidence of bleeding at the 24-hour mark was observed in 40 out of 138 patients, equating to a rate of 29%. Antiplatelet therapy was initiated in 54 out of 138 patients (39%), based on the indication-contraindication status following the control CT scan conducted after 24 hours. Among the patients, 71 out of 138 (52%) exhibited good collateral flow (defined as >50% collateral flow), while 11 out of 138 patients (8%) received salvage therapy (refer to Table 2).

Table 2. NIHSS score and other general information				
		Min-Max	Median	Mean±SD/n (%)
NIHSS score				
Admission		4.0-22.0	10.0	10.4±3.3
24th hour		0.0-25.0	4.0	6.2±5.0
3rd month MRS		0.0-6.0	2.0	2.2±2.1
First pass recanalization	(-)			81 (58.6)
	(+)			57 (41.4)
Distal embolism	(-)			78 (57)
	(+)			60 (43)
sICH in 24 hours	(-)			98 (71)
	(+)			40 (29)
Antiaggregant therapy	(-)			84 (61)
	(+)			54 (39)
Tan score	(-)			28 (20)
	<50%			39 (28)
	50-99%			51 (37)
	100%			20 (15)
MRS: Modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, sICH: symptomatic intracranial hemorrhage				

Patients were categorized into three groups based on their scores on the NIHSS, the MRS, and the presence or absence of intracranial hemorrhage. Within these categories, the NIHSS scores were further divided into four groups: 0-5, 6-10, 11-20, and ≥21. The MRS scores were classified into three groups: 0-2, 3-5, and 6. Additionally, patients were grouped according to the presence or absence of intracranial hemorrhage at the 24-hour mark. The times for symptom onset and recanalization did not show significant differences (p>0.05) among the groups classified by NIHSS scores of 0-5, 6-10, 11-20, and ≥21. Furthermore, the values for door imaging, door-to-TPA administration, and door puncture did not differ significantly (p>0.05) across the same NIHSS score groups (see Table 3).

Table 3. Relationship of qualitemetric measures with NIHSS score						
		NIHSS score 0-5	NIHSS score 6-10	NIHSS score 11-20	NIHSS score ≥21	p
Symptom puncture time	Mean±SD	310.8±227.7	223.2±159.6	269.6±176.6	165.0±	0.450 ^K
	Median	287.5	170.0	210.0	165.0	
Symptom recanalization time	Mean±SD	374.4±232.6	274.6±160.1	333.0±188.3	220.0±	0.258 ^K
	Median	349.5	220.0	271.0	220.0	
Puncture recanalization time	Mean±SD	63.6±16.4	51.6±18.0	61.1±29.7	55.0±	0.203 ^K
	Median	60.0	50.0	52.5	55.0	
Door imaging time	Mean±SD	20.9±18.8	18.1±14.6	19.7±16.5	9.0±	0.616 ^K
	Median	15.0	15.0	15.0	9.0	
Door TPA time	Mean±SD	62.0±27.5	52.9±19.8	43.7±18.7	±	0.056 ^K
	Median	55.0	50.0	40.0	0.0	
Door puncture time	Mean±SD	65.0±17.6	57.3±17.0	54.0±17.8	50.0±	0.186 ^K
	Median	72.5	60.0	52.5	50.0	
First pass recanalization						
First pass	n (%)	8 (40.0)	47 (53.4)	44 (69.8)	1 (100)	p>0.05 ^{X²}
Repeating	n (%)	4 (20.0)	18 (20.5)	16 (25.4)	0 (0.0)	
K Kruskal-Wallis (Mann-Whitney U test) / X² Chi-squaretest (Fischer test); NIHSS: National Institutes of Health Stroke Scale, TPA: tissue plasminogen activator						

The times for symptom puncture and symptom recanalization did not exhibit significant differences ($p>0.05$) among the groups categorized by MRS scores of 0-I-II, III-IV-V, and VI. Additionally, no significant differences ($p>0.05$) were observed between the MRS 0-I-II, III-IV-V, and VI groups regarding puncture recanalization, door imaging, door iv tPA administration, and door puncture values.

However, the TICl stage was significantly higher ($p<0.05$) in the MRS 0-I-II group compared to the MRS III-IV-V and VI groups. Furthermore, the first-pass recanalization rate was significantly higher ($p<0.05$) in the MRS III-IV-V group than in the MRS 0-I-II group. No significant difference ($p>0.05$) was found in the first-pass recanalization rate between the MRS VI group and the MRS 0-I-II and III-IV-V groups (see Table 4).

Table 4. Comparison of MRS groups

			¹ MRS 0-I-II	² MRS III-IV-V	³ MRS VI	p
Symptom puncture time	Mean±SD		256.6±178.9	237.3±156.7	240.4±179.2	0.910 ^K
	Median		200.0	185.0	180.0	
Symptom recanalization time	Mean±SD		310.9±182.8	310.0±168.1	296.3±194.6	0.792 ^K
	Median		230.0	262.5	225.0	
Puncture recanalization time	Mean±SD		54.0±18.6	71.9±37.5	52.3±20.3	0.062 ^K
	Median		51.0	62.0	45.0	
Door imaging time	Mean±SD		18.8±17.3	20.2±12.3	18.4±13.5	0.327 ^K
	Median		15.0	15.0	15.0	
Door TPA time	Mean±SD		49.9±19.7	59.9±19.7	46.1±24.8	0.061 ^K
	Median		45.0	55.0	40.0	
Door puncture time	Mean±SD		55.5±16.7	62.0±20.3	54.8±17.0	0.246 ^K
	Median		60.0	60.0	50.0	
TICI	0	n (%)	2 (2.2)	5 (20.8)	6 (26.1)	0.000 ^X
	II A	n (%)	2 (2.2)	4 (16.7)	1 (4.3)	
	II B	n (%)	22 (24.2)	6 (25.0)	7 (30.4)	
	II C	n (%)	12 (13.2)	6 (25.0)	4 (17.4)	
	III	n (%)	53 (58.2)	3 ¹ (12.5)	5 ¹ (21.7)	
First pass recanalization						
First pass	n (%)		59 ² (64.8)	23 (95.8)	18 (78.3)	0.008 ^X
Repeating	n (%)		32 (35.2)	1 (4.2)	5 (21.7)	
K Kruskal-Wallis (Mann-Whitney U test) / X ² Chi-square test; ¹ Difference with MRS 0-I-II group p<0.05, ² Difference with MRS III-IV-V group p<0.05; MRS: Modified Rankin Scale. TPA: tissue plasminogen activator. TICI: treatment in cerebral ischemia						

K Kruskal-Wallis (Mann-Whitney U test) / X² Chi-square test; ¹Difference with MRS 0-I-II group $p<0.05$, ²Difference with MRS III-IV-V group $p<0.05$; MRS: Modified Rankin Scale, TPA: tissue plasminogen activator, TICl: treatment in cerebral ischemia

At the 24-hour mark, there were no significant differences ($p>0.05$) in symptom puncture time and symptom recanalization time between the groups with and without bleeding. Additionally, at 24 hours, the parameters of door imaging, door iv tPA, and door puncture value also did not exhibit significant differences ($p>0.05$) between the two groups. However, within the group that experienced bleeding

at 24 hours, the TICl stage was significantly lower ($p<0.05$) compared to the group without bleeding. Furthermore, the MRS score at three months was significantly higher ($p<0.05$) in the bleeding group than in the non-bleeding group at the 24-hour assessment. Lastly, the tan score in the bleeding group at 24 hours was significantly lower ($p<0.05$) than that of the non-bleeding group (see Table 5).

Table 5. Comparison of groups with and without intracranial hemorrhage

		sICH (-)		sICH (+)		p
		Mean±SD/n (%)	Median	Mean±SD/n (%)	Median	
Symptom puncture time		248.1±176.3	180.0	256.3±171.5	197.5	0.609 ^m
Symptom recanalization time		306.0±183.0	227.5	313.6±178.9	252.5	0.644 ^m
Puncture recanalization time		57.6±24.3	57.5	54.9±23.7	54.5	0.398 ^m
Door imaging time		17.6±13.5	15.0	22.9±20.5	15.0	0.127 ^m
Door TPA time		50.4±19.3	45.0	53.8±28.3	45.0	0.961 ^m
Door puncture time		56.3±18.0	60.0	57.1±16.4	56.5	0.877 ^m
TICl	0	10 (10.5)		3 (7.1)		0.000^X
	IIA	3 (3.1)		4 (9.5)		
	II B	21 (21.8)		14 (33.3)		
	II C	15 (15.6)		7 (16.7)		
	III	47 (49.0)		14 (33.3)		
First pass recanalization	First pass	66 (68.0)		34 (82.9)		0.074 ^X
	Repeating	31 (32.0)		7 (17.1)		
3rd month MRS		1.6±0.0	1.0	3.2±1.0	2.0	0.001^m

^mMann-Whitney U test / X² Chi-square test; sICH: symptomatic intracranial hemorrhage, TPA: tissue plasminogen activator, TICl: treatment in cerebral ischemia, MRS: Modified Rankin Scale

DISCUSSION

This study, conducted at a stroke center that has recently completed its first year of operation, presents novel insights into the relationship between treatment duration and perfusion achieved through endovascular recanalization.

In our study, the cohort of patients who underwent MT predominantly consisted of an elderly population, with a mean age of 69.5 years. The distribution of gender and the prevalence of comorbid conditions varied across the literature; in our study, the proportion of female patients was 45%, which was equal to that of male patients. The following comorbidities were observed: hypertension in 63% of patients, atrial fibrillation in 54%, coronary artery disease in 39%, diabetes in 21%, obesity in 27%, and a history of stroke in 19%. Additionally, 11% of the patients were receiving warfarin, while 17% were on newer generation oral anticoagulants (2-7).

In the study, the durations for door-imaging, door-TPA, and door-puncture were consistent with international quality guidelines as well as the timeline outlined in the quality guidelines published by the Ministry of Health (8,13-15). Compliance with these standards was achieved through frequent in-service training and tailoring emergency department operations to acute stroke management.

Teamwork, experience, and effective coordination are critical components in stroke centers. Chatterjee et al. (16,17) found that the density of the emergency department did not influence imaging and thrombolysis times for patients presenting with acute stroke. In contrast, Reznick et al. reported that increased crowding was associated with prolonged time from patient arrival to imaging. Furthermore, Arrate et al. demonstrated that stroke severity significantly impacted the time from arrival to imaging, identifying stroke severity as the primary determinant of patient management and care timelines (18). Additionally, another study indicated that patients with NIHSS scores ranging from 16 to 25 had a higher likelihood of completing the imaging procedure within 25 minutes, while patients with scores exceeding 25 experienced delays in imaging due to medical complications, such as loss of airway control (19). In our study, which categorized patients based on NIHSS scores of 0-5, 6-10, 11-20, and ≥ 21 , we observed that the NIHSS score did not significantly affect the duration from the patient's presentation in the emergency department to the initiation of effective treatment, consistent with the findings of Sauser et al. (20). This result can be explained by the fact that the same procedures are applied to all patients in the emergency department in case of stroke rather than the severity of the stroke.

In previous studies, the impact of early reperfusion on favorable clinical outcomes has been established; however, due to the limitations associated with patient selection, there is a pressing need for larger, data-driven investigations (13-15,21). It has been observed that patients who undergo early revascularization tend to exhibit improved functional outcomes. Specifically, a shorter duration of vessel

occlusion is associated with fewer sequelae, which may contribute to enhanced patient outcomes (22-26). In our study, the time to symptom recanalization did not show a significant difference among the MRS groups 0-I-II, III-IV-V, and VI. Nevertheless, a significant correlation was identified between the modified TIC1 score and both clinical outcomes and successful recanalization. Furthermore, our findings indicated that the incidence of symptomatic intracranial hemorrhage was significantly lower in patients demonstrating good recanalization, underscoring the critical importance of effective endovascular treatment over merely early intervention. Additionally, consistent with existing literature, the MRS scores were higher, and the tan scores were significantly lower in the hemorrhagic group compared to the non-hemorrhagic group, suggesting that multiple factors influence favorable clinical outcomes (27,28).

CONCLUSION

In our study, we did not identify a correlation between stroke severity and the quality-metric times observed in the emergency department. It is possible that different outcomes may emerge if studies are conducted with larger populations. A well-trained team and effective interdepartmental coordination are essential for more efficient and timely treatment of acute stroke. The coordination of all components within the neurology and emergency medicine departments, which is critical in the context of acute stroke, should be meticulously organized with respect to diagnosis and time management. Acute stroke patients should be treated quickly and effectively regardless of NIHSS intensity. There should be an experienced team and a standardized in-hospital procedure for acute stroke patients.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: This study received approval from the Clinical Studies Ethics Committee of University of Health Sciences Haseki Training And Research Hospital (Decision No: 261-2023) and was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2095-2128. Erratum in: *Lancet*. 2013;381:628.
2. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intra-arterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11-20. Erratum in: *N Engl J Med*. 2015;372:94.
3. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372:2285-95.

4. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296-306.
5. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344-418. Erratum in: *Stroke*. 2019;50:e440-1.
6. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378:708-18.
7. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378:11-21.
8. T.C. Sağlık Bakanlığı Sağlık Hizmetleri Genel Müdürlüğü Araştırma, Geliştirme ve Sağlık Teknolojisi Değerlendirme Dairesi Başkanlığı. Akut İskemik İnme Tanı ve Tedavi Rehberi, Version 1.0. Ankara: Çankaya. Republic of Turkey Ministry of Health. 2020;14-43.
9. Di Somma S, Paladino L, Vaughan L, et al. Overcrowding in emergency department: an international issue. *Intern Emerg Med*. 2015;10:171-5.
10. Barber PA, Demchuk AM, Zhang J, et al. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS study group. Alberta Stroke Program Early CT Score. *Lancet*. 2000;355:1670-4. Erratum in: *Lancet* 2000;355:2170.
11. Zhang S, Chen W, Tang H, et al. The prognostic value of a four-dimensional CT angiography-based collateral grading scale for reperfusion therapy in acute ischemic stroke patients. *PLoS One*. 2016;11:e0160502.
12. Zaidat OO, Castonguay AC, Linfante I, et al. First-pass effect: A new measure for stroke thrombectomy devices. *Stroke*. 2018;49:660-6.
13. Mueller-Kronast NH, Zaidat OO, Froehler MT, et al. STRATIS Investigators. Systematic evaluation of patients treated with neurothrombectomy devices for acute ischemic stroke: primary results of the STRATIS registry. *Stroke*. 2017;48:2760-8.
14. Saver JL, Goyal M, van der Lugt A, et al. HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279-88.
15. Sheth SA, Jahan R, Gralla J, et al. SWIFT-STAR trialists. Time to endovascular reperfusion and degree of disability in acute stroke. *Ann Neurol*. 2015;78:584-93.
16. Chatterjee P, Cucchiara BL, Lazarciuc N, et al. Emergency department crowding and time to care in patients with acute stroke. *Stroke*. 2011;42:1074-80.
17. Rezek MA, Murray E, Youngren MN, et al. Door-to-imaging time for acute stroke patients is adversely affected by emergency department crowding. *Stroke*. 2017;48:49-54.
18. Olascoaga Arrate A, Freijo Guerrero MM, Fernández Maiztegui C, et al. Use of emergency medical transport and impact on time to care in patients with ischemic stroke. *Neurologia (Engl Ed)*. 2019;34:80-8.
19. Kelly AG, Hellkamp AS, Olson D, et al. Predictors of rapid brain imaging in acute stroke: analysis of the Get With the Guidelines-Stroke program. *Stroke*. 2012;43:1279-84.
20. Sauser K, Bravata DM, Hayward RA, et al. A national evaluation of door-to-imaging times among acute ischemic stroke patients within the Veterans Health Administration. *J Stroke Cerebrovasc Dis*. 2015;24:1329-32.
21. Zaidat OO, Castonguay AC, Nogueira RG, et al. TREVO stent-retriever mechanical thrombectomy for acute ischemic stroke secondary to large vessel occlusion registry. *J Neurointerv Surg*. 2018;10:516-24.
22. Mishra SM, Dykeman J, Sajobi TT, et al. Early reperfusion rates with IV tPA are determined by CTA clot characteristics. *AJNR*. 2014;35:2265-72.
23. Behrens L, Möhlenbruch M, Stampfl S, et al. Effect of thrombus size on recanalization by bridging intravenous thrombolysis. *Eur J Neurol*. 2014;21:1406-10.
24. Seners P, Delepiepierre J, Turc G, et al. Thrombus length predicts lack of post-thrombolysis early recanalization in minor stroke with large vessel occlusion. *Stroke*. 2019;50:761-4.
25. Ospel JM, Singh N, Almekhlafi MA, et al. Early recanalization with alteplase in stroke because of large vessel occlusion in the ESCAPE trial. *Stroke*. 2021;52:304-7. Erratum in: *Stroke*. 2021;52:e92.
26. Saver JL. Time is brain—quantified. *Stroke*. 2006;37:263-6.
27. Liebeskind DS, Saber H, Xiang B, et al. Collateral circulation in thrombectomy for stroke after 6 to 24 hours in the DAWN trial. *Stroke*. 2022;53:742-8.
28. Liebeskind DS, Jahan R, Nogueira RG, et al. Early arrival at the emergency department is associated with better collaterals, smaller established infarcts and better clinical outcomes with endovascular stroke therapy: SWIFT study. *J Neurointerv Surg*. 2016;8:553-8.



Our Surgical Treatment Results for Suprarenal Masses: Single-Center Study

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Abstract

Aim: The study was focused on examining the results of surgical management of adrenal tumors treated at our center as well as comparing different types of surgeries especially laparoscopic and open approaches.

Material and Method: We retrospectively analyzed data from 82 patients who underwent surgery for adrenal masses at Dicle University Medical Faculty between 2010 and 2020. Patients were categorized into laparoscopic and open surgery groups based on surgical technique, and further classified as functional/non-functional and benign/malignant according to tumor characteristics. Demographic data, tumor characteristics, surgical outcomes, and complications were evaluated.

Results: The mean age of patients was 45.3 ± 14.2 years, with females comprising 58.5% of the cohort. Laparoscopic surgery was performed in 70.7% of cases, while 29.3% underwent open surgery. The mean operative time was significantly shorter in the laparoscopic group (115.4 ± 32.6 minutes) compared to the open surgery group (148.8 ± 45.3 minutes) ($p < 0.05$). Intraoperative blood loss was significantly lower in the laparoscopic group (150 ± 75 ml vs 325 ± 180 ml, $p < 0.05$). Functional tumors were present in 26.8% of patients, while 73.2% had non-functional tumors. Histopathological evaluation revealed benign tumors in 84.1% of cases and malignant tumors in 15.9%.

Conclusion: Laparoscopic approach represents a safe and effective method for surgical treatment of adrenal masses in selected patients. However, open surgery should be preferred for large tumors and cases with suspected malignancy. Treatment planning should be individualized for each patient, with surgical approach selection based on tumor characteristics and patient-specific factors.

Keywords: Surgical management, adrenal masses, laparoscopic adrenalectomy

INTRODUCTION

The implementation of minimally invasive techniques in the surgical management of adrenal masses has significantly improved patient outcomes (1). The recognition of functional hormonally active tumors constitutes a significant step in the treatment approach within adjuvant treatment (2). Particularly, laparoscopic adrenalectomy has offered a less invasive approach, reducing complication rates and enhancing patient comfort (3). Moreover, extensive retrospective analyses have demonstrated that large adrenal tumors can be managed more effectively through open surgery (4). According to a study, tumor classification and its degree of malignancy are determined ultimately by the pathological and clinical

findings which are compiled after surgical intervention (5). Additionally, advances in preoperative imaging techniques have improved the accuracy of pre-surgical diagnosis (6).

Using minimally invasive methods in the surgical treatment of adrenal masses is a contemporary approach which targets the improvement of clinical outcome with the reduction of complications. It is proposed in this study that laparoscopic approaches are allegedly less destructive in nature and are therefore likely to enable faster recovery and lower postoperative complications. As a supporting hypothesis, factors such as tumor size and hormonal secretion play a determinative role in surgical method selection, suggesting that particularly large tumors can be treated more effectively through open surgery.

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The selection of surgical approach is influenced not only by technical advantages but also by the patient's general health status and comorbidities. Recent research on minimally invasive approaches in the surgical treatment of adrenal masses provides significant data for improving both surgical outcomes and patient satisfaction. Particularly, retroperitoneoscopic adrenal tumor enucleation has emerged as an effective method for safely removing small adrenal tumors with low malignancy potential. This method that has been used offers survival to functional adrenal tissue and therefore decreases the risk of adrenal insufficiency (7). Furthermore, innovations in endourological surgery, such as the use of disposable ureteroscopes and laser lithotripsy methods, are enhancing the efficacy of minimally invasive procedures (8). Moreover, it has been demonstrated that the use of artificial intelligence programs enhances clinical efficiency during the procedure's decision making in urology surgery (9). All of them taken together suggest that adrenal surgical procedures ought to be modified appropriately to the needs of specific patients.

The main aim of the current study was to evaluate the demographic, tumor characteristics, surgical techniques and outcomes of patients who surgically treated adrenal masses in our clinic. Open surgery and minimally invasive laparoscopic surgery methods are compared, surgery of functional and non functional adrenal tumors is evaluated in terms of the results of the therapy applied and the postoperative complications encountered are examined. In this light, we hope to add to the existing literature based on our single center experience and help surgeons with respect to their selection of devices and methods, especially for adrenal mass removal.

MATERIAL AND METHOD

Study Design and Patient Selection

This retrospective cohort study, titled "Our Surgical Outcomes in Adrenal Mass Treatment: A Single-Center Study," was conducted at the Department of General Surgery, Dicle University Faculty of Medicine. The study was designed according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies. Primary outcomes were defined as operative time, blood loss, and complication rates, while secondary outcomes included length of hospital stay and conversion rates. Sample size calculation was performed using G*Power 3.1.9.7 software, with 80% power, 0.05 type I error, and 0.5 effect size, yielding a total of 82 patients, of whom 70.7% (n=58) comprised the laparoscopic group and 29.3% (n=24) the open surgery group. Patient allocation to surgical groups was based on tumor characteristics, surgeon preference, and patient-specific factors, following our institution's standardized protocol for adrenal surgery. Data from 82 patients who underwent adrenalectomy for adrenal masses between January 2010 and January 2020 were retrospectively analyzed.

The study included patients over 18 years of age who underwent adrenalectomy for adrenal masses, had complete surgical and pathology records, and comprehensive preoperative imaging and laboratory examinations. Exclusion criteria encompassed patients under 18 years of age, those with incomplete surgical and follow-up records, and patients operated on for non-adrenal pathologies. Data collection was performed independently by two researchers using a standardized data extraction form, with any discrepancies resolved through consensus. The study protocol was approved by the Ethics Committee of Dicle University Faculty of Medicine (approval number: 197, dated 25.03.2021).

Preoperative Assessment

Medical records of included patients were reviewed to document basic demographic information including age, sex, and body mass index, along with presenting complaints, comorbidities, and American Society of Anesthesiologists (ASA) scores. Body Mass Index (BMI) was calculated using the formula kg/m^2 based on patients' height and weight measurements. ASA scores were categorized according to the American Society of Anesthesiologists' classification as ASA I (healthy), ASA II (mild systemic disease), and ASA III (severe systemic disease). Comorbid conditions were determined through evaluation of existing diagnoses, current medications, and preoperative consultations, and were classified according to the ICD-10 coding system.

All patients underwent preoperative evaluation by endocrinologists. Blood cortisol and aldosterone levels were measured, along with plasma renin activity. Twenty-four-hour urinary metanephrine, normetanephrine, and vanillylmandelic acid levels were assessed. Patients underwent 1 mg dexamethasone suppression testing. Ultrasonography was the preferred initial imaging modality. Computed tomography (CT) or magnetic resonance imaging (MRI) was performed when deemed necessary. Preoperative biopsy was conducted in cases with suspected malignancy.

Surgical Method and Follow-up

Selection of surgical approach was based on tumor size, malignancy potential, and patient comorbidities. For laparoscopic procedures, a lateral retroperitoneal approach was employed using four ports. Open surgery was performed through a subcostal incision. Operative time, blood loss volume, and conversion rates from laparoscopic to open surgery were documented. Drainage tubes were placed in all patients. Postoperative complications (hemorrhage, surgical site infection, intestinal obstruction), length of hospital stay, duration of drain placement, and blood transfusion requirements were evaluated. Blood transfusions were administered to patients whose hemoglobin levels fell below 8 g/dl. Reasons for conversion from laparoscopic to open surgery (uncontrollable bleeding, severe adhesions, unexpected anatomical variations, tumor invasion into surrounding tissues, and technical difficulties) were recorded.

Pathological Examination and Metastatic Assessment

All resected specimens were examined by experienced pathologists. Tumor type, size, and malignancy status were determined. Tumor diameters were categorized into three groups: less than 4 cm, 4-6 cm, and greater than 6 cm. For metastatic tumors, patients' past medical records and imaging results were reviewed to identify the primary site of disease.

Statistical Analysis

Data analysis was performed using SPSS 25.0 software. The Kolmogorov-Smirnov test was employed for the evaluation of normality of data distribution. Numerical data were expressed as mean±standard deviation, while categorical data were presented as numbers and percentages. Independent samples t-test was used for comparing numerical data with normal distribution between two groups, while the Mann-Whitney U test was employed for non-normally distributed data. Chi-square test was used for comparing categorical variables, with Fisher's exact test applied when expected values were less than 5. One-way analysis of variance (ANOVA) with post-hoc Bonferroni test was used for comparisons involving more than two groups. For post-hoc analyses, the Bonferroni

correction was applied, with significance levels determined by dividing $p=0.05$ by the number of comparisons.

Logistic regression analysis was performed to identify factors influencing conversion from laparoscopic to open surgery. The regression model included age, sex, BMI, ASA score, tumor size, functional status, and suspicion of malignancy as independent variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

Analysis of demographic and clinical characteristics of the 82 patients included in the study revealed a mean age of 45.3 ± 14.2 years, with 58.5% female and 41.5% male patients. The mean body mass index was 27.4 ± 4.2 kg/m². According to ASA scoring, the majority of patients were classified as ASA II (54.9%), followed by ASA I (24.4%) and ASA III (20.7%). The most common presenting complaint was abdominal pain (31.7%), followed by hypertension (23.2%) and weight gain (9.8%). In 35.3% of patients, masses were discovered incidentally. Among comorbid conditions, hypertension was most prevalent (42.7%), followed by diabetes mellitus (26.8%), cardiovascular diseases (15.9%), and COPD (4.9%) (Table 1).

Table 1. Demographic and clinical characteristics		
Parameter	Value	p-value
Age (years) (mean±SD, min-max)	45.3±14.2 (17–75)	0.023*
Gender, n (%)		0.034*
Female	48 (58.5)	
Male	34 (41.5)	
BMI (kg/m²) (mean±SD)	27.4±4.2	0.045*
ASA score, n (%)		0.041*
ASA I	20 (24.4)	
ASA II	45 (54.9)	
ASA III	17 (20.7)	
Presenting symptoms, n (%)		0.028*
Abdominal pain	26 (31.7)	
Hypertension	19 (23.2)	
Weight gain	8 (9.8)	
Incidental	29 (35.3)	
Comorbidities, n (%)		0.037*
Hypertension	35 (42.7)	
Diabetes mellitus	22 (26.8)	
Cardiovascular disease	13 (15.9)	
COPD	4 (4.9)	

p<0.05 statistically significant; BMI: body mass index, ASA: American Society of Anesthesiologists, COPD: chronic obstructive pulmonary disease, SD: standard deviation

Regarding tumor characteristics, 51.2% of masses were located on the left side, 42.7% on the right side, and 6.1% were bilateral. The mean tumor size was 5.6 ± 2.4 cm. Functional assessment revealed that 26.8% of tumors were functional, while 73.2% were non-functional. Ultrasonography was the

most commonly used diagnostic method (70.7%), followed by MRI (17.1%) and CT (12.2%). Preoperative biopsy was performed in 22% of patients. Hormonal activity analysis showed excess cortisol in 11%, excess aldosterone in 6.1%, and excess catecholamine in 9.7% of cases (Table 2).

Table 2. Tumor characteristics

Parameter	Value	p-value
Tumor location, n (%)		0.031*
Right	35 (42.7)	
Left	42 (51.2)	
Bilateral	5 (6.1)	
Tumor size (cm) (mean±SD)	5.6±2.4	0.028*
Functional status, n (%)		0.042*
Functional	22 (26.8)	
Non-functional	60 (73.2)	
Radiological diagnostic method, n (%)		0.035*
USG	58 (70.7)	
CT	10 (12.2)	
MRI	14 (17.1)	
Preoperative biopsy, n (%)	18 (22.0)	0.044*
Hormonal activity type, n (%)		0.039*
Cortisol excess	9 (11.0)	
Aldosterone excess	5 (6.1)	
Catecholamine excess	8 (9.7)	

p<0.05 statistically significant; SD: standard deviation, USG: ultrasonography, CT: computed tomography, MRI: magnetic resonance imaging

In terms of surgical approach, 70.7% of patients underwent laparoscopic surgery, while 29.3% received open surgery. The mean operative time was 115.4±32.6 minutes in the laparoscopic group and 148.8±45.3 minutes in the open surgery group. Intraoperative blood loss was measured at 150±75 ml in the laparoscopic group and 325±180 ml in the open group. Conversion from laparoscopic to open surgery was necessary in 14.6% of cases. The mean length of hospital stay was 7.4±3.5 days, with drain removal occurring at 3.6±1.2 days postoperatively. Blood transfusion was required in 12.2% of patients (Table 3).

Table 3. Surgical characteristics and postoperative outcomes

Parameter	Value	p-value
Surgical approach, n (%)		0.027*
Laparoscopic	58 (70.7)	
Open	24 (29.3)	
Operation time (min) (mean±SD)		0.031*
Laparoscopic	115.4±32.6	
Open	148.8±45.3	
Intraoperative blood loss (mL) (mean±SD)		0.022*
Laparoscopic	150±75	
Open	325±180	
Conversion rate, n (%)	12 (14.6)	0.038*
Hospital stay (days) (mean±SD)	7.4±3.5	0.025*
Drain duration (days) (mean±SD)	3.6±1.2	0.042*
Blood transfusion requirement, n (%)	10 (12.2)	0.036*
Morbidity, n (%)		0.029*
Bleeding	4 (4.9)	
Wound infection	5 (6.1)	
Ileus	2 (2.4)	
Mortality, n (%)	0 (0)	1.000

p<0.05 statistically significant; SD: standard deviation, min: minutes, mL: milliliters

Analysis of functional status and patient distributions revealed that 73.2% of patients had non-functional tumors, while 26.8% had functional tumors. In terms of tumor type distribution, 84.1% were benign and 15.9% were malignant, with localization showing 51.2% left-sided, 42.7% right-sided, and 6.1% bilateral placement (Figure 1).

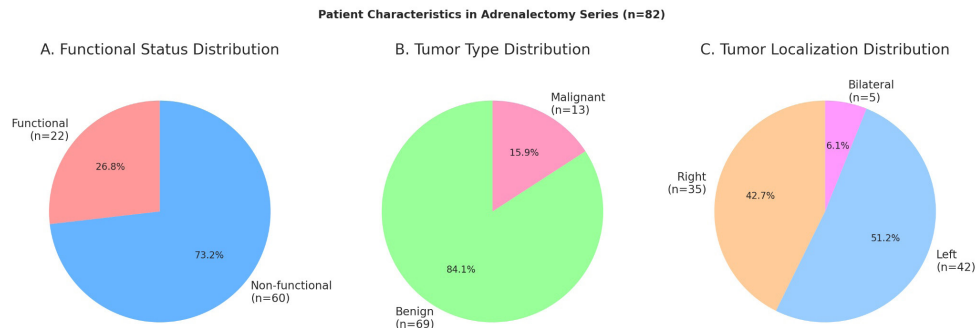


Figure 1. Distribution of patient characteristics in adrenalectomy series; **A.** Functional status distribution, **B.** Tumor type distribution, **C.** Tumor localization distribution

When evaluating surgical approach characteristics and complications, comparison between laparoscopic and open surgery showed significant differences in operative time and blood loss amounts. Analysis of postoperative complications revealed similar rates of hemorrhage, wound infection, and ileus in both groups (Figure 2).

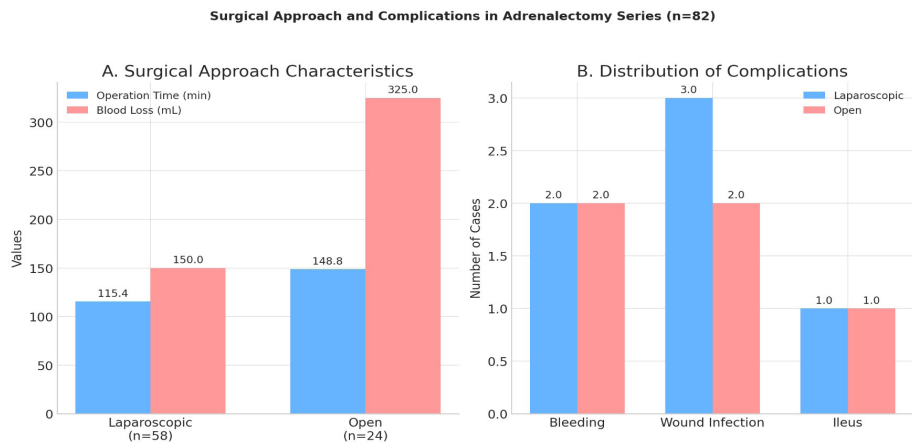


Figure 2. Surgical approach and complications in adrenalectomy series; **A.** Surgical approach characteristics (operation time and blood loss), **B.** Distribution of postoperative complications

Histopathological evaluation most commonly identified pheochromocytoma (24.4%) and adrenocortical neoplasia (25.6%), followed by adrenocortical adenoma (22%), metastatic cancer (15.8%), myelolipoma (7.3%), and ganglioneuroma (4.9%). Regarding malignancy status, 84.1% of patients had benign tumors, while 15.9% had malignant lesions. When categorized by tumor diameter, the majority of cases fell within the 4-6 cm range (47.6%), followed by >6 cm (29.2%) and <4 cm (23.2%) groups (Table 4).

Table 4. Histopathological results		
Parameter	Value	p-value
Histopathological diagnosis, n (%)		0.032*
Adrenocortical adenoma	18 (22.0)	
Pheochromocytoma	20 (24.4)	
Adrenocortical neoplasia	21 (25.6)	
Myelolipoma	6 (7.3)	
Ganglioneuroma	4 (4.9)	
Metastatic cancer	13 (15.8)	
Malignancy status, n (%)		0.028*
Benign	69 (84.1)	
Malignant	13 (15.9)	
Tumor size categories, n (%)		0.035*
<4 cm	19 (23.2)	
4–6 cm	39 (47.6)	
>6 cm	24 (29.2)	
p<0.05 statistically significant; n: number, cm: centimeters		

In the comparative analysis of functional and non-functional tumors, operation time was significantly longer in the functional group (138.6±42.8 vs 112.4±35.2 minutes). Similarly, blood loss volume was higher in the functional group (285±145 vs 168±95 ml). The mean length of hospital

stay was 8.6±3.8 days for functional tumors compared to 6.4±2.9 days in the non-functional group. Complication rates were 31.8% in the functional group and 6.7% in the non-functional group. Functional tumors also demonstrated larger diameters (6.8±2.4 vs 5.2±1.8 cm) (Table 5).

Table 5. Comparison of functional vs. non-functional tumors			
Parameter	Functional (n=22)	Non-functional (n=60)	p-value
Operation time (min) (mean±SD)	138.6±42.8	112.4±35.2	0.024*
Blood loss (mL) (mean±SD)	285±145	168±95	0.018*
Hospital stay (days) (mean±SD)	8.6±3.8	6.4±2.9	0.031*
Complication rate, n (%)	7 (31.8%)	4 (6.7)	0.028*
Tumor size (cm) (mean±SD)	6.8±2.4	5.2±1.8	0.022*
p<0.05 statistically significant; n: number, SD: standard deviation, min: minutes, mL: milliliters, cm: centimeters			

In metastatic adrenal gland tumors, the mean tumor size was 11.4±2.5 cm. Among these metastatic tumors, six were due to pancreatic adenocarcinoma and two were neuroendocrine tumor metastases. Histopathological examination of 36 patients who underwent laparoscopic adrenalectomy revealed 11 pheochromocytomas, 6 myelolipomas, 8 adenomas, 9 neoplasias, and 2 ganglioneuromas. Among 15 patients who underwent open adrenalectomy, 7 had metastatic tumors, 3 had pheochromocytomas, and 5 had adrenocortical neoplasia. In 8 cases excluding metastatic tumors, surgery was initiated laparoscopically but converted to open procedure.

Regarding postoperative complications, hemorrhage occurred in two patients total, one from each surgical group. Blood transfusion was administered to patients whose hemoglobin levels fell below 8 g/dl, and they were managed with medical treatment. Patients were discharged without requiring secondary surgical intervention. Drains were used in all patients and removed on postoperative day 3, except in the two patients with hemorrhage, whose drains were removed on postoperative day 7.

DISCUSSION

This research, which focuses on the surgical treatment of adrenal masses, intends to assess the results of surgical techniques applied at our facility and assess the results based on the use of either open or laparoscopic approaches. From what we have found, the advantages that come with performing minimally invasive surgery are more than enough to warrant its use as it has lower complications and faster recovery periods. However, in cases involving large tumors or those with high malignancy risk, open surgical approaches have proven more effective, particularly regarding surgical control. Moreover, the utilizing imaging and hormonal evaluations prior to the procedure has also been indicated to improve diagnostic accuracy parameters, hence increasing quality of surgical results. These data reinforce the necessity of optimizing surgical method selection based on tumor characteristics and patient-specific factors.

The findings obtained in this study reveal both commonalities and distinct variations when compared with existing literature regarding the clinical and demographic characteristics of adrenal incidentalomas. In this case, the average age of 45.3±14.2 years should be noted as it is significantly at the lower end of the spectrum of age as documented in the literature. According to published research, the prevalence of incidentalomas typically increases with age, with the average age at diagnosis ranging between 55-62 years (10,11). The explanation we may find for this younger age distribution in our study is purely demographic factors or differences in diagnostic methods.

Regarding gender distribution, our study identified a female predominance of 58.5%. This finding aligns with existing literature documenting a slightly higher prevalence of adrenal incidentalomas in women compared to men (10,12). For instance, Bancos and colleagues reported that women comprised 55% of incidentaloma cases, while men accounted for 45%. Abdominal pain emerged as the primary presenting complaint, accounting for 31.7% of cases. Although literature predominantly characterizes incidentalomas as asymptomatic, abdominal pain has been recognized as a frequent catalyst for initiating imaging studies (11). The incidental detection rate in our study was 35.3%, which falls within the reported literature range of 4-42% (10,11). In terms of comorbidities, hypertension (42.7%) and diabetes (26.8%) emerged as the most prevalent concurrent conditions. The literature consistently reports high frequencies of these comorbidities among patients with incidentalomas. For instance, Lee and colleagues documented hypertension prevalence ranging from 36-58% and diabetes prevalence between 20-40% (10). While our findings generally align with these ranges, the lower diabetes rate observed in our study may be attributed to population-specific variations. These results, it should be noted, are in line with the national and international literature on the diagnosis and clinical approach to patients with adrenal incidentalomas. However, observed variations in population age and incidentaloma prevalence

may reflect regional differences in clinical practice patterns. These prior factors may be critically reviewed in later research as they may have implications as far as patient care as well as the outcomes.

The predominant utilization of laparoscopic surgery at 70.7% demonstrates how this minimally invasive approach enhances patient outcomes. Fu et al. reported that laparoscopic surgery, compared to open surgery, correlates with reduced blood loss (-115.27 mL) and shorter hospital stays (-3.17 days) (13). In our study, blood loss was significantly lower in the laparoscopic surgery group compared to open surgery (150 mL vs 325 mL, $p < 0.05$). This notable difference in blood loss can be attributed to several factors, including better visualization and more precise dissection in laparoscopic surgery, while the higher blood loss in open surgery may be related to the management of more complex cases. Among the 12 cases (14.6%) that required conversion from laparoscopic surgery to open surgery, 3 cases (25%) were due to uncontrollable bleeding, and these cases were analyzed within the open surgery group. Comparing operative durations, laparoscopic surgery demonstrated shorter procedure times compared to open surgery (115.4 min vs. 148.8 min). Danwang et al. (2020) reported that laparoscopic surgery provides temporal advantages even in obese patients (14). Our conversion rate to open surgery was recorded at 14.6%, which aligns with literature-reported rates ranging between 3-5% (15). This outcome illustrates the limitations of the laparoscopic approach, particularly in cases presenting technical challenges. Regarding length of hospital stay, laparoscopic surgery group patients were discharged earlier with an average stay of 7.4 days. These achievements prove the efficiency of laparoscopic surgery as opposed as to open surgery because of shorter recovery time and lower complication rates (13). In conclusion, laparoscopic surgery should be the primary choice for suitable patients. However, open surgery maintains its significance in cases involving large tumors or complex anatomical situations (15).

In our study, analysis of adrenal tumor characteristics revealed a predominant localization in the left (51.2%) and right (42.7%) adrenal glands. Consistent with literature findings, there was a higher frequency of tumors in the left adrenal gland (16). The mean tumor size was determined to be 5.6 ± 2.4 cm, demonstrating concordance with dimensions reported in retrospective analyses (17). Functional tumors constituted 26.8% of cases, aligning with previously reported ranges of 20-30% (18). Pheochromocytoma emerged as one of the most frequent pathologies at 24.4%, while adrenocortical neoplasms accounted for 25.6% of cases. These findings correspond with the incidence of pheochromocytoma reported across various series (16). Furthermore, the malignancy rate was identified as 15.9%, supporting the previously established range of 12-20% in earlier studies (18).

In comparing surgical outcomes between functional and non-functional adrenal tumors, operative duration was notably longer in the functional group (138.6 min), a finding previously correlated with surgical challenges in hormone-active tumors (19). The elevated complication rate of 31.8% observed in functional tumors can be attributed to hormone-related perioperative hemodynamic fluctuations and thromboembolic risks (20). Additionally, the larger tumor size in the functional group (6.8 cm) supports the understanding that these tumors typically demonstrate enhanced growth potential due to hormonal activity (21). Length of hospital stay was significantly prolonged in cases involving functional tumors (8.6 days), a finding associated with the complexities of postoperative steroid management (19).

As far as the assessment of the adrenalectomy safety and outcomes is concerned, complication rates are very important. Our study documented post-adrenalectomy complications including bleeding (4.9%), surgical site infections (6.1%), ileus (2.4%), and transfusion requirements (12.2%), with zero mortality. These results tend to fall into the same range as values reported in the existing literature. Parente et al., in their multicenter study, reported an overall complication rate of 26.8%, with hemorrhage, wound infections, and postoperative ileus emerging as the most frequent complications (22). Their study emphasized that open surgical approaches significantly elevated complication risks. Similarly, Vlk et al. demonstrated that open surgical approaches, compared to laparoscopic procedures, were associated with increased complication rates and prolonged postoperative recovery periods (23).

Regarding transfusion requirements, our observed rate of 12.2% appears favorable compared to other studies reported in the literature. For instance, Parente et al. documented an intraoperative transfusion requirement rate of 18.3% due to bleeding complications (22). This disparity may be attributed to advancements in surgical techniques and increased surgeon experience levels.

Finally, the zero mortality rate observed in our study demonstrates the overall safety profile of adrenalectomy procedures. Mortality rates reported in the literature typically range between 0-0.8% (22). It is this evidence, which offers support to the statement, that risks minimal when undertaking the adrenalectomy procedures, is subjected to the selection of appropriately experienced surgeons.

The 15.8% rate of metastatic adrenal tumors identified in our study aligns with previously reported rates in the literature. For instance, Dages et al. reported that adrenal metastasis rates typically range between 10-20% (24). The mean tumor size of 11.4 ± 2.5 cm also demonstrates concordance with literature findings, where final analyses indicate metastatic adrenal tumors generally exceed 10 cm in diameter (25). The high incidence of pancreatic neuroendocrine tumors (panNETs) among primary

neuroendocrine neoplasms is a reflection of their relative frequency and clinical significance. Recent imaging-based analyses have shown that panNETs often present with advanced metastatic disease at diagnosis, which suggests that they may have an early propensity for dissemination, especially to the liver and regional lymph nodes (26).

Our study has several limitations. First, its single-center experience and retrospective design inherently limits the generalizability of findings. Due to a relatively small sample size, power for subgroup analyses may have been limited. However, the strength of the study includes a longer follow-up, extensive surgical and pathological data, and functional and non-functional tumors. Moreover, the detailed comparison between laparoscopic and open surgical results is also somewhat informative. Future research needs to be multicenter, prospective with larger patient cohorts especially with long term oncological outcomes for minimally invasive techniques with quality of life measures included. Also, researching robotic surgery for adrenal masses is a very meaningful discussion for the future of medicine.

CONCLUSION

In summary, laparoscopic surgery is a safe and effective method to surgically manage adrenal masses when adequate patient selection is performed. We showed that laparoscopic adrenalectomy is associated with shorter length of hospital stay, less blood loss and lower rates of complications. However, open surgery plays an important role in large tumors with malignancy suspicion. Surgical management of functional tumours requires high alertness and careful control of hormones, particularly with regard to the perioperative period.

Preoperative scans and hormonal mapping can be particularly useful for formulating the appropriate operative technique. Our experience shows us that each patient has unique treatment requirements, given this, the appropriate surgical methodology should select focusing tumor characteristics, patient factors as well as the surgeon's expertise.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: The study protocol was approved by the Ethics Committee of Dicle University Faculty of Medicine (approval number: 197, dated 25.03.2021).

REFERENCES

1. Fascetti-Leon F, Scotton G, Pio L, et al. Minimally invasive resection of adrenal masses in infants and children: results of a European multi-center survey. *Surg Endosc.* 2017;31:4505-12. Erratum in: *Surg Endosc.* 2017;31:4513.
2. Lenert JT, Barnett CC Jr, Kudelka AP, et al. Evaluation and surgical resection of adrenal masses in patients with a history of extra-adrenal malignancy. *Surgery.* 2001;130:1060-7.
3. Economopoulos KP, Mylonas KS, Stamou AA, et al. Laparoscopic versus robotic adrenalectomy: a comprehensive meta-analysis. *Int J Surg.* 2017;38:95-104.
4. Terzolo M, Ali A, Osella G, Mazza E. Prevalence of adrenal carcinoma among incidentally discovered adrenal masses. *Arch Surg.* 1997;132:914-9.
5. Lucchi M, Dini P, Ambrogio MC, et al. Metachronous adrenal masses in resected non-small cell lung cancer patients: therapeutic implications of laparoscopic adrenalectomy. *Eur J Cardiothorac Surg.* 2005;27:753-6.
6. Uttinger KL, Reibetanz J, Diers J, et al. Volume-outcome relationship in adrenal surgery from 2009-2017 in Germany—a retrospective study. *Eur J Endocrinol.* 2023;188:lvac013.
7. Yan H, Cao G, Cui X, et al. Retroperitoneoscopic enucleation adrenalectomy: a viable surgical option for small nonsecreting adrenal tumors with low potential of malignancy. *Transl Androl Urol.* 2023;12:1713-22.
8. Tzelvels L, Juliebø-Jones P, Somani B. Editorial: the evolution of minimally invasive urologic surgery: innovations, challenges, and opportunities. *Front Surg.* 2024;11:1525713.
9. Peng L, Liang R, Zhao A, et al. Amplifying Chinese physicians' emphasis on patients' psychological states beyond urologic diagnoses with ChatGPT - a multicenter cross-sectional study. *Int J Surg.* 2024;110:6501-8.
10. Bancos I, Prete A. Approach to the patient with adrenal incidentaloma. *J Clin Endocrinol Metab.* 2021;106:3331-53.
11. Okroj D, Rzepecka A, Kłosowski P, et al. Review of diagnostic modalities for adrenal incidentaloma. *J Clin Med.* 2023;12:3739.
12. Lee JM, Kim MK, Ko SH, et al. Clinical Guidelines for the Management of Adrenal Incidentaloma. *Endocrinol Metab (Seoul).* 2017;32:200-18.
13. Fu SQ, Zhuang CS, Yang XR, et al. Comparison of robot-assisted retroperitoneal laparoscopic adrenalectomy versus retroperitoneal laparoscopic adrenalectomy for large pheochromocytoma: a single-centre retrospective study. *BMC Surg.* 2020;20:227.
14. Danwang C, Agbor VN, Bigna JJ. Obesity and postoperative outcomes of the patients with laparoscopic adrenalectomy: a systematic review and meta-analysis. *BMC Surg.* 2020;20:194.
15. Davey MG, Ryan ÉJ, Donlon NE, et al. Comparing surgical outcomes of approaches to adrenalectomy - a systematic review and network meta-analysis of randomised clinical trials. *Langenbecks Arch Surg.* 2023;408:180.
16. Wang J, Yang B, Sun S, Zhang Y. Perioperative factors influencing the difficulty of retroperitoneal laparoscopic adrenalectomy: a single-center retrospective study. *BMC Urol.* 2022;22:22.
17. Samsel R, Cichocki A, Roszkowska-Purska K, et al. Adrenal metastases - long-term results of surgical treatment, single-centre experience. *Contemp Oncol (Pozn).* 2020;24:29-33.
18. Sabet FA, Majdzadeh R, Mostafazadeh Davani B, et al. Likelihood ratio of computed tomography characteristics for diagnosis of malignancy in adrenal incidentaloma: systematic review and meta-analysis. *J Diabetes Metab Disord.* 2016;15:12.

19. Aydin H, Dural AC, Sahbaz NA, et al. Hormonally active adrenal tumors; challenges and outcomes for different surgical approaches. *Sisli Etfal Hastan Tip Bul.* 2021;55:325-32.
20. Indrawan DH, Prapiska FF, Warli SM et al. Functional and non-functional types of adrenal tumors: a case series [version 1; peer review: 1 approved with reservations, 1 not approved]. *F1000Research.* 2021;10:675.
21. Herrera-Martínez AD, Rebollo Román Á, Pascual Corrales E, et al. Adrenal incidentalomas and other endocrine-related adenomas: how much does cortisol secretion matter?. *Cancers (Basel).* 2023;15:4735.
22. Parente A, Kamarajah SK, Thompson JP, et al. Risk factors for postoperative complications after adrenalectomy for pheochromocytoma: multicentre cohort study. *BJS Open.* 2023;7:zrad090.
23. Vlk E, Ebbehøj A, Donskov F, et al. Outcome and prognosis after adrenal metastasectomy: nationwide study. *BJS Open.* 2022;6:zrac047.
24. Dages KN, Kohlenberg JD, Young WF Jr, et al. Presentation and outcomes of adrenal ganglioneuromas: a cohort study and a systematic review of literature. *Clin Endocrinol (Oxf).* 2021;95:47-57.
25. Thompson LH, Ranstam J, Almquist M, et al. Impact of adrenalectomy on morbidity in patients with non-functioning adrenal cortical tumors, mild hypercortisolism and Cushing's syndrome as assessed by national and quality registries. *World J Surg.* 2021;45:3099-107.
26. Lee L, Ito T, Jensen RT. Imaging of pancreatic neuroendocrine tumors: recent advances, current status and controversies. *Expert Rev Anticancer Ther.* 2018;18:837-60.



Is Serum Tryptase a Dependable Biomarker for Diagnosing and Tracking Rheumatoid Arthritis?

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Abstract

Aim: Our aim in this study was to demonstrate that rheumatoid arthritis (RA) patients have an increase in serum tryptase concentrations and that this correlates with the level of disease activity.

Material and Method: The research involved 43 patients RA and 37 healthy participants as the control group. The average ages of the patients and the control group were 52.53±11.10 and 48.41±12.79 years, respectively. Sociodemographic information of all participants was recorded. Disease Activity Score 28 (DAS28), Health Assessment Questionnaire (HAQ) and Visual Analog Scale (VAS) scores were calculated after detailed examination to determine disease activity. Total serum tryptase concentrations were evaluated using enzyme-linked immunosorbent assay (ELISA).

Results: Serum tryptase levels were higher in the RA group compared to the healthy group and a statistically significant difference was found ($p<0.001$). A meaningful connection was detected between serum tryptase concentrations and DAS28, VAS and HAQ scores in RA patients ($p<0.05$). Erythrocyte sedimentation rate (ESR) and serum tryptase levels showed a notable and significant association ($p<0.05$). There was no statistically significant correlation between serum tryptase concentrations and C-reactive protein (CRP) ($p>0.05$).

Conclusion: The findings reveal that serum tryptase levels are upregulated in subjects with RA and demonstrate a correlation with disease activity. Serum tryptase may contribute to inflammation in RA.

Keywords: Biomarker, diagnosing, rheumatoid arthritis, serum tryptase

INTRODUCTION

Rheumatoid arthritis (RA) is a persistent intractable inflammatory entity of uncertain origin, typically accompanied by symmetrical polyarthritis. Along with the disease, various tissues and organs may be affected. In addition to the devastating damage it causes to joints, RA is connected to higher rates of morbidity and mortality, largely due to associated comorbidities and systemic effects. The inflammatory pathway in RA is stimulated by numerous cytokines, resulting in damage to the synovial joints and irreversible joint deterioration. Although RA is a common rheumatic disease, its prevalence has been reported as 0.5-1% (1-3).

Mast cells (MCs) originating in the bone marrow are particularly

reliant on stem cell factors to sustain their survival. Although they are primarily responsible for allergic inflammation, they can also cause chronic inflammation through the secretion of various chemokines and cytokines (4). MCs exist in two forms: tryptase-positive MCs (MCT) and MCs positive for both tryptase and chymase (MCTC). MCTC cells are found in normal synovium, while MCT cells increase in rheumatic diseases and may play a role in inflammation. Tryptase, a tetrameric serine protease, is primarily synthesized by MCs and stored in their secretory granules. Upon activation of MCs, tryptase is released through degranulation, along with other stored mediators, into the extracellular environment. This release plays a pivotal role in various immunological responses, including inflammation, tissue remodeling and immune modulation (5,6).

CITATION

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Serum tryptase is also involved in the etiopathogenesis of many diseases (7-9). The most important function of tryptase in these diseases is its pro-inflammatory effect. Elevated tryptase levels have been associated with allergic inflammation-related conditions such as allergic asthma and other mast cell-mediated diseases (10,11). Tryptase exerts its pro-inflammatory effects through various mechanisms. One such mechanism is the hypothesis of cytokine release and cell activation. In this case, tryptase stimulates endothelial cells to excrete pro-inflammatory cytokines, including interleukin-8 (IL-8) and interleukin-1 beta (IL-1 β), which promote leukocyte recruitment and adhesion. Additionally, tryptase activates microglia and astrocytes in the central nervous system, leading to the release of tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and reactive oxygen species via the protease-activated receptor 2 (PAR-2)-mitogen-activated protein kinase (MAPK)-NF- κ B signaling pathway (12-14). Secondly, tryptase contributes to tissue remodeling and matrix degradation by activating matrix metalloproteinases and other proteolytic enzymes. This activity is particularly important in diseases like asthma, where tryptase-induced airway remodeling and hyperresponsiveness are observed (10,11). Third, tryptase enhances the production of neutrophil extracellular traps, a system by which neutrophils capture and destroy pathogens. This interaction further amplifies the inflammatory response. (15). Fourth, in conditions such as inflammatory bowel disease, tryptase activates fibroblasts through the PAR-2/Akt/mTOR signaling pathway, triggering fibrosis and leading to excessive extracellular matrix deposition (9). Finally, tryptase plays a role in cardiovascular diseases by stimulating endothelial cell activation, increasing platelet-activating factor production, and inducing neutrophil adhesion, which contributes to vascular inflammation and damage (16,17). In conclusion, tryptase appears to be a key mediator in various inflammatory processes. Its ability to trigger the TNF- α , IL-6, and IL-1 β pathways, which are crucial in the pathogenesis of RA, may explain its significant role in this disease. Tryptase's role in these mechanisms positions it as a promising target for therapeutic interventions in inflammatory diseases.

This study sought to evaluate the link between serum tryptase levels and disease activity in RA, as well as to assess the potential of tryptase as a biomarker for inflammatory response. Given the limited data regarding the role of tryptase in RA pathogenesis, this study aims to make an important and novel contribution to the field.

MATERIAL AND METHOD

Participants

This cross-sectional, single-centre study was performed in the Physical Therapy and Rehabilitation Clinic of a Recep Tayyip Erdoğan University Training and Research Hospital with 43 RA patients diagnosed based on the 2010 American College of Rheumatology (ACR) diagnostic criteria and 37 healthy individuals as the control group. A detailed history was taken, and systemic and rheumatologic examinations were performed in all participants. Sociodemographic,

clinical, and laboratory measurements were obtained from RA subjects for comparison with the control group. Subjects with a history of malignancy, those under 18 or over 75 years of age, those with advanced heart failure, advanced renal failure, acute infections, demyelinating diseases, idiopathic anaphylaxis, unexplained abdominal pain and/or cramping and/or syncope, other rheumatic diseases, psoriasis, atopic dermatitis, food allergies, drug allergies, venom allergies, allergic rhinitis, asthma or allergic rhinitis were ostracised from the study.

Consent for the research design was granted by the Clinical Research Ethics Committee of the Faculty of Medicine of a Recep Tayyip Erdoğan University (Ethics Committee approval date: 12.12.2014, decision no: 2014/167).

The sample size determination for this study was conducted using the G Power 3.1 software. With an alpha level of 0.5, an effect size of 0.66, and a target power of 80%, the analysis indicated that each group should consist of at least 36 participants (7).

Clinical Measurements

Disease Activity Score 28 (DAS28) is a widely used measure to determine disease activity in RA patients and reflects the person's current disease status. It considers swelling and tenderness in 28 joints, the erythrocyte sedimentation rate (ESR) value, and the patient's general health assessment or pain assessment. DAS28 scores below 2.6 were considered, indicating remission, 2.6 to just under 3.2 represented low disease activity, 3.2 to 5.1 indicated intermediate disease activity, and scores above 5.1 were categorized as high disease activity (18).

Visual Analog Scale (VAS) was used to estimate the violence of the disease. Patients were asked to mark a 10 cm line where one end represented the best period of the disease and the other the worst, with the current state marked in between. The distance from the zero point was measured in centimetres (0-10 cm) (19).

The Health Assessment Questionnaire (HAQ) contains 20 questions, organized into 8 domains: dressing, toileting, hygiene, rising, reaching, eating, gripping, walking, and other everyday activities. This questionnaire evaluates the last week. Each subsection was scored independently and a single HAQ score ranging from 0 to 3 was determined by averaging the scores of the 8 subsections (20).

Laboratory Analysis

Serum C-reactive protein (CRP) levels were quantified with an Abbott autoanalyzer (Architect C1600; Abbott, USA). Normal CRP values ≤ 0.5 mg/dL were considered. Serum specimens were preserved at -80°C until the day of analysis for measurement of total tryptase concentrations. Serum tryptase concentrations were assayed utilizing an enzyme-linked immunosorbent assay (ELISA) kit from Cloud-Clone Corp. (Houston, TX 77082, USA). The coefficients of variation (CV) for inter-assay and intra-assay precision were $<12.0\%$ and $<10.0\%$, respectively, with a sensitivity of 14.1 pg/mL.

Statistical Analysis

IBM SPSS version 22 was used to analyze the research data. Mean, standard deviation, number, percentage and median (range) values of the research data were presented. Pearson Chi-Square, Yates Corrected Chi-Square and Fisher Exact Tests were used to examine categorical variables. The normality of data scatter, kurtosis and skewness values were statistically evaluated using the Kolmogorow Smirnow test. Student's t-test was used for comparisons between two independent groups in normally distributed data; Mann-Whitney U test was used for comparisons of non-normally distributed data, and Kruskal-Wallis test was used for comparisons of three independent groups. When meaningful comparisons were found between the three groups as a result of the Kruskal-Wallis test, Bonferroni correction was performed to determine the source of the differences. The relationships among variables were analyzed through Spearman's rank correlation method, and the level of statistical significance was defined as $p<0.05$.

RESULTS

80 individuals were analyzed. Of the participants, 43 (53.8%) were RA patients, while the remaining 37 (46.3%) were otherwise healthy subjects forming the healthy group. Sociodemographic data of the patient and control groups were analyzed and no significant discrepancy was observed between them (Table 1). Statistically significant differences were obtained regarding ESR, CRP and tryptase levels between RA patients and control group ($p<0.001$).

ESR, CRP and tryptase levels were detected significantly higher in RA patients than in the control group (Table 2). In RA patients, tryptase levels showed a moderate, positive, and statistically significant correlation with VAS, DAS28, HAQ scores, and ESR values (correlation coefficients: $r=0.350$, $r=0.501$, $r=0.320$, $r=0.420$, respectively; $p<0.05$). However, there was no significant correlation between tryptase levels and disease duration or CRP levels ($p>0.05$) (Table 3). Significant disparities were detected between RA patients with different levels of disease activity in terms of VAS and HAQ scores as well as ESR, CRP and tryptase levels ($p<0.05$). Post-hoc binary comparisons suggested that significant variations in VAS and HAQ scores, as well as CRP and tryptase levels, resulted from groups of individuals with high disease activity. On the contrary, the significantly different ESR values were between patients with low and high disease activity. RA patients with high disease activity had significantly higher VAS and HAQ scores, CRP and tryptase levels compared to those who had low or moderate disease activity (Table 4). Statistical data on other laboratory investigations in the RA group are presented in Table 4. A statistically significant difference in tryptase levels was observed between Rheumatoid factor (RF)-negative and RF-positive RA patients ($p<0.05$). The level of tryptase was notably greater in RF-positive RA patients compared to those who were RF-negative. No significant difference was found between anti-cyclic citrullinated peptide (Anti-CCP) negative and positive RA patients ($p>0.05$) (Tables 5,6).

Table 1. Sociodemographic comparison between patient and control groups			
	RA (n=43)	Control (n=37)	p
Age (years)	52.53±11.10	48.41±12.79	0.101
Gender			
Male	7 (16.3)	5 (13.5)	0.975
Female	36 (83.7)	32 (86.5)	
Educational level			
Illiterate	13 (30.2)	6 (16.2)	0.183
Primary school graduate	21 (48.8)	17 (45.9)	
Secondary/high school graduate	6 (14.0)	6 (16.2)	
College/university graduate	3 (7.0)	8 (21.7)	
Height (cm)	160.74±6.79	163.24±7.06	0.111
Body weight (kg)	76.21±14.04	73.81±13.05	0.434
BMI (kg/m²)	29.50±5.23	27.71±4.64	0.111
BMI: body mass index; continuous variables are presented as "mean ± standard deviation", and categorical variables as "number (column percentage)"			

Table 2. Distribution of laboratory values between patient and control groups					
	RA (n=43)		Control (n=37)		p
	$\bar{X}\pm SD$	Median (min-max)	$\bar{X}\pm SD$	Median (min-max)	
ESR (mm/h)	33.49±24.39	26 (6-103)	15.97±9.14	15 (2-37)	<0.001
CRP (mg/dL)	1.38±1.86	0.59 (0.09-7.35)	0.39±0.27	0.30 (0.09-1.31)	<0.001
Tryptase (pg/mL)	14.06±6.56	10.78 (6.13-35.01)	8.75±1.63	8.78 (5.01-13.48)	<0.001
$\bar{X}$: mean, SD: standard deviation, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein					

Table 3. The association of serum tryptase levels with disease-related variables in RA patients			
	Tryptase		
	r	p	
VAS	0.350*	0.022	
HAQ	0.320*	0.037	
ESR	0.420**	0.005	
CRP	0.278	0.071	
DAS28	0.501**	0.001	
*p<0.05, **p<0.01; ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, VAS: Visual Analog Scale, HAQ: Health Assessment Questionnaire, DAS28: Disease Activity Score 28			

Table 4. Distribution of clinical characteristics and laboratory values of RA patients according to disease activity							
	Disease activity						p
	Low (n=10)		Moderate (n=15)		High (n=18)		
	$\bar{X}\pm$ SD	Median (min-max)	$\bar{X}\pm$ SD	Median (min-max)	$\bar{X}\pm$ SD	Median (min-max)	
Disease duration (months)	85.20±53.80	72 (12-192)	107.60±88.25	84 (12-324)	89.33±91.41	48 (12-300)	0.518
VAS	2.60±1.08	2.5 (1-5)	4.00±1.60	4 (1-6)	6.28±2.24 ^{ab}	6 (1-10)	<0.001
HAQ	0.58±0.56	0.37 (0-1.5)	0.87±0.36	0.87 (0.25-1.75)	1.62±0.66 ^{ab}	1.81 (0.25-2.5)	<0.001
DMARD use							
Non-user [n (%)]	2 (20.0)		1 (6.7)		1 (5.6)		0.411
User [n (%)]	8 (80.0)		14 (93.3)		17 (94.4)		
Biological drug use							
Non-user [n (%)]	7 (70.0)		11 (73.3)		16 (88.9)		0.398
User [n (%)]	3 (30.0)		4 (26.7)		2 (11.1)		
RF							
Negative [n (%)]	8 (80.0)		5 (33.3)		6 (33.3)		0.034
Positive [n (%)]	2 (20.0)		10 (66.7)		12 (66.7)		
Anti-CCP							
Negative [n (%)]	5 (50.0)		5 (33.3)		5 (27.8)		0.491
Positive [n (%)]	5 (50.0)		15 (66.7)		13 (72.2)		
ESR (mm/h)	14.40±8.20	12 (6-29)	28.53±14.33	22 (15-65)	48.22±28.26 ^a	39.5 (13-103)	<0.001
CRP (mg/dL)	0.54±0.39	9.68 (6.13-17.73)	0.55±0.32	0.41 (0.27-1.38)	2.54±2.42 ^{ab}	1.49 (0.39-7.35)	0.004
Tryptase (pg/mL)	10.12±3.27	9.68 (6.13-17.73)	13.23±7.52	10.22 (8.01-35.01)	16.95±5.98 ^{ab}	15.97 (8.01-29.77)	0.003
$\bar{X}$: mean, SD: standard deviation, %: percentage, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, VAS: Visual Analog Scale, HAQ: Health Assessment Questionnaire, DMARD: disease-modifying antirheumatic drug, RF: rheumatoid factor, Anti-CCP: anti-cyclic citrullinated peptide antibody							
^a Post-hoc pairwise comparison showed a significant difference with the "low" disease activity group (p<0.017); ^b Post-hoc pairwise comparison showed a significant difference with the "moderate" disease activity group (p<0.017); ^c Post-hoc pairwise comparison showed a significant difference with the "high" disease activity group (p<0.017)							

Table 5. Tryptase levels in RA patients according to RF status					
	RF negative (n=19)		RF positive (n=24)		p
	$\bar{X}\pm SD$	Median (min-max)	$\bar{X}\pm SD$	Median (min-max)	
Tryptase (pg/mL)	10.41±2.96	9.91 (6.13-17.73)	16.96±7.22	15.65 (8.66-35.01)	0.001
$\bar{X}$: mean, S: standard deviation, %: percentage, RF: rheumatoid factor					

Table 6. Tryptase levels of RA patients according to anti-CCP status					
	Anti-CCP negative (n=15)		Anti-CCP positive (n=28)		p
	$\bar{X}\pm SD$	Median (min-max)	$\bar{X}\pm SD$	Median (min-max)	
Tryptase (pg/mL)	11.97±6.71	10.49 (6.92-35.01)	15.18±6.32	14.12 (6.13-29.77)	0.070
$\bar{X}$: mean, S: standard deviation, %: percentage, Anti-CCP: anti-cyclic citrullinated peptide					

DISCUSSION

Our research demonstrated that serum tryptase levels were markedly higher in RA patients than in the control group, with a notable relationship linking higher tryptase levels and greater disease activity. Tryptase levels exhibited a positive correlation with DAS28, VAS, HAQ scores, and ESR, whereas no significant link was identified with CRP levels. This evidence suggests on the possibility role of tryptase levels as a surrogate biomarker for the severity and progression of RA.

MCs are heterogeneous cells of bone marrow origin with multiple functions. They manage a wide range of functions in innate and gained immunity, including re-vascularization, inflammation, hypersensitivity reactions, vascular system regulation (21,22). MCs contain granules that store many substances. These granules contain proinflammatory structures, including proteoglycans and tryptase. When MCs are stimulated and activated, these granules are released into the environment, and hypersensitivity and inflammation develop (23). Recent studies demonstrating the presence of MCs in the synovium of RA patients and the classification of synovitis according to the density of these cells prove that MCs play an active role in the development of this disease and that the disease shows a heterogeneous structure. MCs secrete a number of chemokines in response to antigenic substances and subsequently cause inflammation, re-vascularization and edema formation in the regional tissue (24). In a study, it has been shown that synovial MCs are found at high rates in patients with RA and inflammation increases in direct proportion to the number of MCs and is associated with high disease activity (25). Kim et al.'s study revealed that MCs and tryptase levels were increased in the synovial tissues of RA patients, and this elevation promoted the differentiation of osteoclasts (26). According to a review by Rivellese et al., the presence of synovial MCs in untreated early RA patients was closely linked to heightened synovial and systemic inflammation, as well as increased disease activity. This connection highlights the significant role of MCs in driving RA pathology and points to their potential as a key focus for early therapeutic interventions (27). All these findings confirm that MCs and tryptase contribute to inflammation in RA.

Guo and colleagues' research revealed that serum tryptase levels were notably elevated in patients with both early and late-stage RA compared to healthy individuals. They investigated the presence of anti-tryptase antibodies in RA serum samples, considering that for a molecule to be recognized as an autoantigen involved in the etiopathogenesis of a disease, antibodies against these antigens must be present. They found that these antibodies were present in RA patients but not in patients with osteoarthritis or systemic lupus erythematosus. Again, when they examined synovial fluid samples of RA patients, they found the presence of tryptase and anti-tryptase antibodies. When compared with synovial fluids of osteoarthritis patients, they showed that these antibodies

were absent. They also found a positive correlation between tryptase levels and DAS28, RF and anti-CCP in RA patients, but not with CRP and ESR (7). Similarly, in our study, serum tryptase concentration was found to be higher in RA patients compared to controls. In our study, we found a positive correlation between serum tryptase levels and DAS28, RF and ESR in RA patients. These findings support that tryptase may play an active and prominent role in disease activity and inflammation in RA. Research exploring the connection between anti-CCP and tryptase is scarce in the existing literature. Unlike the study by Guo et al., although no correlation was found between anti-CCP and tryptase in our study, tryptase levels were higher in the anti-CCP positive group. This may be due to the variability in the antigen responses of autoantibodies.

A study by Rossini et al. found no significant increment in serum tryptase concentrations in patients with early RA versus healthy controls. Additionally, a negative association has also been reported between CRP and serum tryptase levels in the same study. As a result, the authors suggested that tryptase may possess an anti-inflammatory role in RA (28). We enrolled only late RA patients in our study and similar to Guo's study; we detected the serum tryptase values were markedly elevated in RA patients relative to the control group. These conflicting results may arise from tryptase playing a more dominant role at different stages of inflammation or from the variability in antigen responses of autoantibodies. Factors such as patient selection, prolonged disease duration, comorbidities developing over the course of the disease, and the medications used could have influenced the outcomes.

In a study by Kim and colleagues investigating osteoclastogenesis in RA patients, they reported elevated serum tryptase levels, consistent with our study. However, no information regarding disease activity was provided in that study (26). In this article, we categorized disease activity into three groups—mild, moderate, and high—and demonstrated that tryptase levels increase as disease activity rises. To our knowledge, no other research in the literature has measured tryptase levels by classifying RA patients according to disease activity, making our research unique in this respect.

Another subject investigated in our study is the relationship between CRP and tryptase. CRP is a member of the pentraxin super family and its synthesis increases in inflammatory conditions. It is mainly regulated by IL-6 and IL-1 β cytokines and synthesised from the liver. CRP is increased in many inflammatory events (29). When we analysed the relationship between CRP levels and serum tryptase, similar to the findings of Guo and colleagues, we did not observe a relationship between CRP and serum tryptase levels. Another study showed a negative correlation between serum trptase and CRP (7,28). This suggests that CRP and tryptase may be activated through different pathways and may be due to the temporal variation of the inflammatory response.

ESR is a test that measures the rate at which erythrocytes sediment. It is used in the diagnosis and monitoring of infectious processes, inflammatory conditions and a number of diseases. ESR is a low specificity test that is influenced by many factors. It may be incompatible with CRP in some diseases such as RA (30). In this study, we found a statistically meaningful distinction between ESR and tryptase concentrations, which differs from Guo and colleagues study (7). This discrepancy is presumably relevant to differences in disease activity and phenotypic heterogeneity in our RA group compared to Guo's study. Considering that ESR may objectively reflect the state of active inflammation, the correlation between ESR and tryptase levels suggests that serum tryptase could serve as an important indicator in assessing disease activity in RA.

The role of tryptase on inflammation in RA led the researcher to investigate the presence of tryptase in other inflammatory diseases. Paolino et al. investigated serum tryptase levels in patients with psoriasis and found that serum tryptase levels were in the normal range in psoriasis patients, but higher levels were found in patients with psoriatic arthritis (PsA) and scalp involvement. As a result, they argued that tryptase showed proinflammatory effect (31). In another study by Chimenti et al., it was reported that tryptase levels upregulated in patients with psoriasis and PsA and may contribute to joint damage as a result of stimulation of matrix metalloproteinases in these patients (32). In another study on sarcoidosis patients, serum tryptase concentrations were raised in sarcoidosis patients versus the control group. However, no distinction was observed between progressive and stable sarcoidosis groups (8). Considering these findings, it can be inferred that tryptase is a key factor in promoting systemic inflammation.

CONCLUSION

We believe that tryptase exerts pro-inflammatory effects. In our research, we detected a notable increase in tryptase levels as disease activity intensified. The positive association observed in the tryptase levels and ESR further supports this hypothesis. This correlation suggests the potential for targeting tryptase or its signaling pathways as a new therapeutic approach in RA. Additionally, the exact mechanisms by which tryptase contributes to RA pathogenesis remain unclear. Further investigation is necessary to clarify its contribution to disease mechanisms and its efficacy as a therapeutic target. Monitoring serum tryptase levels may also aid in classifying patients according to disease severity and tailoring treatment regimens accordingly. Patients with high tryptase levels may potentially benefit from more aggressive anti-inflammatory and immunomodulatory therapies.

Study Limitations

The main restriction of our study is that other cytokine levels implicated in the mechanism of disease pathogenesis, synovial fluid cytokine and tryptase levels,

and histological sampling of the inflamed tissue were not analyzed. Additionally, the sample size was relatively small, and the study was cross-sectional, limiting the ability to establish causality between elevated tryptase levels and RA progression. Various treatment methods that could influence cytokine levels and the relationship between tryptase and other variables were used by patients.

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REFERENCES

1. Afifi N, B MM, Abdel Ghani AM, Mohamed Ali Hassan HGE, Behiry ME. Value of albumin-fibrinogen ratio and CRP-albumin ratio as predictor marker of disease activity in Egyptian RA patients, correlated with musculoskeletal sonography. *Open Access Rheumatol.* 2020;12:241-8.
2. Chen S, Ying H, Du J, et al. The association between albumin-dNLR score and disease activity in patients with rheumatoid arthritis. *J Clin Lab Anal.* 2019;33:e22695.
3. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *N Engl J Med.* 2011;365:2205-19.
4. Metcalfe DD, Baram D, Mekori YA. Mast cells. *Physiol Rev.* 1997;77:1033-79.
5. Sprinzl B, Greiner G, Uyanik G, et al. Genetic regulation of tryptase production and clinical impact: hereditary alpha tryptasemia, mastocytosis and beyond. *Int J Mol Sci.* 2021;22:2458.
6. Theoharides TC, Valent P, Akin C. Mast cells, mastocytosis, and related disorders. *N Engl J Med.* 2015;373:163-72.
7. Guo Y, Wu Q, Ni B, et al. Tryptase is a candidate autoantigen in rheumatoid arthritis. *Immunology.* 2014;142:67-77.
8. Bargagli E, Mazzi A, Mezzasalma F, et al. The analysis of tryptase in serum of sarcoidosis patients. *Inflammation.* 2009;32:310-4.
9. Liu B, Yang MQ, Yu TY, et al. Mast cell tryptase promotes inflammatory bowel disease-induced intestinal fibrosis. *Inflamm Bowel Dis.* 2021;27:242-55.
10. Zhang MQ, Timmerman H. Mast cell tryptase and asthma. *Mediators Inflamm.* 1997;6:311-7.
11. Numerof RP, Simpson PJ, Tanaka R. Tryptase inhibitors: a novel class of anti-inflammatory drugs. *Expert Opin Investig Drugs.* 1997;6:811-7.
12. Compton SJ, Cairns JA, Holgate ST, Walls AF. The role of mast cell tryptase in regulating endothelial cell proliferation, cytokine release, and adhesion molecule expression: tryptase induces expression of mRNA for IL-1 beta and IL-8 and stimulates the selective release of IL-8 from human umbilical vein endothelial cells. *J Immunol.* 1998;161:1939-46.

13. Zhang S, Zeng X, Yang H, et al. Mast cell tryptase induces microglia activation via protease-activated receptor 2 signaling. *Cell Physiol Biochem*. 2012;29:931-40.
14. Zeng X, Zhang S, Xu L, et al. Activation of protease-activated receptor 2-mediated signaling by mast cell tryptase modulates cytokine production in primary cultured astrocytes. *Mediators Inflamm*. 2013;2013:140812.
15. Pejler G, Alanazi S, Grujic M, et al. Mast cell tryptase potentiates neutrophil extracellular trap formation. *J Innate Immun*. 2022;14:433-46.
16. Meyer MC, Creer MH, McHowat J. Potential role for mast cell tryptase in recruitment of inflammatory cells to endothelium. *Am J Physiol Cell Physiol*. 2005;289:C1485-91.
17. Mohajeri M, Kovanen PT, Bianconi V, et al. Mast cell tryptase - Marker and maker of cardiovascular diseases. *Pharmacol Ther*. 2019;199:91-110.
18. Prevoo ML, van 't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum*. 1995;38:44-8.
19. Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain*. 1983;17:45-56.
20. Küçükdeveci AA, Sahin H, Ataman S, et al. Issues in cross-cultural validity: example from the adaptation, reliability, and validity testing of a Turkish version of the Stanford Health Assessment Questionnaire. *Arthritis Rheum*. 2004;51:14-9.
21. Traina G. Mast cells in human health and diseases 2.0. *Int J Mol Sci*. 2024;25:6443.
22. Nassar A, Wagura E, Loukas M. Mast cells and arteriogenesis: a systematic review. *Cardiovasc Pathol*. 2025;75:107716.
23. Oštrić Pavlović I, Radović S, Krtinić D, et al. Tryptase: the silent witness of past and ongoing systemic events. *Medicina (Kaunas, Lithuania)*. 2024;60:1380.
24. Min HK, Kim KW, Lee SH, Kim HR. Roles of mast cells in rheumatoid arthritis. *Korean J Intern Med*. 2020;35:12-24.
25. Rivellesse F, Mauro D, Nerviani A, et al. Mast cells in early rheumatoid arthritis associate with disease severity and support B cell autoantibody production. *Ann Rheum Dis*. 2018;77:1773-81.
26. Kim KW, Kim BM, Won JY, et al. Regulation of osteoclastogenesis by mast cell in rheumatoid arthritis. *Arthritis Res Ther*. 2021;23:124.
27. Rivellesse F, Rossi FW, Galdiero MR, et al. Mast cells in early rheumatoid arthritis. *Int J Mol Sci*. 2019;20:2040.
28. Rossini M, Viapiana O, Zanoni G, et al. Serum levels of tryptase suggest that mast cells might have an antiinflammatory role in rheumatoid arthritis: comment on the article by Rivellesse et al. *Arthritis Rheumatol*. 2016;68:769.
29. Zhou HH, Tang YL, Xu TH, Cheng B. C-reactive protein: structure, function, regulation, and role in clinical diseases. *Front Immunol*. 2024;15:1425168.
30. Bray C, Bell LN, Liang H, et al. Erythrocyte sedimentation rate and C-reactive protein measurements and their relevance in clinical medicine. *WMJ*. 2016;115:317-21.
31. Paolino G, Di Nicola MR, Currado M, et al. Serum tryptase levels in patients with psoriasis: a pilot study for a possible useful biomarker. *Clin Exp Dermatol*. 2022;47:178-9.
32. Chimenti MS, Sunzini F, Fiorucci L, et al. Potential role of cytochrome c and tryptase in psoriasis and psoriatic arthritis pathogenesis: focus on resistance to apoptosis and oxidative stress. *Front Immunol*. 2018;9:2363.



Effects of Walking on Mobility, Balance and Anthropometric Measurements in Individuals with Mechanical Low Back Pain

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Abstract

Aim: This study aims to investigate the effects of walking on mobility, balance and anthropometric measurements.

Material and Method: Our study included individuals with mechanical low back pain, who were randomly assigned to experimental and control groups. After the waist and hip circumference measurements of the participants who completed the personal information form, a 40-meter fast walking test was performed together with the Timed Up and Go test. The experimental group practiced treadmill walking while the control group continued to take normal care. Evaluations were performed before and after treatment. The results were evaluated in SPSS 22 software program.

Results: No significant differences were observed regarding the demographic characteristics of the participants in our study. However, a notable improvement was identified in the outcomes of the mobility evaluation test ($p < 0.05$). Statistically significant differences were also observed in anthropometric measurements in the low back and hip region ($p < 0.05$).

Conclusion: As a result of our study, it was shown that walking exercise produced significant changes in mobility, balance and anthropometric measurements of individuals.

Keywords: Mechanical low back pain, walking, mobility

INTRODUCTION

Low back pain that is not caused by any known specific pathology, usually originating from in the lumbosacral region or other soft tissues around these discs, is called mechanical low back pain (1,2). Mechanical low back pain is very widespread and ranks among the major causes of disability globally. It is also the second most frequent complaint reported in primary health care settings (3). Furthermore, mechanical low back pain has been reported to affect 23% of the global population, with a recurrence rate ranging from 24% to 80% within a year (4,5). Low back pain is a multifactorial condition influenced by environmental, occupational, personal, and physical factors. According to the literature, risk factors include age, gender, occupation, socio-cultural status, stress, smoking, and obesity (6,7).

A comprehensive evaluation is essential for developing

an effective treatment plan for mechanical low back pain. In this evaluation, patient history, physical examination, imaging and laboratory methods should be used together (8-10). Both pharmacologic and non-pharmacologic methods are used to treat mechanical low back pain. Bed rest, heat treatments, electrotherapy, ultrasound, mobilization, and manipulation are examples of non-pharmacological methods (11-13). In recent years, activities such as walking and cycling have been included in non-pharmacological treatment programs. In the literature, there are studies investigating the effects of walking on individuals with mechanical low back pain (14). These studies generally focus on the effects of walking on pain, functionality and depression (15,16).

The purpose of this research was to explore the influence of walking activity on balance, mobility, and anthropometric measurements in individuals with mechanical low back pain.

CITATION

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MATERIAL AND METHOD

The Scientific Research and Publication Ethics Committee of Artvin Çoruh University approved our work. The approval letter, dated 16.04.2024, with the number "E-18457941-050.99-132258" on it, was issued.

The participants in our research were students from the Department of Physiotherapy at Artvin Çoruh University. Participants who consented to participate were included after being informed about the study.

Inclusion criteria;

- Agreeing to participate in the research,
- Signing the consent form created for the research,
- Over 18 years of age,
- Having been diagnosed with mechanical low back pain as a result of clinical evaluation by a physician,
- Not having any history of surgery.

Exclusion criteria;

- Being under 18 years of age,
- Not signing the consent form,
- Previous surgical operation,
- Exposure to low back pain due to a known cause,
- Having physiotherapy and rehabilitation treatment within the last six months,
- Having medical treatment for low back pain within the last six months.

Students diagnosed with mechanical low back pain through clinical evaluation conducted by the university infirmary physician were included in the study. All individuals who agreed to participate in the study and signed the consent form were asked to fill out a personal information form. The participants were then randomly divided into experimental and control groups.

Anthropometric measurements were performed by trained researchers in accordance with standard procedures. A stadiometer was used for height measurement. Participants were asked to stand upright and barefoot, and the headpiece was lowered to the highest point of the head. The first measurement was taken in this way, and after a few seconds of rest, the participants' height was measured again in the same position. The average of the obtained results was then calculated. A calibrated Seca 813 digital scale was used for weight measurement. Participants were weighed in light clothing and without shoes for the first measurement. After stepping off the scale and resting for a few seconds, they were asked to step back on for a second measurement. The average of the two obtained values was calculated. All measurement procedures were conducted in accordance with the standards specified by the World Health Organization (WHO) and relevant literature (17). The measurement parameters included height, body weight, waist circumference, hip circumference, and body mass index (BMI). All measurements were conducted in an environment where participants were in an appropriate position and in a relaxed state.

The participants' waist circumference was measured at the umbilicus level, while hip circumference was measured at the most prominent point of the gluteal region, ensuring the tape was parallel to the ground. The BMI of the participants was calculated by dividing body weight in kilograms by the square of height in meters. The Timed Up and Go Test was used to measure participants' mobility, while the 40-Meter Fast-Paced Walk Test was applied to evaluate short-distance walking speed and direction-changing activities. Before the assessment, the tests were explained to the individuals, and a trial test was conducted before starting the actual evaluation. After the first assessment, participants in the experimental group began a moderate-paced 20-minute walk on a Voigt treadmill at a speed of 5 km/h. The walking sessions were performed five times per week (once per day) for three weeks. Individuals in the control group followed physiotherapists' recommendations by maintaining proper posture, engaging in light physical activities, and avoiding situations that could trigger pain (such as strenuous movements) while continuing their daily routines.

The data collection instruments included a descriptive information form, the Timed Up and Go Test, the 40-Meter Fast-Paced Walk Test, and anthropometric measurements.

The Descriptive Information Form was created by researchers based on a literature review. It consists of six questions covering participants' age, height, weight, BMI, smoking status, and family income level.

The Timed Up and Go Test was used for this assessment, in which participants were seated in a chair with a 3-meter walking distance marked ahead, instructed to stand up, walk to the marked endpoint, return, and sit back down, while the time taken to complete the task was recorded (18).

In the 40-Meter Fast-Paced Walk Test, a hard-surfaced area is marked with a 10-meter distance between the start and finish points. Traffic cones are placed 2 meters behind the start line and 2 meters beyond the finish line. Participants are instructed to walk between the start and finish lines while turning around the cones. The time taken for every 10-meter segment is recorded (19).

In anthropometric measurements, participants' waist circumference was measured at the umbilicus level, while hip circumference was measured at the most prominent point of the gluteal region, ensuring the tape was parallel to the ground. Measurements were repeated before and after the test. To minimize error, each measurement was taken twice, and the average of the obtained values was used for calculations (20).

The timed get-up-and-walk test required the participant to leave the chair, walk to the end of the room, return, and sit in the chair. The amount of time that passed was noted (18).

40-meter fast tempo walking test; In the test, an area of 10 meters is determined between the start and end points on a hard surface. Then traffic cones are placed 2 meters behind the start line and 2 meters ahead of the finish line. The participant is instructed to walk between the start and finish lines while maneuvering around the cones. While the participant is doing this, the elapsed time for every 10 meters is recorded (19).

The sample size in this study was determined based on data from a previous study examining the temporal and kinematic parameters of individuals with chronic low back pain. The effect size was calculated using the mean and standard deviation values of Timed Up and Go Test scores (18). In this study, the effect size for the groups was 1.5653. Using the G*Power 3.1.9.4 software with effect size=1.5653, alpha=0.05, and power=0.95, the total sample size was calculated as 24.

Statistical Analysis

The data obtained in the study were analyzed using SPSS 22.0 software. A significance level of $p < 0.05$ was considered for all statistical analyses. The Kolmogorov-Smirnov test was used to assess the normality of the data distribution. Descriptive statistics were presented as mean±standard deviation for normally distributed continuous variables, median and interquartile range for non-normally distributed variables, and frequency and percentage (%) for categorical variables. Group comparisons were conducted using the One-Way ANOVA and Kruskal-Wallis H test.

RESULTS

No significant difference was seen when comparing the demographic information of the study and control groups ($p > 0.05$) (Table 1).

Table 1. Analysis of demographic information of the participants

		Experimental group (n=39)		Control group (n=39)		p-value
Age	Mean±SD	20.00±1.25		20.00±2.00		F=1.127
	Median (Min-Max)	20.5 (18-25)		21 (18-26)		p=.533
BMI	Mean±SD	21.94±4.99		20.83±3.65		$\chi^2=1.565$
	Median (Min-Max)	21.8 (17.8-25.8)		22.2 (18.3-26.1)		p=.353
		Number (n)	Percent (%)	Number (n)	Percent (%)	
Gender	Male	15	38.46	15	42.30	$\chi^2=.384$
	Female	24	61.54	24	57.70	p=.825
Smoking	Yes	7	19.23	9	23.07	$\chi^2=.118$
	No	32	80.77	30	76.93	p=.943

F: One Way ANOVA Test, χ^2 : Chi-Square test

When the pre-test results of the experimental and control groups were compared, no statistically significant difference was found, whereas a statistically significant difference was detected in the post-test results between the groups ($p=0.004$, $p < 0.05$). When the pre-test and post-

test results were compared in the control group, there was no statistically significant difference ($p=0.230$, $p > 0.05$). When the pre-test and post-test results were compared in the experimental group, there was a statistically significant difference ($p=0.004$, $p < 0.05$) (Table 2).

Table 2. Comparison of the experimental and control groups in the timed up and go test pre-test and post-test

		Experimental group (n=39)	Control group (n=39)	t value	p value	
Timed up and go test (s)	Pre test	Mean±SD	8.8068±1.81	8.9072±1.40	0.98	0.330
		Median (Min-Max)	8.75 (7.90-9.80)	8.75 (7.55-9.90)		
	End test	Mean±SD	7.5088±1.40	8.9571±2.30	-2.97	0.004*
		Median (Min-Max)	7.45 (6.90-8.20)	8.80 (7.60-9.95)		
Within-group comparison (pre and post)		t=-3.025	t=1.503	-	-	
p-value		0.004*	0.230	-	-	
t (Independent): Independent samples t-test. t (Dependent): Dependent samples t-test. *p<0.05						

t (Independent): Independent samples t-test, t (Dependent): Dependent samples t-test, * $p < 0.05$

When the experimental and control groups were compared, no significant difference was observed between the pre-test and post-test ($p>0.05$). Similarly, no statistical difference was found between pre-test and post-test measurements

in the control group ($p=0.511$, $p>0.05$). However, a statistically significant difference was identified between pre-test and post-test measurements in the experimental group ($p=0.034$, $p<0.05$) (Table 3).

Table 3. Comparison of the experimental and control groups in the 40 meter rapid tempo walking test pre-test and post-test						
			Experimental group (n=39)	Control group (n=39)	t test	p test
40 meter rapid tempo walking test (m/s)	Pre test	Mean±SD	2.3917±0.25	3.2072±0.10	-1.29	0.244
		Median (Min-Max)	2.995 (2.66-3.33)	3.240 (2.85-3.24)		
	End test	Mean±SD	3.4207±0.18	3.1090±0.12	1.85	0.114
		Median (Min-Max)	3.35 (3.10-3.80)	3.09(2.85-3.33)		
Within-group comparison (pre and post)			t=-3.73	t=0.74	-	-
p-value			0.034*	0.511	-	-
t (Independent): Independent samples t-test, t (Dependent): Dependent samples t-test, *p<0.05						

Participants in the study and control groups low back circumference anthropometric measurements did not differ statistically significantly before walking ($p>0.05$), but after walking, a significant difference was discovered in favor of the study group ($p<0.05$) (Table 4).

When comparing the pre-test hip circumference anthropometric measurements of the experimental and control groups, no statistically significant difference

was found ($p=0.924$, $p>0.05$). Similarly, there was no significant difference between the groups in the post-test measurements ($p=0.461$, $p>0.05$). Within-group analysis revealed a statistically significant difference between the pre-test and post-test measurements in the experimental group ($p=0.006$, $p<0.05$). When the pre-test and post-test results were compared within the groups, walking was observed to produce a statistically significant change in hip circumference measurements (Table 4).

Table 4. Comparison of anthropometric measurements of experimental and control groups at pre-test and post-test						
			Experimental group (n=39)	Control group (n=39)	t test	p test
Anthropometric measurement of low back circumference (cm)	Pre test	Mean±SD	101.604±2.75	102.450±2.06	0.515	0.625
		Median (Min-Max)	95.2 (89-101)	91 (82-100)		
	End test	Mean±SD	100.48±2.55	102.220±2.28	0.271	0.796
		Median (Min-Max)	93 (88-98)	90.5 (82-99)		
Within-group comparison (Pre vs. Post)			t=3.865	t=2.012	-	-
p-value			0.031*	0.138	-	-
Anthropometric measurement of hip circumference (cm)	Pre test	Mean±SD	107.604±2.75	107.450±2.06	0.100	0.924
		Median (Min-Max)	109 (103-115)	109.5 (104-115)		
	End test	Mean±SD	102.48±2.55	107.220±2.58	-0.432	0.667
		Median (Min-Max)	105 (100-109)	109.32 (104-115)		
Within-group comparison (Pre vs. Post)			t=6.926	t=1.532	-	-
p-value			0.006*	0.010*	-	-
t (Independent): Independent samples t-test, t (Dependent): Dependent samples t-test, *p<0.05						

DISCUSSION

Walking is a widely recommended physical activity to improve health and support activities of daily living (21). In this study, the effects of walking activity on mobility, balance and anthropometric measurements were examined. Our study aims to provide important information on how walking can be used more effectively in clinical practice and to contribute to the literature.

In a study conducted by Suh et al., (2019), the effectiveness of lumbar stabilization exercises and walking activity on low back pain was examined. They included 48 participants in their study and divided the participants into 4 groups by randomization method. They applied flexibility exercises to the first group, walking to the second group, stabilization exercises to the third group and walking activity with stabilization exercises to the fourth group. In their study, they used the VAS scale to measure pain at rest and during physical activity as the primary outcome measure and the frequency of medication use, Oswestry disability index, beck depression questionnaire and lumbar muscle strength as secondary outcome measures. According to the results of their study, the reduction of back pain and increase in muscle strength were more significant in the stabilization and walking groups compared to the other group. The authors also recommended walking and stabilization exercises for chronic low back pain (22).

A study by Arkesteijn et al. (2022) examined how walking and static work programs affected older women's posture, stimulation of muscles, and acute low back pain. The study involved 14 elderly women. A improved silent standing task and a 30-minute walking task were used to evaluate changes in trunk contractions, lower and higher spine angles, postural influence, and back discomfort. The results, although not statistically significant, indicate a decline in acute back pain and an increase in the upper spine flexion angle (23).

In a study conducted by Seay et al. (2011), the effects of low back pain on the pelvis and trunk during walking and running were examined. Runners participated in the study. The runners were asked to walk on a treadmill with increments of 0.8 m/s. Pelvis and trunk data were collected during the last 20 seconds of each phase. Coordination analysis measured the portion of the walking cycle spent on trunk movement only, pelvis movement only, in-phase, and antiphase relationships for each group. In the group with low back pain, a reduction in coordinated movement between the pelvis and trunk was found, despite low disability levels (24). In our study, it was observed that walking activity provided significant improvements in the experimental group on the timed up-and-go and 40-meter walk tests. Our study also showed that walking had significant effects on mobility and performance.

In a study conducted by Tekin et al., (2020), the effectiveness of an aerobic exercise program in patients with non-specific low back pain was investigated. The participants included in their study were divided into

experimental and control groups by randomization method and the participants in the experimental group were given home exercises in addition to aerobic exercise while the control groups were only given home exercise program. The participants were assessed for pain level, spinal flexibility, lumbar muscle endurance, depressive symptom presence and severity, disability, and quality of life before treatment, after treatment, and three months after treatment. According to the results of the study, significant improvement was found in all evaluations in the study group, while significant improvement was found in pain, spinal flexibility and physical component of quality of life in the control group. Compared to the control group, the positive change in the evaluation parameters over time was significantly higher in the experimental group (25).

In a study conducted by Li et al. (2020), the effects of walking activity on body mass index, low back circumference, and other health indicators in the working population were explored. The study evaluated participants' walking behavior, height, weight, and low back circumference measurements before and after the intervention. The results indicated that walking exercises were effective in reducing both body mass index and low back circumference (26). In our study, it was found that walking had a positive effect on reducing low back circumference in the study group.

In a study conducted by Melam et al. (2016) examined the effects of aerobic exercise and brisk walking on body mass index, anthropometric measurements and blood pressure in overweight. The participants in the study were assigned to three groups using a randomization method. The primary group was selected as aerobic exercises and diet; the second group as brisk walking and diet; and the third group as the control group. The interventions were continued for 10 weeks and a re-evaluation was performed at the end of 10 weeks. As a result of the study, it was found that the participants in the aerobic exercise and diet group saw more positive effects than those in the brisk walking and diet group. In addition, changes in all variables were significant in the brisk walking and diet group, yet the control group showed no significant differences (27).

A study by Guessogo et al. (2016) examined the effect of a 24-week repetitive short-term walking-based training program on the physical fitness of black Cameroonian obese women. Participants in the study were divided into three groups: premenopausal women, postmenopausal women, and the control group. A 90-minute rehabilitation protocol was performed for all groups except the control group. The first 20 minutes of this program consisted of warm-up exercises, while the remaining time consisted of main exercises and cooling exercises. Metabolic, cardiorespiratory and anthropometric measurements were performed by the researchers at the beginning and end of the study. As a result of the study, there were no significant differences in the measurements of the participants in the

control group, while significant differences were found in metabolic, cardiorespiratory and anthropometric values for the other two groups (28). In our study, the participants in the experimental group were made to walk at a moderate pace and anthropometric measurements were performed. As a result of our study, significant differences were found in anthropometric variables in consistent with the literature. Although our study found significant results of walking on mobility, balance and anthropometrics, further studies are needed to contribute to the literature on this subject.

Despite these positive findings, our study has limitations. The short study duration prevented long-term evaluations. The fact that the participants were young adults makes it unclear whether the findings are applicable to older individuals or other populations. Further research involving longer follow-up periods and different age groups is needed.

CONCLUSION

Walking exercises may be an effective method for improving mobility, balance, and anthropometric measurements in individuals with mechanical low back pain. Additionally, moderate-paced walking was found to significantly reduce waist and hip circumference. Future studies should investigate the long-term effects of walking interventions on low back pain management.

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REFERENCES

1. Akeda K, Yamada J, Linn E, et al. Platelet-rich plasma in the management of chronic low back pain: a critical review. *J Pain Res.* 2019;12:753-67.
2. El-Sayed A, Hadley C, Tessema F, et al. Back and neck pain and psychopathology in rural sub-Saharan Africa: evidence from the Gilgel Gibe Growth and Development Study, Ethiopia. *Spine. (Phila Pa 1976).* 2010;35:684-9.
3. Traeger A, Buchbinder R, Harris I, Maher C. Diagnosis and management of low-back pain in primary care. *CMAJ.* 2017;189:E1386-95.
4. Andersson GB. Epidemiological features of chronic low-back pain. *Lancet.* 1999;354:581-5.
5. Will JS, Bury DC, Miller JA. Mechanical low back pain. *Am Fam Physician.* 2018;98:421-8.
6. Hoy D, Brooks P, Blyth F, Buchbinder R. The epidemiology of low back pain. *Best Pract Res Clin Rheumatol.* 2010;24:769-81.
7. Ünde Ayyat P, Aydın ON, Oğurlu M. Risk factors associated with lower back pain in the Polyclinic of Algology. *AĞRI* 2012;24:165-70.
8. Hutchins TA, Peckham M, Shah LM, et al. ACR appropriateness criteria® low back pain: 2021 update. *J Am Coll Radiol.* 2021;18:S361-79.
9. Parfenov V, Golovacheva V. Diagnosis and treatment of acute low back pain. *Ter Arkh.* 2019;91:155-9.
10. Casser H-R, Seddigh S, Rauschmann M. Acute lumbar back pain: investigation, differential diagnosis, and treatment. *Dtsch Arztebl Int.* 2016;113:223-34.
11. Myrtos CD. Low back disorders. Evidence-based prevention and rehabilitation. *J Can Chiropr Assoc.* 2012;56:76.
12. Polat M, Karaoğlu B. Approach to lumbar pain: recognition treatment. *Klinik Tıp Aile Hekimliği.* 2017;9:13-21.
13. Yaraşır E, Pirinçci E, Deveci SE. Complementary and alternative treatment in low back pain. *Archives Medical Review Journal.* 2018;27:93-108.
14. Pocovi N, de Campos T, Christine Lin C, et al. Walking, cycling, and swimming for nonspecific low back pain: a systematic review with meta-analysis. *J Orthop Sports Phys Ther.* 2022;52:85-99.
15. Ünal A, Yelda K, Gülsüm T, et al. Factors affecting pain intensity and disability level in patients with low back pain: a cross-sectional study. *Gevher Nesibe Journal of Medical & Health Sciences.* 2023;8:75-83.
16. Kim H, Min TJ, Kang SH, et al. Association between walking and low back pain in the Korean population: a cross-sectional study. *Ann Rehabil Med.* 2017;41:786-92.
17. de Onis M, Habicht JP. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. *Am J Clin Nutr.* 1996;64:650-8.
18. Buraschi R, Pollet J, Villafañe JH, et al. Temporal and kinematic analyses of timed up and go test in chronic low back pain patients. *Gait Posture.* 2022;96:137-42.
19. Aily JB, da Silva AC, de Noronha M, et al. Concurrent validity and reliability of video-based approach to assess physical function in adults with knee osteoarthritis. *Phys Ther.* 2024;104:pzae039.
20. Turan E, Savut B, Kulaksızoğlu M, et al. Diyabetli hastalarda bel, boyun ve ayak bileği çevresinin kesim nokta değerleri. *Selçuk Tıp Derg.* 2015;31:24-6.
21. Ungvari Z, Fazekas-Pongor V, Csiszar A, Kunutsor SK. The multifaceted benefits of walking for healthy aging: from blue zones to molecular mechanisms. *Geroscience.* 2023;45:3211-39.
22. Suh JH, Kim H, Jung GP, et al. The effect of lumbar stabilization and walking exercises on chronic low back pain: a randomized controlled trial. *Medicine (Baltimore).* 2019;98:e16173.
23. Arkesteijn M, Jones R, Low DC. The effect of walking and stationary work on the acute back pain, muscle activation, posture and postural control of older women. *Ergonomics.* 2022;65:866-76.
24. Seay JF, Van Emmerik RE, Hamill J. Influence of low back pain status on pelvis-trunk coordination during walking and running. *Spine (Phila Pa 1976).* 2011;36:E1070-9.

25. Tekin V, Akçay Ş, Şengül İ, et al. Effect of aerobic exercise program in patients with non-specific chronic low back pain. *Cukurova Med J.* 2020;45:1372-83.
26. Li YC, Zhao YF, Yang XZ, et al. Effects of short-term intervention of walking on body mass index, waist circumference, and related indicators of working population. *Zhonghua Yu Fang Yi Xue Za Zhi.* 2019;53:212-7.
27. Melam GR, Alhusaini AA, Buragadda S, et al. Impact of brisk walking and aerobics in overweight women. *J Phys Ther Sci.* 2016;28:293-7.
28. Guessogo WR, Temfemo A, Mandengue SH, et al. Effect of 24-week repeated short-time walking based training program on physical fitness of black Cameroonian obese women. *J Exerc Rehabil.* 2016;12:90-8.



A Comparative Study Evaluating Tonsillolith and Stylohyoid Ligament Ossification on Cone Beam Computed Tomography and Panoramic Radiography: A Retrospective Study

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Abstract

Aim: Dentists frequently encounter soft tissue calcifications in their routine practice. Stylohyoid ligament calcification or ossification (SHLO) is a common incidental finding on radiographs. Tonsillolith is a calcified structure formed as a result of chronic and recurrent inflammation in the crypts of the tonsils. The purpose of this study was to compare the prevalence of tonsillolith and SHLO and mean length of SHL obtained using cone beam computed tomography (CBCT) and panoramic radiography (PR) images.

Material and Method: In this study, CBCT and PR images of a total of 289 patients (mean age 41.87 years), including 157 females and 132 males, were evaluated. The prevalence of tonsilloliths and SHLO was recorded as present/absent, and SHL lengths were measured as the linear distance between the base and the apex of the stylohyoid process on CBCT and PR images. The SHL lengths greater than 30 mm were labeled as SHLO and used in the prevalence statistics. Wilcoxon test used for the relationship between SHL/SHLO lengths obtained by two different imaging methods and McNemar test for the prevalence of tonsillolith obtained by two different imaging methods.

Results: The prevalence of tonsillolith was found to be 7.4% with PR and 23.5% with CBCT, the prevalence of SHLO was 34.78% with PR and 43.25% with CBCT, and the mean SHL length was 28.67 mm with PR and 30.88 mm with CBCT. The prevalence of SHLO and tonsillolith was found to be higher in CBCT than in PR, and the measured mean SHL length was greater. This difference was statistically significant. No statistically significant differences were observed between genders with respect to SHL length and SHLO prevalence. The prevalence of tonsillolith in males was found to be statistically significantly higher than in females.

Conclusion: In cases where the length of the SHL is of critical importance for SHLO or when there is a suspicion of Eagle syndrome, CBCT is more suitable imaging technique instead of PR. This is also the case for tonsillolith evaluations, as the CBCT eliminates superimpositions.

Keywords: Cone-beam computed tomography, heterotopic ossification, palatine tonsil, panoramic radiography

INTRODUCTION

Dentists frequently encounter soft tissue calcifications (STC) in their routine practice. The majority of STC cases are asymptomatic and identified as incidental findings on radiographic images (1). Calcium salt accumulation in soft tissue that lacks organization is classified as heterotopic calcification, whereas organized calcium salt accumulation is defined as heterotopic ossification. Heterotopic calcification is classified into three categories: dystrophic, idiopathic, and metastatic. These categories are based on the mechanism, etiology, and localization of

the calcification (2). Dystrophic calcification represents a specific form of heterotopic calcification observed in degenerate, diseased, or dead tissues of individuals who have normal levels of calcium and phosphate in their serum (3). It frequently manifests following inflammatory, traumatic, or infectious processes (4). These calcifications are found primarily in the area of the head and neck. They are relatively common in the general population. Most calcifications are asymptomatic and are incidentally identified through imaging techniques commonly employed in dentistry (2).

CITATION

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Styloid process is a pointed and cylindrical bone process. It originates from the inferior aspect of the petrous part of the temporal bone, moving in an antero-inferior direction. The inferior part of the styloid process close to the carotid vessels (5,6). Stylohyoid ligament, originates from the styloid process and connects the temporal and hyoid bones (5). Stylohyoid ligament calcification or ossification (SHLO) is a common incidental finding on radiographs (1,7). A length of 30 mm or more is considered calcified/elongated (6,8,9). Eagle syndrome, which is characterized by elongation of this ligament, is associated with some symptoms (10). Pain can be felt in the throat, front of the neck and ear. The view of SHLO is not pathognomonic for Eagle syndrome. Symptoms of Eagle syndrome can vary from mild discomfort to acute neurological and reflected pain (11). SHLO; in the region between the posterior aspect of the ramus mandible and the cervical vertebra, there is a radiopaque image in a structure similar to a dry tree branch, which becomes thinner as it moves downward (12).

Tonsilloliths are calcified structures formed in the crypts of the tonsil due to chronic recurrent inflammation (13). On clinical examination, it is usually apparent as yellowish plaques on the tonsillar surface. While smaller tonsilloliths are usually symptomless, bigger ones can cause a variety of symptoms. These include pain, bad breath, foreign body sensation, earaches, irritation, difficulty swallowing, bad taste (14). They can be single or several, one-sided or both-sided. The size of the tonsilloliths can vary from a few millimeters up to several centimeters in size. Tonsilloliths can be seen on routine panoramic radiographs (PR). In the PR images, it is seen in the form of single or multiple radiopacities superimposed on the middle part of the mandibular ramus. Tonsilloliths appear lateral to the oropharyngeal airway on cone beam computed tomography (CBCT) axial sections. Their density is similar to that of cortical bone (15).

Although these calcifications are visible on PR, that is one of the traditional imaging modalities commonly used in dentistry, it has some limitations compared to CBCT (15). The proximity of anatomical structures in the head and neck region leads to distortion, magnification, superimposition and ghost images in the radiographic images. These limitations in PR can lead to inadequate diagnosis and detection of calcifications. With CBCT, the diagnosis and location of the calcification can be accurately determined due to the three-dimensional imaging (16,17).

In cases where STCs are close to bone, it may be difficult to determine whether the calcification is in bone or soft tissue. In such cases, patient history, clinical examination, radiographs taken from a different angle, or other imaging modalities may be useful (2). Today, CBCT is widely used in maxillofacial imaging because of its lower radiation dose and high spatial resolution of bone structures compared to computed tomography (CT). Incidental findings such as STCs can be diagnosed with CBCT (16). The localization, number, shape and distribution of STCs should be considered for correct diagnosis. Knowledge

of soft tissue anatomy is necessary for the diagnosis of calcifications (18).

The purpose of this study was to compare the prevalence of tonsillolith and SHLO and mean length of SHL obtained using CBCT and PR images. In addition, it was also aimed to examine the relationship between the prevalence of tonsillolith and mean length of SHL/SHLO and the age groups and the gender.

MATERIAL AND METHOD

This study designed as retrospective radiological study and received ethical approval from Kütahya University Non-Interventional Clinical Research Ethics Committee with protocol number 2024/05-14 dated April 22, 2024. A total of 795 CBCT images from the image archive of the Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Kütahya Health Sciences University, were examined between January 1, 2022 and January 1, 2023, and the dates of the CBCT's were recorded. The radiographic images of patients who obtained CBCT and PRs within the same week were included in the study. All PRs were acquired using the Morita Veraview EPOCS 2D (Japan) unit at 65-90 kVp and 6-10 mA. Instrumentarium brand device was used to acquire all CBCT images (Palo Dex Group Oy Nahkelantie 160 FI-04300 TUUSULA, FINLAND) using 89 kVp, 4-12 mA values. OnDemand 3D Dental (Cybermed, Seoul, South Korea) imaging software used for CBCT measurements. The measurements on the PR were performed using TRtek Medical software (İstanbul, Türkiye). Acer Veriton VZ4880G monitor (23.8-inch, 1920 X 1080 resolution) used for CBCT and PR image evaluations.

Inclusion and Exclusion Criteria

The CBCT images with an 8*15 cm field of view (FOV), where the entire length of the SHL can be seen, were included in the study. Patients without bone metabolic disorders, over 18 years of age, with PR and CBCT images obtained in the same week were included in the present study. Patients in which the entire SHL could not be observed, patients with bone metabolism diseases and patients under the age of 18 were excluded from the study. Furthermore, radiographs with motion artefacts and poor diagnostic quality were excluded.

A priori power analysis with a 5% significance level and an estimated effect size of 0.33, along with a desired study power of 95%, indicated that a minimum number of 262 patients would be required for this investigation (G*Power: Statistical Power Analyses for Windows; Dusseldorf, Germany). A total of 795 CBCTs were analyzed in the present study. Of these, 483 were excluded from the study because they lacked a comparable PR image captured within the same week, 15 were excluded since they were radiographic images of individuals under 18 years of age, and 8 were excluded due to the presence of radiographic artifacts. The final analysis included 289 CBCT and PR images. The study's flow chart is presented in Figure 1.

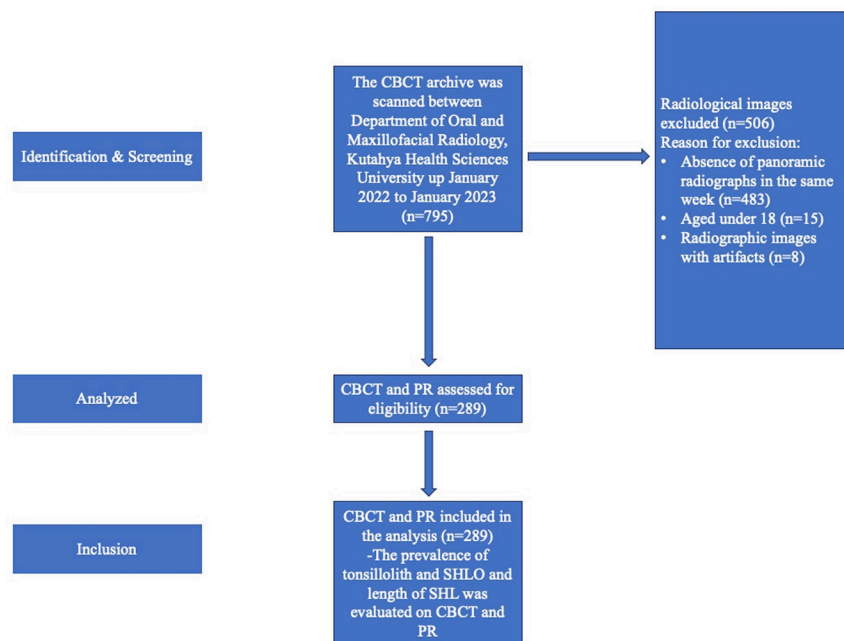


Figure 1. Study flowchart

Evaluations and Measurements on PR and CBCTs

An Oral and Maxillofacial Radiology specialist (A.T.) with three years of experience, in a quiet room with low-level lighting, performed all measurements and evaluations. Measurements and evaluations were repeated twice at two weeks interval. For STCs seen on PR images (Figure 2) (19), only tonsillolith and SHLO were examined. For the prevalence of tonsilloliths, tonsilloliths were labeled as presence/absence.

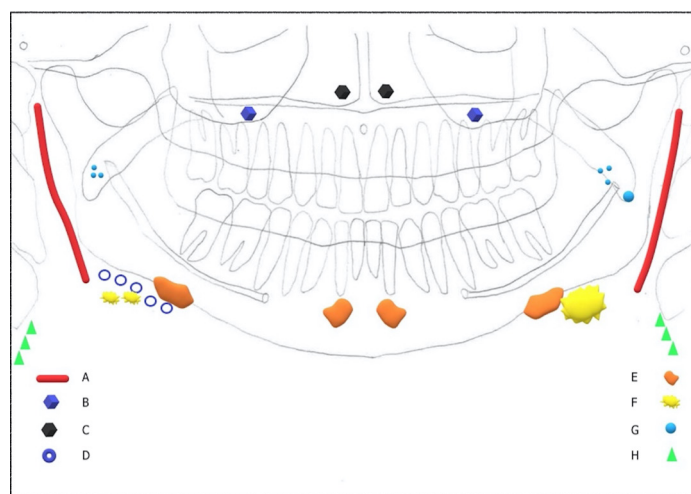


Figure 2. Soft tissue calcifications; A: Stylohyoid ligament ossification, B: Antrolith, C: Rhinolith, D: Phlebolith, E: Sialolith, F: Calcified lymph node, G: Tonsillolith, H: Carotid artery calcification

Detection of Tonsilloliths on CBCT and PR: Tonsilloliths appear as single or multiple radiopacities superimposed on the midsection of the mandibular ramus in PRs, particularly in the region where the dorsal surface of the tongue crosses the oropharyngeal airways (15) (Figure 2). In axial section of CBCT images, tonsilloliths are identified in the soft tissue adjacent to the medial aspect of the mandibular ramus and the lateral wall of the oropharyngeal airway (15) (Figure 3).

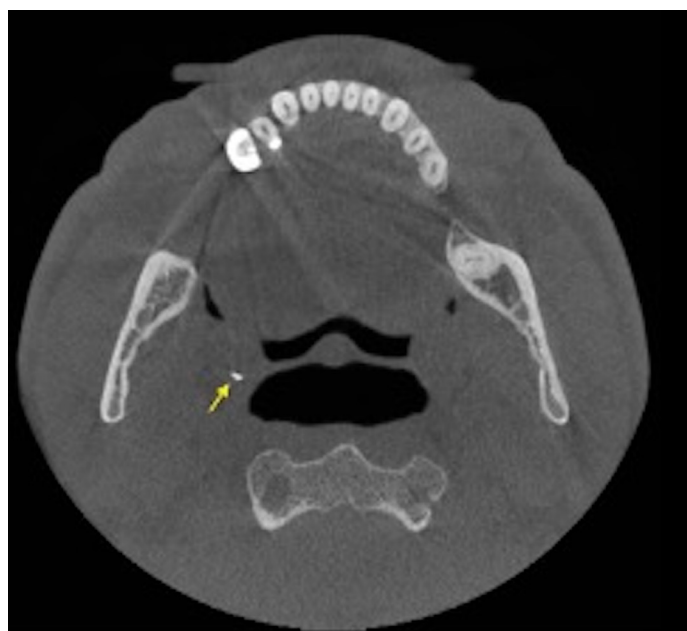


Figure 3. Tonsillolith on axial section of CBCT

Detection and Measurement of SHL on CBCT and PR: In PRs, SHL originates from the region of the mastoid process, extending through the posteroinferior aspect of the mandibular ramus towards the hyoid bone (15). SHL was measured as the linear distance between the base and the apex of the stylohyoid process on PR (8) (Figure 4). The SHL length was determined by measuring the straight-line distance between the base and the apex of the stylohyoid process on CBCT images (8) (Figure 5). The measurement was made including the non-ossified parts of the SHL. Parasagittal sections were used for SHL measurements on the CBCT image. All SHL measurements were recorded in mm. The SHL lengths greater than 30 mm were labeled as SHLO and used in the prevalence statistics. Age, gender information of the patients was added to the Excel table.



Figure 4. SHL measurement on PR

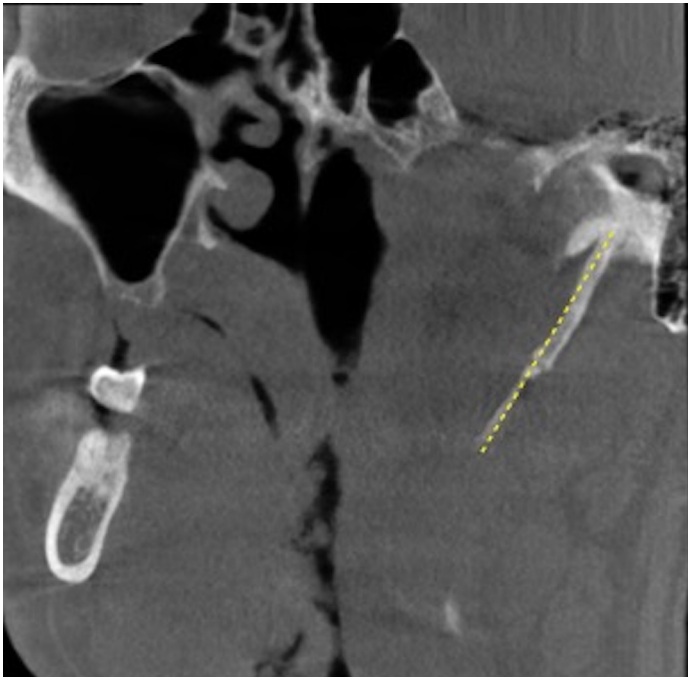


Figure 5. SHL measurement on parasagittal section of CBCT

Statistical Analysis

SPSS software (IBM, SPSS version 26, for Mac, Chicago, IL) was used to investigate the results of this conducted study. Intraclass correlation was used for measurement data, and Goodman-Kruskal tau coefficient was used for categorical

data to evaluate intra-observer agreement. Frequency and descriptive statistics were used for all data. Pearson chi-square test was used to analyze the relationship between tonsillolith with age groups and gender. The Mann-Whitney U test was used to compare the means of two independent groups when the measurement data did not meet the requirements of the parametric test; the Kruskal-Wallis test was used to compare the means of three independent groups. The relationship between the measurement data obtained with two different imaging techniques was analyzed by Wilcoxon test, while the categorical data analyzed by using McNemar test. In statistical analyses, significance level was determined as 5%.

RESULTS

Intraclass agreement test results were good for SHL length measurements (0.823) and excellent for tonsillolith scores (0.973). Second measurements were used for further statistical analysis. A total of 289 patients, 157 females and 132 males, were included in our study. The age of the patients included in our study ranged from 18 to 80 years (mean age 41.87 years). The prevalence of tonsilloliths and SHLO was evaluated on 578 sides, and the length of the SHL was measured on 578 sides. To evaluate the relationship between calcifications and age groups, patients were classified into 3 groups according to age. Patients aged 18-35 years were formed the first group, 35-52 years the second group, and 52-80 years the third group. There were 103 patients in the first group, 98 in the second group, and 88 in the third group.

The prevalence of tonsillolith and SHLO, the soft tissue calcifications examined in our study, are shown in Table 1. The prevalence of tonsillolith and SHLO was found to be higher in the CBCT than in the PR. Table 2 presents the mean, minimum, maximum, and standard deviation values for the lengths of SHL and SHLO. The results of our study indicate that the mean SHL length measured with CBCT was 30.88 mm, while with PR it was 28.67 mm. Additionally, the mean SHLO length was measured as 38.44 mm with CBCT and 37.43 mm with PR.

Table 1. Prevalence of STCs on CBCT and PR					
Imaging techniques	Soft tissue calcifications	Presence		Absence	
		n	%	n	%
CBCT	Tonsillolith	136	23.5	442	76.5
	SHLO	250	43.25	328	56.75
PR	Tonsillolith	43	7.4	535	92.6
	SHLO	201	34.78	377	65.22

Table 2. Descriptive analysis of SHL and SHLO on CBCT and PR						
Imaging techniques	Length	n	Mean	Minimum	Maximum	Standard deviation
CBCT	SHL	578	30.88	7.10	92.45	9.34
	SHLO	250	38.44	30.19	92.45	9.10
PR	SHL	578	28.67	9.12	84.82	8.74
	SHLO	201	37.43	30.11	84.82	8.51

In our study, tonsilloliths were observed statistically significantly more often in males in both PR and CBCT images. They were also observed statistically significantly less frequently in the patient group under

35 years of age than in the other patient groups in both imaging techniques. There was no statistically significant relationship between the second and third age groups (Table 3).

Table 3. Relationship between prevalence of tonsillolith and SHLO with gender and age groups						
Soft tissue calcifications	Demographic data	Imaging techniques		n		p value
				Presence (%)	Absence (%)	
Tonsillolith	Gender	CBCT	Female	255 (81.2)	59 (18.8)	0.003*
			Male	187 (70.8)	77 (29.2)	
		PR	Female	297 (94.6)	17 (5.4)	0.043*
			Male	238 (90.2)	26 (9.8)	
	Age groups	CBCT	18-35 ^a	179 (86.9)	27 (13.1)	0.000*
			35-52 ^b	144 (73.5)	52 (26.5)	
			52-80 ^b	119 (67.6)	57 (32.4)	
		PR	18-35 ^a	201 (97.6)	5 (2.4)	0.002*
			35-52 ^b	178 (90.8)	18 (9.2)	
			52-80 ^b	156 (88.6)	20 (11.4)	
SHLO	Gender	CBCT	Female	183 (58.3)	131 (41.7)	0.417
			Male	145 (54.9)	119 (45.1)	
		PR	Female	215 (68.5)	99 (31.5)	0.074
			Male	162 (61.4)	102 (38.6)	
	Age groups	CBCT	18-35 ^a	131 (63.6)	75 (36.4)	0.006*
			35-52 ^b	94 (47.9)	102 (52.1)	
			52-80 ^b	103 (58.5)	73 (41.5)	
		PR	18-35 ^a	156 (75.7)	50 (24.3)	0.000*
			35-52 ^b	110 (56.1)	86 (43.9)	
			52-80 ^b	111 (63.1)	65 (36.9)	

Pearson chi-square test was used; *p<0.05 was considered statistically significant; There is no statistically significant difference between groups with the same superscripts

Table 4 shows the relationship between mean SHL and SHLO lengths with gender, and age groups. While there was no statistical relationship between mean SHL length and gender, the relationship between mean SHLO length and gender was significant. Male patients with SHLO had longer SHLO lengths than females.

The relationship between SHL length and age group was statistically significant. Accordingly, the mean SHL length of the patient group under 35 years of age was lower than the other groups in both imaging techniques. The relationship between mean SHLO length and age groups was not statistically significant (Table 4).

Table 4. Relationship between SHL and SHLO lengths with gender and age groups							
Soft tissue calcifications	Demographic data	Imaging techniques		n	Mean (mm)	p ¹ value	p ² value
SHL Length	Gender	CBCT	Female	314	29.84	0.126	-
			Male	264	32.10		
		PR	Female	314	27.75	0.155	-
			Male	264	29.77		
	Age groups	CBCT	18-35 ^a	206	29.99	-	0.010*
			35-52 ^b	196	31.60		
			52-80 ^b	176	31.13		
		PR	18-35 ^a	206	27.27	-	0.000*
			35-52 ^b	196	29.31		
			52-80 ^b	176	29.60		
SHLO Length	Gender	CBCT	Female	131	36.40	0.000*	-
			Male	119	40.70		
		PR	Female	99	35.54	0.002*	-
			Male	102	39.27		
	Age groups	CBCT	18-35	75	39.12	-	0.376
			35-52	102	37.48		
			52-80	73	39.12		
		PR	18-35	50	39.26	-	0.131
			35-52	86	36.23		
			52-80	65	37.63		

p¹: Mann Whitney-U test was used, p²: Kruskal-Wallis test was used, * p<0.05 was considered statistically significant; There is no statistically significant difference between groups with the same superscripts

The comparison of the prevalence of tonsillolith and the length of SHL in CBCT and PRs is shown in Table 5. The diagnosis of tonsillolith was found to be statistically significantly higher in CBCT than in PRs. The mean SHL length was found to be statistically significantly higher in CBCT than in PR (Table 5).

Table 5. Comparison of tonsillolith prevalence and SHL length with CBCT and PR						
	Imaging Techniques	Tonsillolith		P ¹	SHL	P ²
		Presence (n, %)	Absence (n, %)		Mean (mm)	
Right	CBCT	74 (25.6)	215 (74.4)	0.000*	31.17	0.000*
	PR	21 (7.3)	268 (92.7)		28.85	
Left	CBCT	62 (21.4)	227 (78.6)	0.000*	30.59	0.000*
	PR	22 (7.6)	267 (92.4)		28.49	
Total	CBCT	136 (23.5)	442 (76.5)	0.000*	30.88	0.000*
	PR	43 (7.4)	535 (92.6)		28.67	
p ¹ : McNemar test was used, p ² : Wilcoxon test was used, * p<0.05 was considered statistically significant						

DISCUSSION

In PRs, structures situated medially concerning the focal trough are subject to higher magnification and distortion. The SHL, particularly its distal end, is situated in a medial position relative to the image layer (5). CBCT imaging is a more effective modality for examining the SHL than PR (20). The orientation of the SHC and its relationship with adjacent anatomical structures can be more accurately assessed on three-dimensional radiographs than on two-dimensional radiographs (21).

The differential diagnosis of tonsilloliths includes pathologies such as osteosclerosis, enostosis, sialolithiasis, lymph node calcification, and phleboliths. When complemented by a CT screening, PR is an effective method for diagnosing these lesions. The use of CBCT images from both sides of the jaw is beneficial for the precise determination of the locations of these calcifications (12,22). Accurate diagnosis of SHLO on PRs can sometimes be difficult due to superimposition of adjacent bony structures. CT overcomes this problem and provides reliable visualization of SHLO features and their relationship to the surrounding anatomy (20).

Tonsilloliths are described in the literature as incidental findings on PRs, but the limitations of this technique make interpretation difficult. In the existing literature, some articles report the prevalence of tonsillolith on panoramic images to be between 2.5% and 18% (22-26). Our study yielded a prevalence rate of 7.4%. Nevertheless, the discrepancy between the prevalence figures reported in some studies was more pronounced (22,23). The discrepancy between studies is thought to be due to differences in the number of samples analyzed. A review of the literature revealed that the prevalence of tonsillolith in studies conducted with CBCT ranged from 2% to 33.2% (27-31). The prevalence of tonsillolith detected in panoramic images was 23.5%. This value was in the range of literature values. This range was generally higher than that observed in PRs. This discrepancy may be due to the fact that CBCT does not produce superposition and creates higher resolution images compared to PR. A number of factors, including sample size, inter-individual variability among patients within a given sample, and differences in the field of view (FOV) of CBCTs, may account for the considerable

variation in the prevalence of tonsilloliths observed in CBCT studies.

In addition to studies that report a statistically higher prevalence of tonsillolith in males (2,22), there are also studies that report a statistically higher prevalence of tonsillolith in females (25). Additionally, in some studies have shown that there is no statistical difference between them (26-28). The prevalence of tonsillolith significantly higher in the male population in the course of our study. The difference in findings may be due to the impact of individual variables, like the presence of tonsillolith, which in some cases may have gone undiagnosed and untreated.

The precise etiology and pathogenesis of tonsillolith are unknown, but repeated flare-ups of inflammation may lead to dystrophic calcification of the tonsil crypts. It is believed that the likelihood of developing this dystrophic calcification increases with increasing age. In the present study, the relationship between age groups and the incidence of tonsillolith showed statistical significance. According to this relationship, tonsillolith increased with age. There are a number of studies in the literature that are in agreement with this outcome (25,27,32). However, there are also inconsistent studies (26,28,31). This difference is likely due to differences in mean age between study populations.

The styloid ligament ossification typically appears as a thin bony prominence that originates from the styloid process and extends toward, and sometimes contacts, the lesser horn of the hyoid bone. In studies conducted with the use of PR, the prevalence of SHLO has been documented to range between 6.23% and 83.6% (33-35). The SHLO observed in the present study exhibited a prevalence rate of 34.78%, which is consistent with the aforementioned range. The principal reason for this extensive discrepancy in the literature is believed to be the size of the sample population. As the number of samples included in these reviewed articles increased, so also did the prevalence of SHLO. Furthermore, the prevalence of SHLO has been reported to be between 3.14% and 63% in studies conducted with CBCT (27-29,36). The frequency of SHLO observed in this present study was within the above range, occurring in 43.25% of cases. The reason for this wide range of prevalence in the literature may be due to the

varying field of view of CBCT, sample size, and individual differences of the patients included in the sample.

The accepted upper limit for the normal length of SHL is 30 mm, as evidenced in the literature (34). In our study, the mean SHL length measured by PR was 28.67 mm, while the mean SHLO length was 37.43 mm (6,33,34). The outcomes obtained from panoramic images were slightly higher to that of the studies employing PR. In the study conducted by Okabe et al. (37), the mean SHL length was found to be 36.7 mm, which is greater than the outcome of the current study. The inclusion of PRs of only 80-year-old patients in their study may explain this disparity (37).

The mean SHL length measured by CBCT was 30.88 mm, while the mean SHLO length was 38.45mm. As reported by Al-Amad et al. in their CBCT study, the mean SHL length was found to be 30.2 mm on the right and 31.2 mm on the left (7). The mean SHL length observed in our study is similar to that reported in the aforementioned study (31.17 mm on the right and 30.59 mm on the left). In the CBCT studies conducted by Büyük et al. (38) and Andrei et al. (5), the mean SHL was found to be 35.09 and 34.28 mm, respectively. These results were higher than those observed in our study. In a study employing the same imaging technique, İlgüy et al. (39) observed an average SHL length of 25.3 mm. This result differed from our study's, yielding a smaller value. The discrepancies may be attributed to the higher mean age or the different sample sizes.

Conflicting results exist in the literature regarding the relationship between SHLO frequency and SHL length with gender. Some studies have found that the SHL length is statistically significantly greater in males than in females (5,33,37). Additionally, some studies did not find a statistical significance between gender and SHL length (38,39). SHLO frequency was observed to be statistically significantly higher in males than females (28). Conversely, some studies reported no statistically significant relationship between gender and SHLO frequency (7,20), or more SHLO frequency in females (35). In the present study, SHL length and SHLO frequency were not statistically related to gender. It is reported that surgical trauma, local chronic irritation, retention of mesenchymal elements, menopausal endocrine disorders and trauma or mechanical stress during growth may lead to SHL hyperplasia in the literature (40). The lack of knowledge regarding the etiological factors in the patients included in our study may explain this discrepancy. In our study, the relationship between SHLO length and gender was also investigated. The SHLO length was higher in males than in females. Missias et al. (28) came to same conclusion.

Although previous studies have indicated that the correlation between SHLO prevalence and age groups is not statistically significant (9,20,28,35), another research has demonstrated that there is, a statistically significant relationship between the two (33). Our study found that SHLO frequency was significantly lower in patients under 35 years of age than in other age groups. İlgüy et al.

(39) and Büyük et al. (5), who examined the relationship between SHL length and age groups, found no statistical relationship. In our study, the relationship was found to be statistically significant. The mean SHL lengths of patients under the age of 35 were observed to be lower than those in the other age groups over the age of 35. The discrepancy may be attributable to the difference in age groups represented in the studies. In the present study, the relationship between mean ossified SHL lengths and age groups was also investigated. No statistically significant relationship was identified.

Panoramic imaging is an easily accessible method of imaging that uses a low dose of radiation and is used in the majority of dental procedures (22). But the diagnostic limitations of PRs make the identification of soft tissue calcifications challenging (20). In a study conducted by Özdede et al. (31), the detection of tonsilloliths in PR and CBCT was compared. In this study, some tonsilloliths identified in CBCT were not visible in PR. The number of tonsilloliths detected in PR was found to be statistically significantly lower than that detected by CBCT. In a comparative study conducted by Gökçen et al. (8), where PR and CBCT were used, the frequency of elongated SHL was found to be statistically significantly higher in CBCT. In a study conducted by Centurion et al. (20), the tonsillolith and SHL chain were evaluated using PR and CBCT. In their study, the prevalence of tonsilloliths and SHLO detected with PR was found to be statistically lower than that with CBCT. In our study, the prevalence of tonsilloliths was found to be higher in CBCT images, and the mean length of SHL was observed to be longer, in alignment with the findings of the aforementioned studies. The lower results obtained in PR are believed to be attributable to the intrinsic characteristics of the imaging modality, including superposition, magnification, and distortion of the image, as well as the reduction of three-dimensional structures to two dimensions. Furthermore, the detectability of calcifications in PR may be influenced by several factors, including the size of the calcification, the degree of calcification, and individual differences such as bone density.

A limitation of this study was the absence of data regarding tonsillolith size. As a result, an examination of the relationship between the prevalence of tonsilloliths detected by PRs and tonsillolith sizes was not possible. Another limitation of our study is the uncertainty regarding the presence or absence of a history of micro or macro trauma in the included patients, as well as the lack of information concerning the menopausal status of female patients. It is recommended that these factors be taken into consideration in future studies.

CONCLUSION

In conclusion, In the literature, the prevalence, size, and relationship with demographic data of tonsillolith and SHLO have been evaluated with different imaging methods such as PRs, CBCT, and CT; however, comparative studies with PR and CBCT are limited. The prevalence of tonsillolith and

SHLO, as well as the length of SHL, were found to be higher in CBCT images in our study. Furthermore, the occurrence of tonsilloliths and SHL was found to be statistically associated with age groups. The statistical analysis revealed that males had higher tonsillolith prevalence and the mean SHL length. The use of CBCT images as an imaging technique for the detection of these pathologies is more suitable than that of PR, due to the superiority of the imaging features of CBCT images over those of PR. The use of panoramic imaging in the initial assessment, epidemiological evaluation, and screening of calcifications may assist in diagnosing and monitoring these conditions. In circumstances where an accurate measurement of the length of the SHL is crucial for the diagnosis of SHLO or when there is a suspicion of Eagle syndrome, a CBCT evaluation should be conducted instead of a PR. In cases where the length of the SHL is of critical importance for SHLO or when there is a suspicion of Eagle syndrome, CBCT is more suitable imaging technique instead of PR. This is also the case for tonsillolith evaluations, as the CBCT eliminates superimpositions.

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Ethical approval: The research protocol was approved by Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (decision date and approval number: 22.04.2024, 2024/05-14). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration. Since our research is a retrospective study, the informed consent form has not been taken.

REFERENCES

1. Syed AZ. Soft tissue calcifications in the head and neck region. Dent Clin North Am. 2024;68:375-91.
2. Yalcin ED, Ararat E. Prevalence of soft tissue calcifications in the head and neck region: a cone-beam computed tomography study. Niger J Clin Pract. 2020;23:759-63.
3. Scarfe WC, Farman A. Soft tissue calcifications in the neck: Maxillofacial CBCT presentation and significance. AADMRT Currents. 2010;2:2:3-15.
4. de Oliveira Cde N, Amaral TM, Abdo EN, Mesquita RA. Bilateral tonsilloliths and calcified carotid atheromas: case report and literature review. J Craniomaxillofac Surg. 2013;41:179-82.
5. Buyuk C, Gunduz K, Avsever H. Morphological assessment of the stylohyoid complex variations with cone beam computed tomography in a Turkish population. Folia Morphol (Warsz). 2018;77:79-89.
6. Hettiarachchi PVKS, Jayasinghe RM, Fonseka MC, et al. Evaluation of the styloid process in a Sri Lankan population using digital panoramic radiographs. J Oral Biol Craniofac Res. 2019;9:73-6.
7. Al-Amad SH, Al Bayatti S, Alshamsi HA. Stylohyoid ligament calcification and its association with dental diseases. Int Dent J. 2023;73:151-6.
8. Akçiçek G, Kara D, Uysal S, Zengin HY. Comparison of elongation and calcification patterns of styloid process on panoramic and cone beam computed tomography images. European Annals of Dental Sciences. 2023;50:S1-5.
9. Saati S, Foroozandeh M, Alafchi B. Radiographic characteristics of soft tissue calcification on digital panoramic images. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2020;20:e5053.
10. Dey A, Mukherji S. Eagle's syndrome: a diagnostic challenge and surgical dilemma. J Maxillofac Oral Surg. 2022;21:692-6.
11. Badhey A, Jategaonkar A, Anglin Kovacs AJ et al. Eagle syndrome: a comprehensive review. Clin Neurol Neurosurg. 2017;159:34-8.
12. Çitir M, Gündüz K. The prevalence of soft tissue calcification/ossification on panoramic radiography. Selcuk Dent J. 2020;7:226-32.
13. de Moura MD, Madureira DF, Noman-Ferreira LC, et al. Tonsillolith: a report of three clinical cases. Med Oral Patol Oral Cir Bucal. 2007;12:E130-3.
14. Babu BB, Tejasvi MLA, Avinash CK, B C. Tonsillolith: a panoramic radiograph presentation. J Clin Diagn Res. 2013;7:2378-9.
15. Carter LC. Yumuşak doku kalsifikasyon ve ossifikasyonları. In: White SC, Pharoah MJ, eds. Oral radyoloji ilkeler ve yorumlama. 7 edition. Ankara: Palme Yayınevi; 2018;524-41.
16. Scarfe WC, Farman AG, Sukovic P. Clinical applications of cone-beam computed tomography in dental practice. J Can Dent Assoc. 2006;72:75-80.
17. Mısırlıoğlu M, Nalcaci R, Adisen MZ, Yardımcı S. Bilateral and pseudobilateral tonsilloliths: three dimensional imaging with cone-beam computed tomography. Imaging Sci Dent. 2013;43:163-9.
18. Duran MH, Coşgun Baybars S. Evaluation of soft tissue calcifications in the head and neck region on panoramic radiography of edentulous patients. NEU Dent J. 2024;6:208-15.
19. Avsever H, Orhan K. Çene kemiği ve çevre dokuları etkileyen kalsifikasyonlar. Türkiye Klinikleri J Oral Maxillofac Radiol-Special Topics. 2018;4:43-52.
20. Centurion BS, Imada TS, Pagin O, et al. How to assess tonsilloliths and styloid chain ossifications on cone beam computed tomography images. Oral Dis. 2013;19:473-8.
21. Gayathri G, Elavenil P, Sasikala B, et al. 'Stylo-mandibular complex' fracture from a maxillofacial surgeon's perspective-review of the literature and proposal of a management algorithm. Int J Oral Maxillofac Surg. 2016;45:297-303.
22. Ghabanchi J, Haghnegahdar A, Khojastehpour L, Ebrahimi A. Frequency of tonsilloliths in panoramic views of a selected population in southern Iran. J Dent (Shiraz). 2015;16:75-80.
23. Icoz D, Akgunlu F. Prevalence of detected soft tissue calcifications on digital panoramic radiographs. SRM Journal of Research in Dental Sciences. 2019;10:21-5.

24. Takahashi A, Sugawara C, Kudoh T et al. Prevalence and imaging characteristics of palatine tonsilloliths evaluated on 2244 pairs of panoramic radiographs and CT images. *Clin Oral Investig*. 2017;21:85-91.
25. Acikgoz A, Akkemik O. Prevalence and radiographic features of head and neck soft tissue calcifications on digital panoramic radiographs: a retrospective study. *Cureus*. 2023;15:e46025.
26. Maia PRL, Tomaz AFG, Maia EFT, et al. Prevalence of soft tissue calcifications in panoramic radiographs of the maxillofacial region of older adults. *Gerodontology*. 2022;39:266-72.
27. Lopes IA, Tucunduva RM, Handem RH, Capellozza AL. Study of the frequency and location of incidental findings of the maxillofacial region in different fields of view in CBCT scans. *Dentomaxillofac Radiol*. 2017;46:20160215.
28. Missias EM, Nascimento E, Pontual M et al. Prevalence of soft tissue calcifications in the maxillofacial region detected by cone beam CT. *Oral Dis*. 2018;24:628-37.
29. Pette GA, Norkin FJ, Ganeles J et al. Incidental findings from a retrospective study of 318 cone beam computed tomography consultation reports. *Int J Oral Maxillofac Implants*. 2012;27:595-603.
30. Diniz V, Corrêa EDCB, Gonçalves BC et al. Prevalence of soft tissue calcifications in cone beam computed tomography images in the region of head and neck. *Brazilian Dental Science*. 2020;23:6-p.
31. Ozdede M, Akay G, Karadag O, Peker I. Comparison of panoramic radiography and cone-beam computed tomography for the detection of tonsilloliths. *Med Princ Pract*. 2020;29:279-84.
32. Oda M, Kito S, Tanaka T et al. Prevalence and imaging characteristics of detectable tonsilloliths on 482 pairs of consecutive CT and panoramic radiographs. *BMC Oral Health*. 2013;13:54.
33. More CB, Asrani MK. Evaluation of the styloid process on digital panoramic radiographs. *Indian J Radiol Imaging*. 2010;20:261-5.
34. Zokaris N, Siska I, Natsis K et al. Investigation of the styloid process length in a Greek population. *Folia Morphol (Warsz)*. 2019;78:378-88.
35. Guimarães AC, Pozza DH, Guimarães AS. Prevalence of morphological and structural changes in the stylohyoid chain. *J Clin Exp Dent*. 2020;12:e1027-32.
36. Togan B, Gander T, Lanzer M, et al. Incidence and frequency of nondental incidental findings on cone-beam computed tomography. *J Craniomaxillofac Surg*. 2016;44:1373-80.
37. Okabe S, Morimoto Y, Ansai T, et al. Clinical significance and variation of the advanced calcified stylohyoid complex detected by panoramic radiographs among 80-year-old subjects. *Dentomaxillofac Radiol*. 2006;35:191-9.
38. Andrei F, Motoc AG, Didilescu AC, Rusu MC. A 3D cone beam computed tomography study of the styloid process of the temporal bone. *Folia Morphol (Warsz)*. 2013;72:29-35.
39. Ilgüy D, Ilgüy M, Fişekçioğlu E, Dölekoğlu S. Assessment of the stylohyoid complex with cone beam computed tomography. *Iran J Radiol*. 2012;10:21-6.
40. Alpoz E, Akar GC, Celik S, et al. Prevalence and pattern of stylohyoid chain complex patterns detected by panoramic radiographs among Turkish population. *Surg Radiol Anat*. 2014;36:39-46.



Treatments for Knee Cartilage Injuries in Athletes Using PRP and Hyaluronic Acid: A Retrospective Analysis

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Abstract

Aim: This retrospective study seeks to evaluate the clinical outcomes and imaging findings in athletes with knee cartilage injuries treated using autologous platelet-rich plasma (PRP) and hyaluronic acid (HA) injections.

Material and Method: Sixty athletes participated in this investigation, with 30 individuals in the PRP group and 30 in the HA group. PRP was administered via ultrasound-guided intra-articular injections over three sessions, spaced at three-week intervals. Similarly, HA was injected using high molecular weight hyaluronic acid following the same schedule. Clinical evaluation was performed using the Visual Analog Scale (VAS) for pain assessment and the Knee Injury and Osteoarthritis Outcome Score (KOOS) for functional evaluation. Radiological changes were assessed through magnetic resonance imaging (MRI).

Results: Both VAS and KOOS scores demonstrated a greater improvement in the PRP group compared to the HA group ($p < 0.05$). MRI findings revealed more pronounced cartilage regeneration in the PRP group ($p < 0.05$). No statistically significant differences were found between the two groups regarding age, gender, or career duration ($p > 0.05$).

Conclusion: For sportsmen with knee cartilage problems, PRP therapy has been found to be a more successful treatment alternative than HA. PRP offers better outcomes for cartilage regeneration, pain management, and functional enhancement. The long-term effectiveness of these results may be further assessed in prospective randomized studies in the future.

Keywords: Platelet-rich plasma, hyaluronic acid, knee cartilage injuries, biological therapy, clinical outcomes

INTRODUCTION

Cartilage damage represents a significant clinical challenge that hinders athletic performance and can lead to long-term joint complications. This issue is particularly prominent in high-contact sports such as soccer, basketball, and running athletes, where the knee joint is frequently subjected to repetitive stress and direct trauma (1,2). Chondral lesions in these athletes often manifest with pain, restricted range of motion, and reduced functional capacity, which can eventually lead to early career termination and an increased risk of osteoarthritis (3).

Due to the limited intrinsic regenerative capacity of cartilage, treatment strategies primarily focus on biological and mechanical interventions (4). Among biological therapies, platelet-rich plasma (PRP) and hyaluronic acid (HA) have

been widely studied and used for managing knee cartilage injuries (5). PRP, an autologous concentrate enriched with growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF- β), and vascular endothelial growth factor (VEGF), has been shown to exert anti-inflammatory effects and promote cartilage repair (6). In contrast, HA acts by enhancing the viscoelastic properties of synovial fluid, thereby providing mechanical support while alleviating pain (7).

Despite their widespread use, comparative studies evaluating the efficacy of PRP and HA specifically in athletes remain limited. Most existing research has focused on general populations with knee osteoarthritis, failing to account for the unique biomechanical demands of competitive athletes (8). Given the high functional requirements and shorter recovery timelines in sports

CITATION

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medicine, understanding the effectiveness of these treatments in this subgroup is crucial (8).

Furthermore, standardized classification systems for cartilage lesions—such as the Outerbridge and International Cartilage Repair Society (ICRS) grading systems—are underutilized in sports-related cartilage injury studies (9). MRI-based scoring methods, including the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) and Whole-Organ Magnetic Resonance Imaging Score (WORMS), allow for objective assessment of cartilage healing and should be incorporated into clinical evaluations (10). Studies have demonstrated that MOCART scores above 55 at 6 months postoperatively can predict the likelihood of achieving acceptable symptomatic improvement at one year following autologous chondrocyte implantation, highlighting the importance of MRI-based assessment in cartilage repair (11,12).

Previous research has also indicated that integrating cartilage repair techniques with biomechanical interventions, such as patellofemoral realignment procedures, enhances both clinical outcomes and MRI-assessed cartilage appearance (13). Additionally, treatment approaches such as Autologous Matrix-Induced Chondrogenesis (AMIC) have shown promising long-term results when compared to microfracture techniques in managing focal chondral defects (14). Understanding these therapeutic strategies in the context of high-performance athletes is essential for optimizing treatment protocols and improving return-to-sport outcomes (15).

The primary aim of this retrospective study is to evaluate and compare the clinical and radiological outcomes of PRP and HA therapies in competitive soccer players with knee cartilage injuries. By incorporating MRI-based cartilage assessment and a structured classification of athletic participation levels, this study aims to bridge the gap in current literature and provide clinically relevant insights into the management of cartilage injuries in athletes.

MATERIAL AND METHOD

This retrospective study was conducted at a sports medicine and orthopedic trauma center between 2020 and 2023. The study adhered to the principles outlined in the Declaration of Helsinki and was approved by Dicle University Medical Faculty Ethics Committee for Noninterventional Studies (Approval No: 2023/16-42) before data collection began.

A total of 60 athletes with clinically and radiologically confirmed knee cartilage injuries were included in the study. Participants were classified into two treatment groups:

- **PRP Group (n=30):** Received PRP intra-articular injections.
- **HA Group (n=30):** Received HA intra-articular injections.

A detailed patient selection flowchart has been added (Figure 1) to illustrate the inclusion and exclusion process, group allocation, and follow-up outcomes.

Inclusion Criteria: Clinically and MRI-confirmed knee cartilage injury, Participation in high-impact sports (soccer, running athletes, basketball, etc.), Professional or collegiate-level athletic activity for at least three consecutive years prior to injury, Treatment with PRP or HA injections, according to standardized protocols, A minimum follow-up duration of 12 months post-treatment.

Exclusion Criteria: Concurrent surgical intervention or history of previous knee surgery, Systemic inflammatory or rheumatic diseases, Incomplete medical records or loss to follow-up.

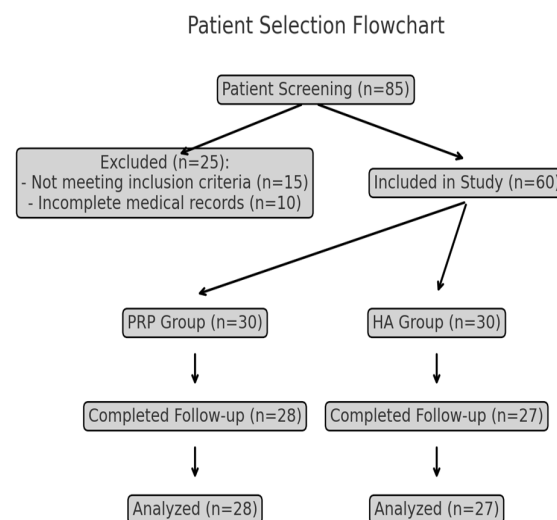


Figure 1. Inclusion and exclusion process, group allocation, and follow-up outcomes

Treatment Protocol

PRP preparation and administration

PRP was prepared using a double centrifugation method to achieve a high concentration of platelets and growth factors (6). A total of 3 mL of PRP was injected intra-articularly into the knee joint under ultrasound guidance at three-week intervals (total of three sessions) (7).

HA injection protocol

High molecular weight HA was administered intra-articularly using a 2 mL dose under ultrasound guidance (8). The injection protocol was identical to the PRP group, consisting of three sessions spaced three weeks apart.

Outcome Measures and MRI Evaluation

1. Pain and Functional Evaluation:

- **Visual Analog Scale (VAS):** Used to assess pain intensity (0=no pain, 10=worst possible pain) before and after treatment (16).
- **Knee Injury and Osteoarthritis Outcome Score (KOOS):** Evaluated functional improvements in sports-related knee injuries (17).

2. MRI-Based Cartilage Assessment:

- All participants underwent pre- and post-treatment MRI scans using a 3.0 Tesla MRI scanner (18).
- Cartilage defects were classified using the Outerbridge and ICRS grading systems (10).
- MRI assessment was conducted using the MOCART scoring system, which evaluates cartilage regeneration on a scale of 0 to 100 (11).
- Cartilage defects were further classified based on anatomical location (e.g., patella, medial/lateral femoral condyle), and MRI findings were analyzed accordingly (9).
- An interobserver reliability analysis was conducted, with two experienced musculoskeletal radiologists independently reviewing the MRI scans.

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0 (IBM, Armonk, NY). Data normality was assessed using the

Kolmogorov-Smirnov test. Paired t-test or Wilcoxon signed-rank test for within-group comparisons. Independent t-test or Mann-Whitney U test for between-group comparisons. Chi-square test for categorical data comparisons. Effect sizes and confidence intervals (95% CI) were reported for VAS, KOOS, and MRI outcomes (19).

Sample size calculation was performed using G*Power 3.1 software, with an effect size of 0.8, $\alpha=0.05$, and power=80%, resulting in a required sample size of 54 participants (20).

Medical records, MRI reports, and athlete performance data from institutional sports medicine databases were used as data sources. The follow-up duration ranged from 12 to 24 months (mean: 16.3±4.2 months).

RESULTS

A total of 55 athletes (PRP: 28, HA: 27) who completed the follow-up period were included in the final analysis. No significant differences were observed between the two groups regarding age, gender distribution, or career duration ($p>0.05$). These data are presented in Table 1.

Table 1. Baseline characteristics of the PRP and HA groups			
Variable	PRP group (n=28)	HA group (n=27)	p-value
Age (years)	28.3±3.4	29.0±3.2	0.532
Gender (male/female)	24/4	23/4	0.749
Career duration (years)	8.1±2.2	8.4±1.9	0.635

The PRP group showed a greater improvement in pain reduction and functional outcomes compared to the HA group. VAS scores decreased significantly in both groups, but the reduction was more pronounced in the

PRP group ($p<0.05$, effect size=0.84). KOOS scores also showed greater improvement in the PRP group ($p<0.05$, effect size=0.78). These data are presented in Table 2.

Table 2. Comparison of clinical outcomes between PRP and HA groups				
Outcome measure	PRP group (Mean±SD, n=28)	HA group (Mean±SD, n=27)	p-value	Effect size (Cohen's d)
VAS (Baseline)	7.8±1.2	7.7±1.3	0.798	-
VAS (Post-treatment)	3.1±1.1	4.4±1.3	0.028	0.84
KOOS (Baseline)	60.1±5.7	59.9±5.8	0.723	-
KOOS (Post-treatment)	85.6±6.1	78.3±5.7	0.018	0.78

Pre- and post-treatment MRI analysis showed significantly better cartilage regeneration in the PRP group compared to the HA group, as reflected by MOCART scores ($p<0.05$, effect size=0.81). MRI-based evaluation also revealed that

cartilage regeneration varied by anatomical location, with the patellar and medial femoral condyle regions showing the most significant improvements. These data are presented in Table 3.

Table 3. MRI-based cartilage regeneration scores (MOCART) by anatomical location				
Anatomical region	PRP group (Pre/Post, n=28)	HA group (Pre/Post, n=27)	p-value	Effect size
Patella	1.2→3.8	1.1→2.7	0.024	0.76
Medial condyle	1.1→3.6	1.0→2.6	0.019	0.79
Lateral condyle	1.3→3.3	1.2→2.5	0.037	0.72

Example MRI scans illustrating cartilage regeneration have been provided in Figure 2.

No serious adverse events were reported in either group. However, mild transient complications were observed. In PRP Group; 3 patients (10.7%) reported transient post-injection knee pain lasting 24–48 hours. In HA Group; 4 patients (14.8%) experienced mild swelling and discomfort at the injection site, resolving within 72 hours. There was no statistically significant difference in adverse event rates between the two groups ($p=0.592$).

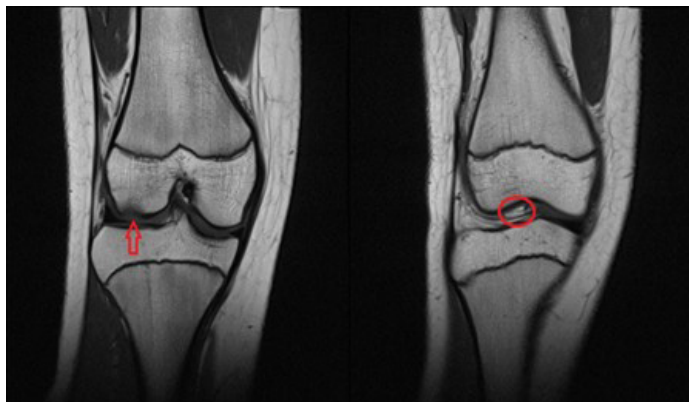


Figure 2. MRI scans after PRP treatments

DISCUSSION

This study compared the clinical and radiological outcomes of PRP and HA injections in competitive athletes with knee cartilage injuries. The results demonstrated that PRP provided superior pain relief and functional improvement compared to HA, as evidenced by greater reductions in VAS scores and higher KOOS improvements. Furthermore, MRI-based cartilage assessments showed that PRP treatment resulted in significantly better cartilage regeneration, particularly in the patellar and medial femoral condyle regions.

The findings of this study align with previous research indicating that PRP is more effective than HA in managing knee cartilage injuries (1,2). Patel et al. reported that PRP injections resulted in superior symptomatic relief compared to HA in early-stage knee osteoarthritis, particularly in active individuals (8). Similarly, Filardo et al. found that PRP provided greater functional improvements than HA in athletes, with better long-term outcomes (3).

However, literature specifically addressing PRP and HA treatments in competitive athletes remains limited. Most studies focus on general populations with degenerative cartilage damage rather than acute or repetitive trauma-induced lesions in high-performance sports (5). A recent meta-analysis by Migliorini et al. suggested that PRP may offer greater regenerative potential due to its growth factor-mediated effects, though long-term comparisons with HA in elite athletes are still lacking (11).

Another crucial aspect of cartilage repair is the use of MRI-based scoring systems for objective assessment

of healing. In this study, MOCART scores demonstrated significantly better cartilage repair in the PRP group, in line with previous findings where PRP-treated patients showed enhanced chondral tissue quality (6). A recent study by Retzky et al. emphasized the importance of MOCART scores in predicting long-term functional recovery in patients undergoing autologous chondrocyte implantation, reinforcing the need for structured imaging-based evaluations (10).

Furthermore, combining PRP with other regenerative techniques has been suggested to enhance cartilage healing. For instance, studies have explored the use of PRP in conjunction with HA, mesenchymal stem cells, or scaffold-based therapies to optimize cartilage repair (21,22). The results of our study indicate that standalone PRP therapy is already superior to HA, supporting its application in sports medicine without requiring additional augmentation.

A study by Dhillon et al. suggested that PRP's efficacy is influenced by the number of injections and the time interval between them, with multiple-session protocols yielding better long-term results (23). This aligns with our treatment protocol, where PRP was administered in three sessions at three-week intervals.

The superior outcomes observed in the PRP group have important implications for sports rehabilitation protocols. Athletes require faster and more effective recovery strategies to return to peak performance, making PRP a potentially more suitable option compared to HA (24).

Studies indicate that PRP reduces recovery time by accelerating tissue repair mechanisms (5). HA primarily functions as a lubricant with some anti-inflammatory properties, while PRP promotes tissue regeneration, leading to faster functional recovery (8). Accordingly, return to sports will be faster.

The enhanced cartilage regeneration associated with PRP may contribute to better joint protection and reduced long-term degenerative risk, which is particularly relevant for competitive athletes (13). Knee osteoarthritis is a significant long-term risk in athletes with cartilage injuries, and PRP may help delay or prevent its progression (22). PRP has greater potential for joint protection and long-term injury prevention.

PRP may serve as an alternative to surgical procedures for cartilage repair in cases where surgery is not an immediate option (2). Studies suggest that PRP can reduce the need for invasive procedures and may delay the progression of cartilage degeneration, especially in active populations (3).

Despite these benefits, the optimal PRP injection protocol remains a topic of debate, with variations in platelet concentration and application techniques influencing clinical outcomes (21). Future studies should focus on standardizing PRP preparation methods to ensure consistency in therapeutic effects.

This study has several limitations that should be acknowledged. As a retrospective study, there is potential for selection bias, and causality cannot be definitively established. A prospective, randomized controlled trial would provide more robust evidence. The follow-up period ranged from 12 to 24 months. Longer-term studies are needed to determine whether the observed cartilage regeneration translates into sustained clinical benefits. While this study classified cartilage defects using the Outerbridge and ICRS grading systems, variability in lesion size and location may influence treatment response. Different PRP preparation methods can lead to variations in platelet concentration and bioactive molecule content, potentially affecting therapeutic efficacy (22). Although interobserver reliability analysis was conducted, a more extensive validation of MRI-based scoring in sports-related injuries would strengthen the findings.

CONCLUSION

This retrospective study compared the clinical and radiologic outcomes of PRP and HA in the treatment of knee cartilage injuries in athletes. The results indicate that PRP treatment is superior to HA in terms of both pain control and functional improvement. Moreover, the PRP therapy was found to promote cartilage regeneration more effectively.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: The study adhered to the principles outlined in the Declaration of Helsinki and was approved by Dicle University Medical Faculty Ethics Committee for Noninterventional Studies (Approval No: 2023/16-42) before data collection began (Date: 14.03.2023).

REFERENCES

- Mandelbaum BR, ElAttrache NS. Articular cartilage repair techniques. Sports Med Arthrosc Rev. 2016;24:43.
- Brittberg, M. New frontiers for cartilage repair, joint preservation and prevention. Journal of Cartilage & Joint Preservation. 2022;2:100060.
- Filardo G, Kon E, Di Martino A, et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. BMC Musculoskelet Disord. 2012;13:229.
- Cole BJ, Pascual-Garrido C, Grumet RC. Surgical management of articular cartilage defects in the knee. J Bone Joint Surg Am. 2009;91:1778-90.
- Kon E, Filardo G, Drobic M, et al. Non-surgical management of early knee osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2012;20:436-49.
- Laudy AB, Bakker EW, Rekers M, Moen MH. Efficacy of platelet-rich plasma injections in osteoarthritis of the knee: a systematic review and meta-analysis. Br J Sports Med. 2015;49:657-72.
- Anitua E, Sánchez M, Orive G, Andía I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. Biomaterials. 2007;28:4551-60.
- Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. Am J Sports Med. 2013;41:356-64.
- Slattery C, Kweon CY. Classifications in brief: outerbridge classification of chondral lesions. Clin Orthop Relat Res. 2018;476:2101-4.
- Retzky JS, Fletcher C, Rzy M, et al. Magnetic resonance observation of cartilage repair tissue (MOCART) scores > 55 at 6 months postoperative predict ability to achieve patient acceptable symptomatic state at minimum 1 year postoperative following autologous chondrocyte implantation for grade IV chondral defects about the patellofemoral joint. Cartilage. 2025;16:17-23.
- Migliorini F, Eschweiler J, Maffulli N, et al. Management of patellar chondral defects with autologous matrix induced chondrogenesis (AMIC) compared to microfractures: a four years follow-up clinical trial. Life (Basel). 2021;11:141.
- Fletcher C, Rzy M, Gomoll A, Strickland S. Treatment of patellar chondral lesions with concomitant matrix-induced autologous chondrocyte implantation, medial patellofemoral ligament reconstruction, and tibial tubercle osteotomy. Arthroscopy Techniques. 2024;13:103059.
- Burger D, Feucht M, Muench LN, et al. Good clinical outcomes after patellar cartilage repair with no evidence for inferior results in complex cases with the need for additional patellofemoral realignment procedures: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2022;30:1752-68.
- Migliorini F, Eschweiler J, Maffulli N, et al. Autologous matrix-induced chondrogenesis (AMIC) and microfractures for focal chondral defects of the knee: a medium-term comparative study. Life (Basel). 2021;11:183.
- Volz M, Schaumburger J, Frick H, et al. A randomized controlled trial demonstrating sustained benefit of Autologous Matrix-Induced Chondrogenesis over microfracture at five years. Int Orthop. 2017;41:797-804.
- Faiz KW. VAS--visuell analog skala [VAS--visual analog scale]. Tidsskr Nor Laegeforen. 2014;134:323.
- Roos EM. 30 years with the Knee injury and Osteoarthritis Outcome Score (KOOS). Osteoarthritis Cartilage. 2024;32:421-9.
- Reed ME, Villacis DC, Hatch GF 3rd, et al. 3.0-Tesla MRI and arthroscopy for assessment of knee articular cartilage lesions. Orthopedics. 2013;36:e1060-4.
- Fritz CO, Morris PE, Richler JJ. Effect size estimates: current use, calculations, and interpretation. J Exp Psychol Gen. 2012;141:2-18.
- Faul F, Erdfelder E, Lang AG, et al. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39:175-91.

21. Nouri F, Babae M, Peydayesh P, et al. Comparison between the effects of ultrasound guided intra-articular injections of platelet-rich plasma (PRP), high molecular weight hyaluronic acid, and their combination in hip osteoarthritis: a randomized clinical trial. *BMC Musculoskelet Disord*. 2022;23:856.
22. Huang HY, Hsu CW, Lin GC, et al. Comparing efficacy of a single intraarticular injection of platelet-rich plasma (PRP) combined with different hyaluronans for knee osteoarthritis: a randomized-controlled clinical trial. *BMC Musculoskelet Disord*. 2022;23:954.
23. Dhillon J, Decilveo AP, Kraeutler MJ, et al. Third-generation autologous chondrocyte implantation (cells cultured within collagen membrane) is superior to microfracture for focal chondral defects of the knee joint: systematic review and meta-analysis. *Arthroscopy*. 2022;38:2579-86.
24. Bosco F, Giai Via R, Giustra F, et al. Platelet-rich plasma for jumper's knee: a comprehensive review of efficacy, protocols, and future directions. *Eur J Orthop Surg Traumatol*. 2024;34:91-6.



Comparison and Clinical Utility of Pre- and Postoperative Diffusion Tensor Imaging MRI Findings in Patients with Cervical Spondylotic Myelopathy

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Abstract

Aim: This study aimed to present the cervical diffusion tensor imaging (DTI) results in cervical spondylotic myelopathy (CSM) patients scheduled for operation and follow-up.

Material and Method: This clinical cohort type study was conducted between January 2016 and May 2016 in the neurosurgery clinic of a tertiary hospital. The study included 27 patients diagnosed with cervical spondylotic myelopathy. Surgical treatment was recommended to 15 patients and follow-up to the remaining. Cervical magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) scans were performed, and anteroposterior canal diameters, apparent diffusion coefficient (ADC), and fractional anisotropy (FA) values were calculated.

Results: The mean age was 62.37 ± 7.39 , and 22.2% (n=6) were women. Hoffmann pathological reflex was detected in 11 (40.7%) patients. The preoperative and postoperative AP (4.18 ± 0.85 vs. 6.66 ± 1.00 , $p < 0.001$), ADC (1.49 ± 0.16 vs. 1.30 ± 0.11 , $p = 0.001$), and FA (0.36 ± 0.04 vs. 0.43 ± 0.04 , $p = 0.001$) values were significantly different. The FA values of patients scheduled for follow-up were significantly higher than those who were recommended surgery (0.43 ± 0.04 vs. 0.37 ± 0.04 , $p = 0.001$). A negative correlation was found between FA and ADC values in both preoperative ($r = -0.618$, $p < 0.001$) and postoperative ($r = -0.748$, $p = 0.013$) measurements.

Conclusion: DTI is a radiological tool that can aid in diagnosing CSM and identifying patients requiring surgery or follow-up. Due to its expected clinical benefits, we recommend a more widespread application of this method in patients with CSM.

Keywords: Diffusion tensor imaging, spinal cord diseases, myelopathy, surgery

INTRODUCTION

Cervical spondylosis is a gradually advancing degenerative disorder that results in neural compression secondary to the progressive narrowing of the spinal canal (1). Cervical spondylosis represents a significant etiological factor in spinal cord dysfunction and acquired spastic paraparesis in adults (2). Moreover, degenerative spondylotic alterations are among the primary contributors to the development of myelopathy (3).

Magnetic resonance imaging (MRI) is the preferred diagnostic modality for evaluating suspected cases of cervical spondylotic myelopathy (CSM). This imaging technique provides multiple advantages, including high-

resolution multi-planar visualization, precise delineation of neural structures, a noninvasive nature, and the benefit of avoiding ionizing radiation exposure (4). Although MRI is considered the gold standard for diagnosing CSM, it has certain limitations, most notably its relatively low sensitivity in identifying subtle structural alterations within the spinal cord and surrounding tissues (4). As a result, early diagnosis of CSM before the manifestation of clinical symptoms or the development of histopathological changes in the spinal cord remains a significant challenge. Diffusion-weighted imaging (DWI), an advanced MRI technique that utilizes the Brownian motion of water molecules (Figure 1) to generate contrast, has shown superior sensitivity in detecting early microstructural abnormalities (5,6).

CITATION

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This technique allows for in vivo, noninvasive mapping of water molecule movement within biological tissues. The diffusion properties of water molecules serve as an indicator of tissue microarchitecture, and pathological conditions can significantly disrupt this process, providing valuable insights into underlying structural abnormalities (5). Diffusion tensor imaging (DTI), an advanced variant of DWI, is widely utilized for the detailed visualization and assessment of white matter tracts within the brain and spinal cord, allowing for the evaluation of their microstructural integrity and connectivity (7). Notably, advanced MRI modalities, including DWI and DTI, have demonstrated the potential to enable earlier detection of myelopathy while also enhancing the understanding of its underlying pathological mechanisms (8,9).

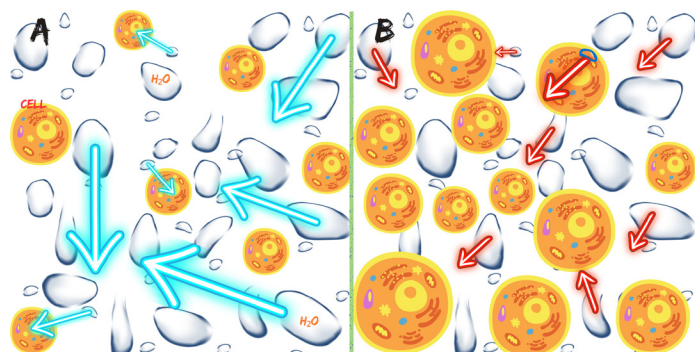


Figure 1. A. The unrestricted diffusion of water molecules in all directions within the tissue is observed; B. A restriction in water molecule movement is observed, accompanied by an increase in anisotropic diffusion along a single direction within the interstitial space

This study aimed to evaluate cervical DTI findings in patients diagnosed with CSM who were either scheduled for surgical intervention or under clinical follow-up. The objective was to provide imaging-based insights to enhance clinical decision-making for physicians and patients.

MATERIAL AND METHOD

Study Design and Patient Population

Our study is a single-center, non-randomized, prospective clinical investigation. The study enrolled 27 patients diagnosed with cervical spondylotic myelopathy, who were followed for at least six months at the Neurosurgery Clinic of Atatürk Training and Research Hospital, operating under the General Secretariat of the Turkish Ministry of Health's Public Hospitals Union, between January 2015 and May 2016. Patients were monitored for at least 6 months. A control group of 10 individuals with normal cervical MRI findings and no active complaints was also included. This research adhered to established ethical guidelines and received formal approval from the hospital's ethics committee. Ethical approval (No: 165 – Date: 11.05.2016) was received from the Yıldırım Beyazıt University Faculty of Medicine, Atatürk Training and Research Hospital Clinical Research Ethics Committee. Informed consent was obtained from all participants prior to their inclusion in the study. Yıldırım Beyazıt University Ankara Atatürk Training and Research Hospital Neurosurgery Clinic is a 30-bed facility that provides outpatient services to approximately 30,000 patients annually.

Participants

The study included 27 patients diagnosed with CSM who were followed for a minimum of six months. Patients aged 40–80 years with at least two levels of CSM and no prior surgical intervention for cervical pathology were eligible for inclusion. Exclusion criteria included patients with a history of surgery for conditions such as neoplasia, infection, traumatic or pathological collapse fractures; those with prior anterior cervical discectomy, foraminotomy, or laminotomy; and patients with poor general health status.

Surgery was recommended for patients with Modified Japanese Orthopedic Association (mJOA) scores of 17 or below, severe clinical symptoms, upper extremity motor strength graded at 4/5 or lower, and a positive Hoffman pathological reflex. Fifteen patients met these criteria, of whom 5 declined surgical intervention. The remaining 10 patients underwent surgery, with 8 receiving open-door laminoplasty and 2 undergoing posterior laminectomy with posterior lateral mass instrumentation. The remaining 12 patients, who did not meet surgical criteria or opted against surgery, were advised to continue with follow-up. Patients who underwent surgical interventions were invited for postoperative follow-up visits and repeat radiological evaluations.

Group 1: Preoperative and postoperative cervical fractional anisotropy (FA) and apparent diffusion coefficient (ADC) measurements were compared in patients who underwent surgery.

Group 2.1: Patients who met surgical criteria but declined surgery.

Group 2.2: Patients who did not meet surgical criteria and were advised for follow-up. Preoperative FA and ADC measurements of these patients were compared with those who underwent surgery.

Group 3: FA and ADC measurements of the asymptomatic control group (Group 3 consists of a 10-member voluntary control group) were compared with those of patients diagnosed with CSM.

Variables

Cervical MRI and DTI were performed for all participants. The anteroposterior (AP) canal diameters, ADC values, and FA values scores were calculated. Additionally, the presence of Hoffman pathological reflexes in patients with CSM was recorded. The primary outcome variable of the study was the ADC values.

In our study, DTI measurements were performed on the cervical cord using a standardized protocol to ensure consistency across all subjects. To minimize variability, we employed the same MRI scanner and acquisition parameters for all patients. Additionally, regions of interest (ROIs) were manually placed by an experienced radiologist following predefined anatomical landmarks to maintain uniformity. To further enhance reproducibility, we utilized inter- and intra-observer reliability assessments.

Statistical Analysis

The suitability of variables, including AP canal diameter, ADC, and FA for normal distribution was assessed using the Shapiro-Wilk test. For variables that did not follow a normal distribution, descriptive statistics were presented as median (interquartile range, IQR). For normally distributed variables, mean±standard deviation (SD) values were provided. Frequency (n) and percentage (%) were used to describe categorical variables, such as patient groups and the presence of Hoffman pathological reflex. Differences in AP canal diameter, ADC, and FA values before and after surgery were analyzed using the paired samples t-test, and the corresponding mean value graphs were generated. The independent samples t-test was used to compare ADC and FA values between the surgical + surgery-declined group and the follow-up group, with relevant mean value graphs plotted. Similarly, differences in ADC and FA values between the CSM group and the control group were also analyzed using the

independent samples t-test, and corresponding graphs were created. Correlation analyses were performed to evaluate the relationships between preoperative and postoperative ADC and FA values. Pearson correlation coefficients were calculated for these relationships. All statistical analyses were conducted using IBM SPSS Statistics, Version 21.0 (IBM Corp., Armonk, NY, USA), and Microsoft Excel 2007 software.

RESULTS

Table 1 summarizes the demographic characteristics of the patient and control groups.

Of the individuals included in the study, 27.0% (n=10) were in the surgical group, 13.6% (n=5) were in the surgery-declined patient group, and 32.4% (n=12) were in the follow-up patient group. The control group consisted of ten asymptomatic individuals. In 26 individuals (70.3%), Hoffman reflex was positive, while in 11 individuals (29.7%), it was negative.

Table 1. Demographic data of patient and control groups				
Groups	n	Mean age±Standard deviation (SD)	Male (n)	Female (n)
Group 1: Patients who met the surgical criteria and underwent surgery	10	61.6±10.7	8	2
Group 2.1: Patients who met the surgical criteria, were recommended surgery but declined the procedure	5	59.4±12.4	4	1
Group 2.2: Asymptomatic CSM patients who were not recommended for surgery and chose follow-up	12	62.0±11.5	8	4
Group 3: Asymptomatic volunteer individuals with no known diagnosis of CSM	10	58.6±11.4	5	5

The mean AP canal diameter of the 37 individuals included in the study was 6.61±2.62 mm (range: 3.30–12.90 mm). The mean ADC was 1.35±0.23×10⁻³ mm²/s (range: 0.85–1.72×10⁻³ mm²/s), while the mean FA was 0.42±0.06 (range: 0.31–0.54).

The preoperative mean AP canal diameter of the 10 patients who underwent surgery was 4.18±0.85 mm, increasing to 6.66±1.00 mm postoperatively. This postoperative increase in AP canal diameter was statistically significant (p<0.001)

(Table 2). The preoperative mean ADC value of the patients was 1.49±0.16×10⁻³ mm²/s, while the postoperative mean was 1.30±0.11×10⁻³ mm²/s. A statistically significant difference was observed between the preoperative and postoperative ADC values (p=0.001), with higher ADC values recorded preoperatively (Table 2). The preoperative mean FA value was 0.36±0.04, increasing to 0.43±0.04 postoperatively. This change was also statistically significant (p=0.001), with lower FA values observed preoperatively compared to postoperative values (Table 2).

Table 2. Comparison of preoperative and postoperative AP, ADC, and FA values				
Parameter	Preoperative Mean±SD	Postoperative Mean±SD	t	p
AP (mm)	4.18±0.85	6.66±1.00	8.537	<0.001
ADC (×10 ⁻³ mm ² /s)	1.49±0.16	1.30±0.11	3.066	0.001
FA (unitless)	0.36±0.04	0.43±0.04	4.739	0.001

t: Paired-sample t-test, SD: standard deviation, AP: anterior-posterior spinal diameter, ADC: apparent diffusion coefficient, FA: fractional anisotropy

The mean ADC value in patients who underwent surgery or declined surgery (Group 2) was 1.49±0.14×10⁻³ mm²/s, compared to 1.42±0.14×10⁻³ mm²/s in the follow-up group (patients not recommended for surgery). There was no statistically significant difference in ADC values between the two groups

(p=0.209) (Table 3). The mean FA value in the surgical and surgery-declined group was 0.37±0.04, while it was 0.43±0.04 in the follow-up group. A statistically significant difference in FA values was observed between the groups (p=0.001), with higher FA values recorded in the follow-up group (Table 3).

Table 3. Comparison of ADC and FA values of patients scheduled for surgery or follow-up

Parameter	Recommended surgery (n=15) Mean±SD	Recommended follow-up (n=12) Mean±SD	t	p
ADC (×10 ⁻³ mm ² /s)	1.49±0.14	1.42±0.14	1.288	0.209
FA (unitless)	0.37±0.03	0.43±0.04	3.964	0.001

t: Independent-samples t-test, SD: standard deviation, ADC: apparent diffusion coefficient, FA: fractional anisotropy

In Group 3, the mean ADC value for the 10 individuals in the control group was 1.06±0.15×10⁻³ mm²/s, compared to 1.46±0.14×10⁻³ mm²/s for individuals diagnosed with CSM. A statistically significant difference in ADC values was observed between the control group and the CSM-diagnosed group (p<0.001). ADC values in the control group were significantly lower than those of patients diagnosed with CSM (Table 4).

Table 4. Comparison of ADC and FA values between the control group and patients with CSM and correlation analysis between FA and ADC in preoperative and postoperative states

Parameter	Control Group (n=10) Mean±SD	Cervical Spondylosis Group (n=27) Mean±SD	t	p
ADC (×10 ⁻³ mm ² /s)	1.06±0.15	1.46±0.14	7.294	<0.001
FA (unitless)	0.48±0.04	0.40±0.05	4.520	<0.001

t: Independent-samples t-test, SD: standard deviation, ADC: apparent diffusion coefficient, FA: fractional anisotropy

A statistically significant moderate negative linear correlation was observed between preoperative fractional anisotropy (FA) values and ADC values (r=-0.618, p<0.001). This indicates that as preoperative FA values increased, preoperative ADC values decreased, and vice versa. Similarly, a strong, negative, linear, and statistically significant correlation was identified between postoperative FA and ADC values (r=-0.748, p=0.013). This suggests that as postoperative FA values increased, postoperative ADC values decreased, and vice versa (Table 5).

Table 5. Correlation analysis between FA and ADC in preoperative and postoperative states

Parameter	Pearson correlation coefficient (r)	p
Preoperative FA and ADC	-0.618	<0.001
Postoperative FA and ADC	-0.748	0.013

ADC: apparent diffusion coefficient, FA: fractional anisotropy

DISCUSSION

The preoperative mean AP canal diameter of the 10 patients who underwent surgery was calculated as 4.18±0.85 mm, increasing to 6.66±1.00 mm postoperatively. The mean ADC value was 1.49±0.16×10⁻³ mm²/s preoperatively and 1.30±0.11×10⁻³ mm²/s postoperatively. The mean FA value increased from 0.36±0.04 preoperatively to 0.43±0.04 postoperatively. The differences in preoperative and postoperative AP canal diameter, FA, and ADC values were statistically significant (Table 2).

In our study, the mean FA value in Group 2, which included patients who underwent surgery and those who were recommended surgery but declined, was 0.37±0.04. In contrast, the mean FA value of patients who were not recommended surgery and were advised for follow-up was 0.43±0.04. A statistically significant difference in FA values was observed between the groups, with higher FA values recorded in the follow-up group (Table 3).

In our study, the mean ADC value of the 10 individuals in Group 3 (control group) was 1.06±0.15×10⁻³ mm²/s,

whereas the mean ADC value of patients diagnosed with CSM was 1.46±0.14×10⁻³ mm²/s. The difference in ADC values between the two groups was statistically significant, with lower ADC values observed in the control group compared to those diagnosed with CSM (Table 4).

Despite being the gold standard for imaging cervical cord pathology, MRI has inherent limitations in quantifying disease severity, offering precise prognostic insights, and capturing early microstructural abnormalities in CSM (10). As a highly sensitive imaging modality, DTI has become increasingly recognized for its ability to reveal microstructural abnormalities beyond the resolution of conventional MRI, utilizing advanced quantitative parameters (10). Significant alterations in DTI metrics can be identified in CSM preceding the development of T2 hyperintensity, emphasizing its role in early disease characterization (11). Using DTI, Kara et al. examined 16 patients diagnosed with CSM who exhibited no spinal cord hyperintensity on T2-weighted MRI, comparing stenotic and non-stenotic cervical canal regions (11). Their findings revealed significant differences in FA and ADC values

between stenotic and non-stenotic segments. Specifically, FA values decreased, while ADC values increased at stenotic levels (11). A meta-analysis of studies investigating DTI in patients with SCM reported a reduction in FA values and an elevation in ADC values (12).

In our study, a comparison of DTI results between the control group (n=10) and patients diagnosed with cervical spondylotic myelopathy (CSM, n=27)—including those who accepted surgery, those who declined surgery, and those advised for follow-up—revealed statistically significant differences in FA and ADC values (Table 4). These findings are consistent with previously reported literature.

The diagnostic utility of MRI, particularly in detecting signal anomalies, remains a subject of debate. While MRI may not reveal definitive evidence of SCM, studies have demonstrated alterations in FA and radial diffusivity (RD) (11,13-15). Shabani et al. assessed perioperative FA values in conjunction with T2 signal intensity on MRI, emphasizing FA as a crucial and reliable prognostic indicator (16). Demir et al. reported that the ADC had an 80% sensitivity in detecting clinically positive myelopathy patients, outperforming T2-weighted imaging at 61%. (9). However, while T2-weighted imaging exhibited a significantly higher specificity (92%) compared to ADC (53%), the lower specificity of ADC is attributed to technical limitations or early spinal cord changes preceding clinical or electrophysiological manifestations (9). However, in our study, MRI values were not measured, which we acknowledge as a limitation of our research.

In a prospective study by Lee et al., FA and ADC values significantly differed between healthy volunteers and patients with SCM, highlighting microstructural alterations in the diseased group (17). Our findings are consistent with those of Lee et al., as presented in Table 4. Similarly, Ellingson et al. highlighted the pivotal role of DTI in assessing disease progression and predicting outcomes in patients who chose to forgo surgical intervention (18). In our study, patients with SCM who were advised for follow-up due to mild findings were compared with those recommended for surgery, revealing a significant difference in FA values and a statistically significant variation in ADC values (Table 3). Similarly, Hori et al. reported that in patients classified based on severe clinical symptoms, FA exhibited a marked decrease, whereas ADC demonstrated an increase (19).

Shabani et al. observed that research examining preoperative and postoperative DTI parameters remains relatively limited (10). Kitamura et al. found no substantial alterations in FA values between the preoperative and postoperative phases in patients who underwent surgery for SCM (20). Wang et al. likewise identified no meaningful correlation between preoperative and postoperative FA and mean diffusivity (MD) parameters in their study (21). In contrast, our study revealed a statistically significant variation in FA and ADC values between the preoperative and postoperative phases (Table 2). Aligned with our results, Guan et al. likewise reported notable variations

in FA values between the preoperative and postoperative periods (22). Our study revealed statistically significant improvements in preoperative and postoperative FA and ADC values among patients who underwent surgical intervention (Table 2).

Jones et al. established a robust correlation between FA and baseline mJOA and Nurick scores (23). Postoperative enhancements in NDI scores, indicative of functional recovery, correlated with preoperative FA values. In patients with severe CSM, those exhibiting disproportionately elevated preoperative FA values attained higher postoperative mJOA scores compared to individuals with lower FA values (23). FA values serve as valuable biomarkers for assessing disease prognosis and predicting clinical outcomes in CSM (10,23). Preoperative FA is the most consistently and strongly correlated parameter with functional outcomes following cervical spondylotic myelopathy surgery (24). Fang et al. employed automated ROI analysis to quantify DTI metrics, including axial diffusion (AD), MD, RD, and FA in CSM patients (25). Their findings indicated elevated AD, MD, and RD values alongside reduced FA values, and uniquely, they identified AD in the DTI-Dorsal Column as the most promising marker for detecting affected segments, diverging from prior literature (25).

Wang et al. recognized reduced FA in the extension position as a robust predictor of restricted neurological recovery after surgery in CSM patients (26). Shao et al. demonstrated that MUSE-DTI provides superior imaging quality relative to conventional DTI and functions as a dependable metric for evaluating disease severity in SCM (27).

Multiple factors persist in complicating DTI measurements, including the distinction between single-level and multilevel disease, the severity and location of maximum compression, patient age, and the specific cervical level assessed, all of which can significantly impact DTI parameters (10,28-30).

When comparing SCM patients recommended for surgery with those not recommended for surgery, FA values were found to be statistically significant, while ADC values were not (Table 3). Additionally, a negative, moderate, linear, and statistically significant relationship was identified between preoperative FA and ADC values. In conclusion, these parameters play a crucial role in facilitating the diagnosis of CSM and enhancing the quality of follow-up care (Tables 4 and 5).

FA and ADC are key DTI metrics that provide valuable insights into microstructural integrity and pathological alterations in the cervical cord (Table 2-4). A decrease in FA typically indicates axonal damage and loss of white matter integrity, while an increase in ADC suggests extracellular edema or neurodegeneration (Figure 1, 2) (Table 2-4). These metrics can aid in assessing disease severity, monitoring progression, and guiding therapeutic strategies (Table 2-4).

Diffusion Tract Bundle Statistics	
Default_1	
Statistic	Value
Number of Tracts	617
Mean FA	0.4447
Mean Diffusivity	0.0033
Mean Radial Diffusivity	0.0026
Mean Axial Diffusivity	0.0017

Tractography Parameters	
Parameter	Value
Tract Length(mm)	50 - 400
Seed points per voxel length	2
Angle Threshold	30
FA Threshold	0.2

Figure 2. FA measurements are monitored using the DWI imaging method via the hospital's electronic database; The two key parameters in DWI are fractional anisotropy (FA) and apparent diffusion coefficient (ADC); FA, an anisotropic parameter, ranges from 0 to 1. A value of 0 indicates unrestricted diffusion, whereas values near 1 suggest a highly anisotropic structure

Our study has several limitations. The primary limitation is the small sample size of both the patient and control groups. Additionally, the lack of a comparison between DTI results and MRI findings represents another constraint. Furthermore, the absence of JOA score evaluation in our study is a noteworthy limitation. We could have delineated the cohort groups more clearly, allowing for a more detailed presentation of the comparisons.

CONCLUSION

Our study demonstrated elevated FA and reduced ADC values in SCM patients compared to healthy controls. Significant alterations in FA and ADC values were evident in both preoperative and postoperative assessments. While FA values differed significantly between SCM patients recommended for surgery and those advised against it, ADC values did not show statistical significance. Furthermore, a moderate, negative, and statistically significant linear correlation was identified between preoperative FA and ADC values. In conclusion, these metrics serve as critical biomarkers for diagnosing CSM and optimizing follow-up care.

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Conflict of interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Tracy JA, Bartleson JD. Cervical spondylotic myelopathy. Neurologist. 2010;16:176-87.

2. Badhiwala JH, Ahuja CS, Akbar MA, et al. Degenerative cervical myelopathy—update and future directions. Nat Rev Neurol. 2020;16:108-24.

3. Al-Ryalat NT, Saleh SA, Mahafza WS, et al. Myelopathy associated with age-related cervical disc herniation: a retrospective review of magnetic resonance images. Ann Saudi Med. 2017;37:130-7.

4. Tsuchiya K, Katase S, Fujikawa S, et al. Diffusion-weighted MRI of the cervical spinal cord using a single-shot fast spin-echo technique: findings in normal subjects and in myelomalacia. Neuroradiol. 2003;45:90-4.

5. Baliyan V, Das CS, Sharma R, Gupta AK. Diffusion weighted imaging: technique and applications. World J Radiol. 2016;8:785-98.

6. Severino R, Nouri A, Tessitore E. Degenerative cervical myelopathy: how to identify the best responders to surgery?. J Clin Med. 2020;9:759.

7. Boucard CC, Hanekamp S, Ćurčić-Blake B, et al. Neurodegeneration beyond the primary visual pathways in a population with a high incidence of normal-pressure glaucoma. Ophthalmic Physiol Opt. 2016;36:344-53.

8. Tohyama S, Walker MR, Sammartino F, et al. The utility of diffusion tensor imaging in neuromodulation: moving beyond conventional magnetic resonance imaging. Neuromodulation. 2020;23:427-35.

9. Demir A, Ries M, Moonen CTW, et al. Diffusion-weighted MR imaging with apparent diffusion coefficient and apparent diffusion tensor maps in cervical spondylotic myelopathy. Radiology. 2003;229:37-43.

10. Shabani S, Kaushal M, Budde MD, et al. Diffusion tensor imaging in cervical spondylotic myelopathy: a review. J Neurosurg Spine. 2020;33:65-72.

11. Kara B, Celik A, Karadereler S, et al. The role of DTI in early detection of cervical spondylotic myelopathy: a preliminary study with 3-T MRI. Neuroradiology. 2011;53:609-16.

12. Guan X, Fan G, Wu X, et al. Diffusion tensor imaging studies of cervical spondylotic myelopathy: a systemic review and meta-analysis. PloS One. 2015;10:e0117707.

13. Lindberg PG, Sanchez K, Ozcan F, et al. Correlation of force control with regional spinal DTI in patients with cervical spondylosis without signs of spinal cord injury on conventional MRI. Eur Radiol. 2016;26:733-42.

14. Mink JH, Gordon RE, Deutsch AL, The cervical spine: radiologist's perspective. Phys Med Rehabil Clin. 2003;14:493-548.

15. Suri A, Chabbara RPS, Mehta VS, et al. Effect of intramedullary signal changes on the surgical outcome of patients with cervical spondylotic myelopathy. Spine J. 2003;3:33-45.

16. Shabani S, Kaushal M, Budde M, et al. Comparison between quantitative measurements of diffusion tensor imaging and T2 signal intensity in a large series of cervical spondylotic myelopathy patients for assessment of disease severity and prognostication of recovery. J Neurosurg Spine. 2019;31:473-9.

17. Lee JW, Kim JH, Park JB, et al. Diffusion tensor imaging and fiber tractography in cervical compressive myelopathy: preliminary results. *Skeletal Radiol.* 2011;40:1543-51.
18. Ellingson BM, Ulmer JL, Kurpad SN, Schmit BD. Diffusion tensor MR imaging of the neurologically intact human spinal cord. *AJNR Am J Neuroradiol.* 2008;29:1279-84.
19. Hori M, Okubo T, Aoki S, et al. Line scan diffusion tensor MRI at low magnetic field strength: feasibility study of cervical spondylotic myelopathy in an early clinical stage. *J Magn Reson Imaging.* 2006;23:183-8.
20. Kitamura M, Maki S, Koda M, et al. Longitudinal diffusion tensor imaging of patients with degenerative cervical myelopathy following decompression surgery. *J Clin Neurosci.* 2020;74:194-8.
21. Wang K, Idowu O, Thompson CB, et al. Tract-specific diffusion tensor imaging in cervical spondylotic myelopathy before and after decompressive spinal surgery: preliminary results. *Clin Neuroradiol.* 2017;27:61-9.
22. Guan L, Chen X, Hai Y, et al. High-resolution diffusion tensor imaging in cervical spondylotic myelopathy: a preliminary follow-up study. *NMR Biomed.* 2017;30:e3769.
23. Jones JGA, Cen SY, Lebel RM, et al. Diffusion tensor imaging correlates with the clinical assessment of disease severity in cervical spondylotic myelopathy and predicts outcome following surgery. *AJNR Am J Neuroradiol.* 2013;34:471-8.
24. Chernysh AA, Loftus DH, Zheng B, et al. Utility of diffusion tensor imaging (DTI) for prognosis and management of cervical spondylotic myelopathy: a PRISMA review. *World Neurosurg.* 2024;190:88-98.
25. Fang Y, Li S, Wang J. et al. Diagnostic efficacy of tract-specific diffusion tensor imaging in cervical spondylotic myelopathy with electrophysiological examination validation. *Eur Spine J.* 2024;33:1230-44.
26. Wang X, Tian X, Zhang Y, et al. Predictive value of dynamic diffusion tensor imaging for surgical outcomes in patients with cervical spondylotic myelopathy. *BMC Med Imaging.* 2024;24:260.
27. Shao H, Liu Q, Saeed A, et al. Feasibility of diffusion tensor imaging in cervical spondylotic myelopathy using MUSE sequence. *Spine J.* 2024;24:1352-60.
28. Wen CY, Cui JL, Liu HS, et al. Is diffusion anisotropy a biomarker for disease severity and surgical prognosis of cervical spondylotic myelopathy?. *Radiology.* 2014;270:197-204.
29. Cui J-L, Li X, Chan T-Y, et al. Quantitative assessment of column-specific degeneration in cervical spondylotic myelopathy based on diffusion tensor tractography. *Eur Spine J.* 2015;24:41-7.
30. Budzik J.-F, Balbi V, Thuc VL, et al. Diffusion tensor imaging and fibre tracking in cervical spondylotic myelopathy. *Euro Radiol.* 2011;21:426-33.



The Importance of Diffusion MRI Imaging in Differentiating Malignant and Benign Breast Lesions

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Abstract

Aim: The aim of this study is to research the separation benign and malignant breast masses with diffusion-weighted magnetic resonance imaging (MRI).

Material and Method: 66 patients (26 benign, 40 malignant) who have taken MRG for any purpose have been incorporated to the research. Routine contrast enhancement dynamic MRI and diffusion weighted imaging (DWI) applied on 66 lesions. Contrast enhancement MRI and DWI characteristics of lesions have been evaluated as retrospective for each lesion. Kinetic curves of contrast enhancement pattern of lesions have been evaluated in accordance with BI-RADS classifications. Apparent diffusion coefficient (ADC) measurements have been obtained numerically from DWI's at work stations. Also, ADC values of normal fibroglandular tissue (NFT) at opposite breast of each patient have been measured. ADC values of NFT, benign and malignant lesions have been compared.

Results: Average ADC values of benign and malignant lesions, NFT in benign and malignant patients, were respectively: $1.535 \times 10^{-3} \text{ mm}^2/\text{s}$, $1.169 \times 10^{-3} \text{ mm}^2/\text{s}$, $1.879 \times 10^{-3} \text{ mm}^2/\text{s}$, $1.852 \times 10^{-3} \text{ mm}^2/\text{s}$. Average ADC values of NFT were statistically significantly higher than values of benign and malignant lesions. Average ADC values of malignant lesions were statistically significantly lower than ADC rates of benign lesions ($p < 0.001$).

Conclusion: Distinguish between benign and malignant breast lesions with ADC values is an auxiliary parameter which can be used together with dynamic contrast enhancement curves of lesions and morphological criteria. In our study, we found that the use of DWI in addition to contrast-enhanced MRI can easily distinguish between NFT, benign and malignant masses. We suggest routine usage of DWI during breast MRI.

Keywords: Magnetic resonance imaging, diffusion, breast cancer, malignant, benign

INTRODUCTION

Breast cancer is one of the most common cancers in women in our country. Mortality rates due to cancer are gradually increasing (1,2). Currently, mammography (MG) is the first radiological diagnostic method used in the evaluation of breast lesions (3). The sensitivity of MG increases with age (4). However, 10% of palpable breast cancers cannot be detected by MG (5). In the evaluation of breast lesions, Magnetic Resonance Imaging (MRI) is used in addition to Ultrasonography (USG) and MG, especially in evaluating multicentricity, breast-sparing surgical planning, distinguishing residual lesions and granulation tissue, and follow-up after treatment (3,6,7). The most important

limitation of MRI is its inability to detect microcalcifications, an important indicator of breast cancer (8). The American Cancer Society (ACS) has developed the MRI BI-RADS classification system and the MRI dictionary to ensure standardization in MRI reports, as in MG (9).

DWI is one of the new techniques and is a method with a short imaging time requires no time and no contrast material. Recently, diffusion weighted imaging (DWI), which reflects the histological structure and cellularity of the tissue, and MRI, which reflects the morphological features and contrast enhancement patterns of the lesion, have been increasingly used in the evaluation of breast lesions (10). Hypercellularity and underdeveloped neovascularity in

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tumoral tissue cause diffusion restriction. Therefore, this difference makes cancer detectable in DWIs (11). DWI was first used by Englander et al. in 1997 (12,13). Sinha et al. used it in 2002 to detect breast masses (14). Diffusion-weighted MRI imaging is known to be effective in showing benign-malignant differentiation as well as tumor aggressiveness in breast lesions (15,16).

The numerical equivalent of diffusion in living tissue is apparent diffusion coefficient (ADC) value. Benign tumors of the breast often have high ADC values. ADC value is affected by tissues characteristics, in fibrotic and necrotic tissues with reduced cellularity. Therefore, the ADC value decreases in masses with dense fibrosis such as fibroadenomas or invasive ductal carcinoma (11,17). It is observed that ADC values of cysts increase according to fluid ratios. Serous substances cause less restriction in diffusion, whereas mucinous substances cause slightly higher diffusion restriction (18-20). In different studies conducted in the literature, it is stated that the specificity will be increased when DWIs are evaluated together in the characterization of breast masses (21).

In our study, we planned to evaluate how the use of DWI findings, one of the functional imaging techniques, in the differentiation of malignant and benign solid breast masses would contribute to the literature.

MATERIAL AND METHOD

Characteristics of Patients

The images of the women undergoing breast MRI due to abnormal MG, USG, and clinical findings in the Radiodiagnostic Department of Dicle University Faculty of Medicine between January 2012 and May 2015 were retrospectively analyzed. Patients receiving chemotherapy and radiotherapy were not included in the study. 66 patients in total were included in the study. Average age of patients was 41.07 (25-76 years). The lesions in the patients were evaluated by the same radiologist. 40 of the lesions were malignant and 26 were benign. The mean age of the patients with malignant lesions was 42.8 years, while it was 38.4 years in those with benign lesions. Ethical approved for the study was obtained from Dicle University Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee (Ethics Committee approval no: 12.06.2015/346).

MRI Protocol

3 Tesla MRI device (Philips Achieva 3.0T MRI Scanner 2013 was used for MRI examination (using a 4-channel double superficial breast wrap, covering the whole breast). The patient was laid on the table in the face down posture and both breast scanning was carried out at the same time. The files of the premenopausal patients who would undergo MRI were scanned and confirmed to be between the 7th and 14th days of the menstrual cycle. In all cases, T1 and T2, fat-suppressed T2 axial view was evaluated. After obtaining fat-suppressed 3D T1-weighted FLASH sequence images, 0.1 mmol/kg gadolinium was injected

intravenously with an autoinjector at a speed of 2 ml/s followed by 20 ml saline.

DWI was achieved prior to dynamically contrast-enhanced views. It was determined that a 2D spine echo- plane imaging (EPI) series was used in axial plane images. A diffusion gradient with a b value of 0 and 600 s\mm² was applied. ADC mapping is automatically generated at the workstations.

Evaluation of MRI

All MR scans were analysed at the central station. The pathology result was unknown while the evaluation was performed. Fat-suppressed non-contrast sections were removed from the contrast-enhanced sections and evaluated. Suspicious lesions were evaluated with the help of T2 images with removal and fat suppression. The lesion type was classified as mass or non-mass according to BI-RADS (11) (Table 1). The mean tumor diameter was measured using T2 images with axial contrast or fat suppression. ADC values of the lesions were calculated by placing them in the peripheral enhancing part of the lesion using the region of interest (ROI). In particular, the ROI was placed in the solid and contrasted part of the lesion. At least three analyses were performed and the values averaged. Care was taken not to place the ROI in areas with necrosis in the middle and not contrasted. The ROI size was kept between 20-25 mm². ADC measurements were also made from the normal breast of each patient, especially from the retroareolar area, and from normal fibroglandular tissues (NFT) (Table 2).

Table 1. MRI BI-RADS classification of malignant and benign lesions			
	Malign (40)	Benign (26)	Total (66)
BI-RADS 1	0	0	0
BI-RADS 2	0	0	0
BI-RADS 3	0	22	22 (33.3%)
BI-RADS 4	1	4	5 (7.5%)
BI-RADS 5	39	0	39 (59.1%)

Table 2. NFT minimum, maximum, average ADC values		
	Benign	Malign
NFT minimum ADC	1.550x10 ⁻³ mm ² /sn	1.560x10 ⁻³ mm ² /s
NFT maximum ADC	2.328x10 ⁻³ mm ² /sn	2.650x10 ⁻³ mm ² /s
NFT mean ADC	1.879x10 ⁻³ mm ² /sn	1.852x10 ⁻³ mm ² /s

Statistical Analysis

The data were evaluated using the SPSS programme. Results are reported as mean±standard variance and as a percentage. It was checked whether the data fit the normal distribution, and an independent sample t-test was used in pairwise comparisons for those that fit the normal distribution and the Mann-Whitney U test was used for those that did not display a normal distribution. Receiver operating characteristic (ROC) analysis was used to calculate the ADC threshold value in the differentiation of benign and malignant lesions.

RESULTS

The study included 66 patients aged 25-76 years. The findings of 66 lesions in 66 operated patients DWI were evaluated. Of the 66 lesions, 26 (39.4%) were benign and 40 (60.6%) were malignant. The age range of patients with benign lesions was 25-67 years (mean age 38.42 years). The definitive diagnosis was made with histopathological diagnosis in 13 (19.6%) benign and 40 malignant (60.8%) lesions, while it was made with radiological follow-up in 13 benign (19.6%) lesions. Lesions were evaluated histopathologically in 53 cases, and radiological follow-up was performed in 13 cases.

Characteristics of Benign Lesions

A totally of 26 tumours were benign. 13 of the 26 benign tumours were evaluated as benign in the histopathological examination. The other 13 lesions were evaluated to be benign after 2 years of follow-up and no histopathological evaluation was required. Of the lesions diagnosed histopathologically, 2 were reported as adenosis, 1 as apocrine metaplasia, 2 as fibroadenomatoid change, 1 as phylloides tumor, and 7 as fibroadenoma.

Characteristics of Malignant lesions

The age range of patients with malignant tumours was 29-76 years (average age 42.80 years). Lesion sizes were between 17-90 (mean size 39.33) mm. For this reason, dimension measurement could not be made. Only 1 of the malignant lesions had a smooth contour.

40 cases with malignant lesions were evaluated histopathologically, and of these, 1 was Ductal Carcinoma Incitu (DCIS), 1 was malignant mesenchymal tumor (MMT), 5 were malignant epithelial tumor (MET), 4 were Invasive Lobular Carcinoma (ILC), and 29 were Invasive Ductal Carcinoma (IDC).

When the patient ages were compared, the mean patient ages in the benign (first group) and malignant (second groups) were 38.42 and 42.80 years, respectively. When the lesion sizes were compared, the mean volume of malignant tumors was measured as 39.33 mm and the mean size of benign tumours was found to be 17.65 mm, and a statistically considerable variance between them was observed ($p<0.05$).

The mean ADC value of NFT was $1.879 (1.550-2.328 \times 10^{-3})$ mm²/s in the primer group and $1.852 (1.560-2.650 \times 10^{-3})$ mm²/s in the seconder group. There was no significance between the average ADC measurements of the NFTs of the two groups ($p=0.653$) (Table 2). There was a statistically considerable variance between the mean ADC results of NFT and lesions ($p<0.05$).

The mean ADC values of benign and malignant lesions were $1.535 \times 10^{-3} (1.206-1.858 \times 10^{-3})$ mm²/s, and $1.169 \times 10^{-3} (0.997-1.597 \times 10^{-3})$ mm²/s, respectively. And there was a statistically considerable variance between these measurements ($p<0.001$) (Table 3).

Table 3. Minimum, maximum and mean ADC values in malignant and benign lesions

	Benign	Malign
Minimum ADC	1.206×10^{-3} mm ² /s	0.997×10^{-3} mm ² /s
Maximum ADC	1.858×10^{-3} mm ² /s	1.597×10^{-3} mm ² /s
Mean ADC	1.535×10^{-3} mm ² /s	1.169×10^{-3} mm ² /s

In the ROC analysis of benign-malignant differentiation of the lesions, the sensitivity 92.3% and the specificity 82.5% when 1.238×10^{-3} mm²/s was taken as the threshold value. Area under the curve: 94.8 (95% confidence interval: 0.901-0.995) (Figure 1).

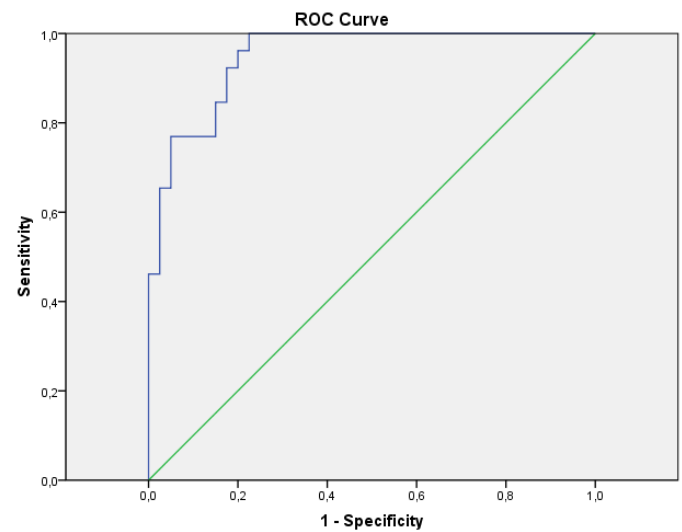


Figure 1. ROC analysis curve of ADC values, area under the curve: 94.8 (95% confidence interval: 0.901-0.995)

DISCUSSION

In this study, we compared the NFT-ADC and ADC ratings malignant and benign lesions to investigate the importance of DWI in benign-malignant differentiation of breast masses. However, in the last years, DWI has been used in breast lesions to make this distinction better. DWI is the most important imaging method that reflects cellularity (22). Many researchers report that the evaluation of DWI features along with the contrast enhancement pattern of breast lesions facilitates the diagnosis (23).

There are significant differences between the mean ADC values of normal breast tissue and benign and malignant breast mases. This difference depends on the physiological characteristics of the lesion, the technical parameters used in imaging, and the different software programs used to statistically evaluate the ADC values found (24). Unfortunately, there is no consensus among the authors about a standard maximum b value that can be used in terms of ADC values in the examination of breast masses. At low b values (<400 mm²/s for breast tissue), the perfusion effect is evident, and ADC values higher than expected are obtained. Especially in invasive ductal carcinoma, the perfusion effect is evident at low b values due to capillary proliferation, and ADC values higher than expected are obtained (24,25).

In studies conducted using different b values in the literature, it was seen that the perfusion effect decreased and ADC values decreased proportionally as the b value increased in the same lesion (24,26). While Partridge et al. used a b value of 600 s/mm², b values such as 750 and 1000 were used in other studies (24,27-29). In our study, a b value of 600 was used.

Palle and Reddy showed that ADC measurements at low b values were higher than ADC measurements at high b values due to perfusion effect. The sensitivity and specificity values for benign and malignant lesions were found to be higher

than other studies with a threshold value of 1.3-1.5x10⁻³ mm²/s and 0.85-1.1x10⁻³ mm²/s, respectively (30).

There is no established threshold value for ADC value in differentiating benign and malignant masses. Different threshold values have been found in many studies (14,24,26-29,31-33) (Table 4). Sinha et al. found the average ADC values in the first DWI for breast masses as 1.01x10⁻³ mm²/s in malign, 1.35x10⁻³ mm²/s in benign lesions, and 1.90x10⁻³ mm²/s in NFT (14). Using ADC values, they were able to make the benign-malignant distinction between lesions with NFT.

Table 4. Sensitivity and specificity ratios for DWI at different b values and cut-off values in the literature and in our study					
Study	Number of lesions	b value (mm ² /s)	Limit value	Sensitivity (%)	Specificity (%)
Pereira (133)	138	250	1.47	81.5	87.7
		500	1.34	91.4	91.2
		750	1.24	91.4	93.0
		1000	1.12	91.0	91.2
Kul (151)	84	1000	0.92	91.5	86.5
Partridge (148)	118	600	1.60	96.0	55.0
Tozaki (147)	124	1000	1.13	97.0	56.0
Stadlbauer (146)	36	1000	1.21	69.0	100
Our work	66	600	1.23	92.3	82.5

Imamura et al. found the mean ADC values to be 0.968x10⁻³ mm²/s in non-mass malignant lesions and 1.238x10⁻³ mm²/s in benign ones. At the threshold value of 1.1x10⁻³ mm²/s, the sensitivity was 68.8% and the specificity was 72.7% (26). Imamura et al. accepted the threshold value as 1.1x10⁻³ mm²/s in the differentiation of non-mass forming formations of malignant-benign character, while Yabuuchi et al. determined this threshold value as 1.30x10⁻³ mm²/s (34).

Partridge found the mean ADC value at 600 mm²/s to be 1.30x10⁻³ mm²/s and 1.71x10⁻³ mm²/s in malignant and benign lesions, respectively. At the threshold value of 1.60x10⁻³ mm²/s, sensitivity was determined to be 96% and specificity was found to be 55% (27,35). In our study, the b value was used as 600, but our threshold value was accepted as 1.238x10⁻³ mm²/s. Different threshold values can be found in studies using the same b values.

In the studies conducted different threshold values were found at different and the same b values. In their study, Pereira et al. found that as the b value increased, the average ADC ratios of benign and malign breast masses decreased compared to each other, and sensitivity and specificity ratios changed. When the b value was selected as 750 mm²/s, they found better sensitivity (91.4%) and better specificity (93%) ratios compared to other b value combinations (0, 250, 500, 750 and 1000 mm²/s) (143) (Table 4). When the threshold value was taken as 1.24x10⁻³ mm²/s at b value 750, sensitivity 91.4%, specificity 93% (24), and when the threshold value was taken as 1.21x10⁻³ mm²/s at b value 1000, sensitivity 69%, specificity 100% (28), while in another study, when

the threshold value was accepted as 1.23x10⁻³ mm²/s at b value 1000, sensitivity 97.4%, specificity 85.7% (29), and in our study, when the ADC threshold value was taken as 1.238x10⁻³ mm²/s, sensitivity 92.3%, and specificity 82.5%. These rates we found are compatible with the literature.

Luo et al. determined ADC values as 1.98x10⁻³ mm²/s in NFT, 1.59x10⁻³ mm²/s in benign lesions, 0.87x10⁻³ mm²/s malignant lesions, and they found a statistically considerable variance in ADC values in the differentiation of NFT-malign-benign lesions (p<0.05). At the threshold value of 1.22x10⁻³ mm²/s, the sensitivity was 88.9% and the specificity was 87.9% (33,36).

In our study, the average ADC values of NFT were found to be statistically significantly higher than the ADC values of malignant and benign lesions (Table 2). A statistically considerable variance was found between the ADC values of malign tumours and benign tumours (p<0.001) (Table 3). When the ADC threshold value was set as 1.238x10⁻³ mm²/s for the identification of benign and malign masses, sensitivity and specificity were 92.3% and 82.5%, respectively.

CONCLUSION

MRI is a common radiologic diagnostic modality for evaluation and identification of breast masses. Contrast-enhanced MRI is very successful in detecting lesions. However, the use of contrast-enhanced MRI alone leads to difficulties in differentiating benign and malignant masses. DWI provides information about morphologic and physiologic changes in tissues caused by some

changes at the cellular level. However, it is difficult to use it alone in the differentiation of breast masses due to its low resolution. For this reason, contrast-enhanced MRI and DWI can be evaluated together in the characteristic features of breast masses. In conclusion, we believe that the use of DWI in addition to contrast-enhanced MRI can easily to separate from each other between NFT, benign and malignant masses. We recommend that DWI should be used routinely to differentiate breast lesions.

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REFERENCES

- Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer*. 2001;37:S4-66.
- Rohan TZ, Mandel JL, Yang HY, et al. Identifying subsets of cancer patients with an increased risk of developing cutaneous melanoma: a surveillance, epidemiology, and end results-based analysis. *JID Innov*. 2024;5:100323.
- Leung JWT. Screening mammography reduced morbidity of breast cancer treatment. *Am J Roentgenol*. 2005;184:1508-9.
- Berg WA. Tailored supplemental screening for breast cancer: what now and what next?. *AJR Am J Roentgenol*. 2009;192:390-9.
- Wolfe JN. Risk for breast cancer development determined by mammographic parenchymal pattern. *Cancer*. 1976;37:2486-92.
- Jamshidi MH, Karami A, Keshavarz A, et al. Magnetic resonance elastography for breast cancer diagnosis through the assessment of tissue biomechanical properties. *Health Sci Rep*. 2024;7:e70253.
- Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology*. 2002;225:165-75.
- Goscini CP, Berman CG, Clark RA. Magnetic resonance imaging of the breast. *Cancer Control*. 2001;8:399-406.
- Illustrated breast imaging reporting and data system (BI-RADS). 5th edition. American College of Radiology (ACR), Reston, VA. 2013.
- Hatakenaka M, Soeda H, Yabuuchi H, et al. Apparent diffusion coefficients of breast tumors: clinical application. *Magn Reson Med Sci*. 2008;7:23-9.
- Tsushima Y, Takahashi-Taketomi A, Endo K. Magnetic resonance (MR) differential diagnosis of breast tumors using apparent diffusion coefficient (ADC) on 1. 5-T. *J Magn Reson Imaging*. 2009;30:249-55.
- Englander SA, Ulug AM, Brem R, et al. Diffusion imaging of human breast. *NMR Biomed*. 1997;10:b348-52.
- Cho E, Baek HJ, Jung EJ, et al. Clinical feasibility of a deep learning approach for conventional and synthetic diffusion-weighted imaging in breast cancer: qualitative and quantitative analyses. *Eur J Radiol*. 2025;182:111855.
- Sinha S, Lucas-Quesada FA, Sinha U, et al. In vivo diffusion-weighted MRI of the breast: potential for lesion characterization. *J Magn Reson Imaging*. 2002;15:693-704.
- Chen X, Li WL, Zhang YL, et al. Meta-analysis of quantitative diffusion-weighted MR imaging in the differential diagnosis of breast lesions. *BMC Cancer*. 2010;10:693.
- Iima M, Honda M, Satake H, et al. Standardization and advancements efforts in breast diffusion-weighted imaging. *Jpn J Radiol*. 2025;43:347-54.
- Rajagopal V, Lee A, Chung JH, et al. Creating individual-specific biomechanical models of the breast for medical image analysis. *Acad Radiol*. 2008;15:1425-36.
- Khaled W, Reichling S, Bruhns OT, et al. Ultrasonic strain imaging and reconstructive elastography for biological tissue. *Ultrasonics*. 2006;44:199-202.
- Luo J, Ying K, Bai J. Elasticity reconstruction for ultrasound elastography using a radial compression: an inverse approach. *Ultrasonics*. 2006;44:e195-8.
- Havre RH, Elde E, Gilja OH, et al. Freehand real-time elastography: impact of scanning parameters of image quality and in vitro intra and interobserver validations. *Ultrasound Med Biol*. 2008;34:1638-50.
- Guo Y, Cai YQ, Cai ZL, et al. Differentiation of clinically benign and malignant breast lesions using diffusion-weighted imaging. *J Magn Reson Imaging*. 2002;16:172-8.
- Anwar R Padhani, Guoying Liu, Dow Mu-Koh, et al. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations neoplasia. 2009;11:102-25.
- Wenkel W, Geppert C, Uder M, et al. Diffusion-weighted imaging in breast MRI-an easy way to improve specificity. *Clinical Woman's Health*. 2007;3:28-32.
- Pereira FP, Martins G, Carvalhaes de Oliveira Rde V. Diffusion magnetic resonance imaging of the breast. *Magn Reson Imaging Clin N Am*. 2011;19:95-110.
- Nicky H.G.M. Peters, Koen L. Vincken, et al. Quantitative Diffusion-Weighted Imaging for differentiation of the benign and malignant breast lesions: The influence of the choice of b-values. *J Magn Reson Imaging*. 2010;31:1100-5.
- Imamura T, Isomoto I, Sueyoshi E, et al. Diagnostic performance of ADC for Non-mass-like breast lesions on MR imaging. *Magn Reson Med Sci*. 2010;9:217-25.
- Partridge SC, Demartini WB, Kurland BF, et al. Differential diagnosis of mammographically and clinically occult breast lesions on diffusion-weighted MRI. *J Magn Reson Imaging*. 2010;31:562-70.
- DePriore MR, Biswas D, Hippe DS, et al. Breast cancer conspicuity on computed versus acquired high b-value diffusion-weighted MRI. *Acad Radiol*. 2021;28:1108-17.

29. Partridge SC, Steingrimsson J, Newitt DC, et al. Impact of alternate b-value combinations and metrics on the predictive performance and repeatability of diffusion-weighted MRI in breast cancer treatment: results from the ECOG-ACRIN A6698 trial. *Tomography*. 2022;8:701-17.
30. Palle L, Reddy B. Role of diffusion MRI in characterizing benign and malignant breast lesions. *Indian J Radiol Imaging*. 2009;19:287-90.
31. Kul S, Cansu A, Alhan E, et al. Contribution of diffusion-weighted imaging to dynamic contrast-enhanced MRI in the characterization of breast tumors. *AJR Am J Roentgenol*. 2011;196:210-7.
32. Tozaki M, Fukuma E. ¹H MR spectroscopy and diffusion-weighted imaging of the breast: are they useful tools for characterizing breast lesions before biopsy?. *AJR Am J Roentgenol*. 2009;193:840-9.
33. Luo JD, Liu YY, Zhang XL, Shi LC. Application of diffusion weighted magnetic resonance imaging to differential diagnosis of breast diseases. *Ai Zheng*. 2007;26:168-71.
34. Yabuuchi H, Matsuo Y, Kamitani T, et al. Non-mass-like enhancement on contrast-enhanced breast MR imaging: lesion characterization using combination of dynamic contrast-enhanced and diffusion-weighted MR images. *Eur J Radiol*. 2010;75:e126-32.
35. Choi BB. Effectiveness of ADC difference value on pre-neoadjuvant chemotherapy mri for response evaluation of breast cancer. *Technol Cancer Res Treat*. 2021;20:15330338211039129.
36. Hottat NA, Badr DA, Lecomte S, et al. Value of diffusion-weighted MRI in predicting early response to neoadjuvant chemotherapy of breast cancer: comparison between ROI-ADC and whole-lesion-ADC measurements. *Eur Radiol*. 2022;32:4067-78.



Aberrant Right Subclavian Artery in Prenatal Diagnosis: A Retrospective Study

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Abstract

Aim: Aberrant right subclavian artery (ARSA) is the most common anomaly of the aortic arch and occurs in 1-2% of the population. Although it is usually asymptomatic, its prenatal detection has gained importance due to associations with chromosomal abnormalities, including trisomy 21 and 22q11.2 microdeletion. This study examines isolated (iARSA) and non-isolated ARSA (niARSA), focusing on diagnostic approaches and neonatal outcomes.

Material and Method: In this retrospective study, 29 pregnancies diagnosed with ARSA between October 2022 and January 2024 were analyzed. Fetuses were classified as iARSA or niARSA based on additional structural or chromosomal findings. Data were collected from high-resolution ultrasound examinations and medical records, and statistical comparisons were performed using SPSS v25.0.

Results: There were a total of 29 cases of ARSA, of which 16 were iARSA (55.2%) and 13 were niARSA (44.8%). Non-invasive prenatal testing was performed in 68.7% of iARSA cases, all of which had normal results. In contrast, invasive testing was performed in 38.5% of niARSA cases, with chromosomal abnormalities detected in two cases (trisomy 21). Neonatal outcomes were favorable in iARSA, with 15 cases discharged without complications. NiARSA cases had higher morbidity, including NICU admissions (46%) and congenital heart defects, which in some cases required surgical intervention.

Conclusion: ARSA is an important marker in prenatal diagnosis. While iARSA generally indicates favorable outcomes, niARSA correlates strongly with unfavorable neonatal outcomes and chromosomal abnormalities. The distinction between iARSA and niARSA is crucial for tailored prenatal management and optimization of neonatal care strategies.

Keywords: Aberrant right subclavian artery, chromosomal abnormalities, congenital heart defects, neonatal outcomes, prenatal diagnosis

INTRODUCTION

Aberrant right subclavian artery (ARSA), the most common anomaly of the branching pattern of the aortic arch, occurs in about 1-2% of the general population (1,2). ARSA results from the failure of normal regression in embryonic development, causing the artery to originate distal to the aortic arch and cross behind the trachea and esophagus toward the right upper limb (2). Although ARSA is usually asymptomatic and considered benign in the general population, it has gained clinical importance as a marker in prenatal diagnosis, especially for chromosomal abnormalities such as trisomy 21 and 22q11.2 microdeletion syndrome (2,3).

The detection of ARSA has been linked to advances in prenatal imaging, particularly the use of color Doppler ultrasonography in the second trimester. Studies report that

ARSA can be identified in 82-95% of cases using the three-vessel and tracheal view, allowing accurate visualization of its progression (1,4). However, ARSA is not only a marker for chromosomal abnormalities, but is also associated with other structural abnormalities that primarily affect the cardiovascular system, such as conotruncal defects (2,4).

Isolated ARSA (iARSA) carries a much lower risk of chromosomal abnormalities than non-isolated ARSA (niARSA), where additional structural or sonographic markers are present. This distinction serves as a basis for clinical decision making, with invasive testing recommended primarily in niARSA cases (2,3). In addition, cell-free DNA testing has been shown to be a non-invasive alternative for chromosomal risk assessment in fetuses with iARSA, demonstrating high sensitivity and specificity for conditions such as trisomy 21 (4,5).

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Despite these advances, there is still a need to clarify the implications of ARSA in different clinical contexts, particularly its association with rare genetic syndromes and long-term neonatal outcomes. This study aims to contribute to the growing body of knowledge by analyzing the co-occurrence of major cardiac and chromosomal abnormalities in fetuses diagnosed with ARSA.

MATERIAL AND METHOD

This retrospective cohort study was conducted in a tertiary perinatology center evaluating pregnancies diagnosed with ARSA by second trimester ultrasonography. Ethical approval was obtained from the local ethics committee before the study began.

The study included pregnant women aged 18–45 years who underwent detailed fetal anomaly screening between October 2022 and January 2024. Cases with ARSA identified on ultrasound were classified as either iARSA or niARSA based on the presence of additional structural abnormalities or sonographic markers, including increased nuchal fold thickness, nasal bone hypoplasia, echogenic bowel, intracardiac echogenic focus, and choroid plexus cysts. Exclusion criteria included pregnancies without ARSA findings on ultrasound or incomplete medical records.

The ultrasound examinations were performed with high-resolution transabdominal ultrasound systems which are Voluson E8 GE ultrasound machine (GE Medical Systems, Milwaukee, WI, USA) equipped with a convex 4–8 MHz transabdominal transducer, by experienced sonographers. The diagnosis of ARSA was confirmed in the three-vessel and tracheal view using color Doppler imaging to identify the typical course behind the trachea (Figure 1).



Figure 1. Ultrasound image of the three-vessel trachea view in a 37 week fetus; An ARSA (arrow) can be visualised arising from the distal aortic arch, coursing towards the right arm; Note the colour scale is set to approximately 20cm/s to enable visualisation of flow within the subclavian artery

Medical records were reviewed to collect data on maternal demographics, prenatal screening results, fetal structural findings, and chromosomal test outcomes. In cases where chromosomal analysis was performed, results were obtained through karyotyping or chromosomal microarray analysis.

The primary outcome was the prevalence of chromosomal abnormalities (e.g., trisomy 21, 22q11.2 microdeletion) and major congenital anomalies in fetuses with ARSA. Secondary outcomes included pregnancy and neonatal outcomes, such as delivery mode, gestational age at delivery, and postnatal complications associated with ARSA.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee at which the studies were conducted (Clinical Research Ethics Committee of Ankara Etlik City Hospital No. 1 (Decision No.: AEŞH-EK-2024-001, date: 31/01/2024) and with the 2013 Helsinki declaration and its later amendments or comparable ethical standards.

The statistical analyzes of this study were carried out using SPSS v25.0 software. Descriptive statistics were presented as median (interquartile range, IQR) for non-normally distributed variables and as percentages for categorical variables. For group comparisons, the Mann-Whitney U test was used for non-normally distributed continuous variables and Pearson Chi-Square was used for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 29 pregnancies with diagnosed ARSA were included in the analysis, of which 16 (55.2%) were classified as iARSA and 13 (44.8%) as niARSA. Table 1 provides an overview of the demographic and clinical characteristics of the groups. The mean maternal age and BMI were similar in the groups (p=0.975 and p=0.638, respectively). The mean gestational age at diagnosis was comparable at 23.06±2.61 weeks for iARSA and 23.30±4.83 weeks for niARSA (p=0.690) (Table 1).

Non-invasive prenatal testing (NIPT) was performed in 68.7% of iARSA cases (11/16), with all results normal. In contrast, no NIPT was performed in any of the niARSA cases. Invasive prenatal testing was performed in 38.5% of niARSA cases (5/13), with chromosomal abnormalities detected in two cases (both trisomy 21). No invasive tests were performed in the iARSA group (Table 2, Table 3).

Neonatal outcomes were significantly different between the groups. In the iARSA group, 15 out of 16 neonates (93.8%) were discharged without complications, while one neonate had to stay in the neonatal intensive care unit (NICU) for 11 days due to transient neonatal tachypnea, congenital pneumonia and other complications, all of which resolved with treatment (Table 4).

Table 1. Demographic and clinical characteristics of pregnant women diagnosed with isolated ARSA and non-isolated ARSA				
	Groups		p-value	
	iARSA (n=16)	niARSA (n=13)		
Age(year) (median) (IQR)	30.5 (11.5)	30.0 (10.5)	0.982	
Body mass index (kg/m ²) (median) (IQR)	27.00 (7.75)	30.00 (5.50)	0.643	
Gravida (median) (IQR)	2 (2)	2 (2)	0.424	
Parity (median) (IQR)	0 (1)	1 (1)	0.777	
Gestational week at the time of diagnosis (week) (median) (IQR)	22.00 (3.50)	23.00 (5.50)	0.690	
Gestational week at birth (week) (median) (IQR)	38.00 (1.75)	37.00 (3.0)	0.173	
Birth weight (gr) (median) (IQR)	3055.00 (272.00)	3305.00 (910.00)	0.430	
Type of delivery (n)				
Spontaneous	5	4		
Cesarean section	11	8	0.525	
Termination	0	1		
Values are presented as median (interquartile range, IQR) for non-normally distributed variables; P-values are calculated using the Mann-Whitney U test for continuous variables and Pearson Chi-Square test for categorical variables; A p-value <0.05 was considered statistically significant; iARSA: aberrant right subclavian artery, ARSA: isolated aberrant right subclavian artery, niARSA: non-isolated aberrant right subclavian artery				

Table 2. Maternal and neonatal characteristics for isolated ARSA cases												
	Age (years)	BMI (kg/m ²)	Gestational age at the time of diagnosis ARSA	Additional ultrasonographic findings	Additional CVS anomalies	PIT	Non-invasive test	Gestational age at delivery	Birth weight	Type of delivery	Gender of the newborn	Results of the prenatal tests
1	20	24	26	None	None	-	-	40	3100	CS	Female	None
2	30	31	23	None	None	-	-	37	3500	CS	Female	None
3	33	33	26.3	None	None	-	-	36	3310	Spontaneous	Male	None
4	22	26	23	None	None	-	-	36	3070	CS	Male	None
5	30	31	20	None	None	-	-	39	3500	CS	Male	None
6	30	25	23	None	None	-	+	39	3600	CS	Female	Normal
7	32	27	22	None	None	-	+	39	3200	CS	Male	Normal
8	27	24	21	None	None	-	+	38	3050	CS	Male	Normal
9	35	32	21	None	None	-	+	37	2790	CS	Female	Normal
10	38	33	22	None	None	-	+	39	3270	CS	Female	Normal
11	29	34	20	None	None	-	+	40	3680	Spontaneous	Female	Normal
12	32	24	23	None	None	-	+	40	3460	Spontaneous	Male	Normal
13	26	24	22	None	None	-	+	39	3060	CS	Male	Normal
14	24	23	20	None	None	-	+	38	2970	Spontaneous	Female	Normal
15	40	31	24	None	None	-	+	38	3010	CS	Female	Normal
16	36	27	22	None	None	-	+	36	2650	CS	Female	Normal
Birth weight is measured in grams (g); Gestational age is presented in completed weeks unless otherwise specified; Results of prenatal tests denote findings of chromosomal or genetic testing when applicable; Neonatal outcomes include complications such as respiratory or cardiac anomalies identified postnatally; ARSA: aberrant right subclavian artery, CS: cesarean section, CVS: cardiovascular system												

Table 3. Maternal and neonatal characteristics for non-isolated ARSA cases												
	Age (years)	BMI (kg/m²)	Gestational age at the time of diagnosis ARSA	Additional ultrasonographic findings	Additional CVS anomalies	PIT	Non-invasive test	Gestational age at delivery	Birth weight	Type of delivery	Gender of the newborn	Results of the prenatal tests
17	22	26	25	Echogenic cardiac	None	-	-	38	2750	Spontaneous	Female	-
18	21	24	30	Polyhydramnios	Type 1 TA, dilated trunkal artery, multiple valve dysplasia	-	-	40	3130	Spontaneous	Male	-
19	34	27	23	Pes equinovarus, scoliosis, renal fusion, single umbilical artery	Agenesis of ductus venosus	-	-	38	3460	CS	Male	-
20	30	26	13	Hydrops fetalis, cystic hygroma, hypoplastic nasal bone	Tricuspid regurgitation	-	-	14	-	Termination		-
21	24	24	20	Echogenic cardiac	None	yes	-	37	2640	CS	Female	Normal
22	25	31	26	PUV	None	yes	-	37	3050	CS	Male	Normal
23	25	24	22	Sandal gap	None	Yes	-	39	3200	CS	Male	Normal
24	27	29	21	Fetal renal pelviectasis	None	Yes	-	40	3300	CS	Male	Normal
25	22	30	25	Single umbilical artery	None	-	-	37	2740	Spontaneous	Male	-
26	44	37	22	Choroid plexus cyst	Mitral valve regurgitation	-	-	36	3020	CS	Female	-
27	42	23	26	Renal pelviectasis	Inlet VSD	yes	-	35	1500	CS	Female	Normal
28	41	30	34	Polyhydramnios, hypoplastic nasal bone	None	-	-	39	3880	Spontaneous	Female	-
29	37	32	27	Renal pelviectasis	DV shunt, inlet VSD	-	-	40	4200	CS	Male	-
Birth weight is measured in grams (g); Gestational age is presented in completed weeks unless otherwise specified (e.g., termination at 14 weeks); Results of prenatal tests denote findings of chromosomal or genetic testing when applicable; Neonatal outcomes include complications such as respiratory or cardiac anomalies identified postnatally; ARSA: aberrant right subclavian artery, VSD: ventricular septal defect, CS: cesarean section, PUV: posterior urethral valve, CVS: cardiovascular system, DV: ductus venosus, TA: truncus arteriosus												

Table 4. Summary of neonatal outcomes based on ARSA subtypes

Type of ARSA	Additional ultrasonographic findings	Neonatal outcomes
1 iARSA	None	Normal outcome
2 iARSA	None	Normal outcome
3 iARSA	None	11 days in NICU; TTN, congenital pneumonia, bilateral PTX, PDA, small secundum ASD
4 iARSA	None	
5 iARSA	None	
6 iARSA	None	
7 iARSA	None	
8 iARSA	None	
9 iARSA	None	
10 iARSA	None	
11 iARSA	None	
12 iARSA	None	
13 iARSA	None	
14 iARSA	None	
15 iARSA	None	
16 iARSA	None	
17 niARSA	Echogenic cardiac finding	
18 niARSA	Polyhydramnios, Type 1 truncus arteriosus, VSD	Operated on the 7th postnatal day, deceased on the 13th postnatal day
19 niARSA	Pes equinovarus, scoliosis, renal fusion, SUA	
20 niARSA	Hydrops fetalis, cystic hygroma, hypoplastic nasal bone	
21 niARSA	Echogenic cardiac finding	
22 niARSA	PUV	
23 niARSA	Sandal gap	
24 niARSA	Fetal renal pelviectasi	
25 niARSA	Single umbilical artery, RDS, IUGR, polyhydramnios, VSD, ASD	
26 niARSA	Choroid plexus cyst	
27 niARSA	Renal pyelectasis, IUGR, ASD, PFO	
28 niARSA	Polyhydramnios, hypoplastic nasal bone	
29 niARSA	Renal pyelectasis, AVSD	

Birth weight is measured in grams (g). Gestational age is presented in completed weeks unless otherwise specified (e.g., termination at 14 weeks); Results of prenatal tests denote findings of chromosomal or genetic testing when applicable; Neonatal outcomes include complications such as respiratory or cardiac anomalies identified postnatally; ARSA: aberrant right subclavian artery, iARSA: isolated aberrant right subclavian artery, niARSA: non-isolated aberrant right subclavian artery, NICU: neonatal intensive care unit , TTN: transient tachypnea of the newborn, PTX: pneumothorax, PDA: patent ductus arteriosus, ASD: atrial septal defect, VSD: ventricular septal defect, CS: cesarean section, PUV: posterior urethral valve, IUGR: intrauterine growth restriction, RDS: respiratory distress syndrome, BPD: bronchopulmonary dysplasia, CVS: cardiovascular system, DV: ductus venosus, TY: tricuspid valve regurgitation

In contrast, the niARSA group exhibited a higher rate of adverse neonatal outcomes, with NICU admission required in 46.1% of cases (6/13). Major complications included respiratory distress syndrome, severe congenital heart defects and chromosomal abnormalities, such as Down syndrome (identified in two cases). Two neonates in this group died due to complications following surgery for congenital anomalies (Table 4). A comparison between niARSA cases with normal chromosomal results and iARSA cases revealed significant differences in neonatal outcomes. Among the eight niARSA cases with normal chromosomal results, three (37.5%) required NICU admission due to complications such as respiratory distress syndrome, IUGR, and congenital anomalies requiring postnatal intervention. In contrast, only one iARSA case (6.3%) required NICU admission, with transient tachypnea of the newborn and congenital pneumonia that resolved with treatment.

The mean birth weight was 3.103 ± 270 g in the iARSA group and 2.910 ± 420 g in the niARSA group ($p=0.668$) (Table 1). The gestational age at birth was slightly lower in the niARSA group (36.9 ± 2.3 weeks) than in the iARSA group (37.8 ± 1.9 weeks), but the difference was not statistically significant ($p=0.173$) (Table 1).

Cesarean section was the predominant mode of delivery in both groups and was performed in 68.7% of all cases. Spontaneous vaginal delivery was performed in 31.3% of cases, with no significant differences between the groups ($p=0.525$) (Table 1).

DISCUSSION

ARSA is a common vascular anomaly with significant impact on prenatal diagnosis and neonatal outcomes. This study evaluates the role of ARSA as a marker of chromosomal and structural abnormalities and compares iiARSA and niARSA cases. The results are consistent with the existing literature and provide insights into clinical practice and prenatal management strategies.

The prevalence of ARSA ranges between 0.5% and 2% in the general population and increases significantly in trisomy 21 cases, with studies reporting rates of 23–30% (2,3). Recent meta-analyses show that isolated ARSA has no significant association with chromosomal abnormalities, with a likelihood ratio (LR+) of almost zero. However, in niARSA the LR+ increases dramatically to 199 when additional markers are present, underlining the diagnostic relevance (2,3).

In this study, niARSA cases had a higher prevalence of chromosomal abnormalities, particularly trisomy 21 and 22q11.2 deletion syndromes, which is consistent with other reports. Previous studies have shown that 22q11.2 deletion syndrome, which is associated with congenital heart defects such as truncus arteriosus, is significantly correlated with ARSA (1,2). In addition, ventricular septal defects and other cardiac malformations are the most common structural anomalies in niARSA cases (6).

Neonatal outcomes in iARSA cases were predominantly favorable, which is consistent with previous literature stating that isolated ARSA rarely leads to significant complications (7,8). In our study, 94% of iARSA neonates were discharged without requiring a prolonged stay in the NICU, emphasizing the limited clinical impact of this condition in the absence of additional abnormalities. However, the niARSA cases had a markedly different profile. Adverse neonatal outcomes such as RDS, low birth weight and prolonged ICU stays were significantly more common in this group. Structural anomalies, including ventricular septal defects (VSD) and other congenital heart defects, contributed to the increased morbidity and in some cases required early surgical intervention (1,6,9). This discrepancy underscores the importance of distinguishing between iARSA and niARSA prenatally to effectively tailor postnatal care strategies.

The use of NIPT in pregnancies with ARSA is a critical factor. In iARSA cases, NIPT has been shown to be a highly reliable tool for ruling out chromosomal abnormalities, obviating the need for invasive procedures such as amniocentesis or chorionic villus sampling (7-9). This is consistent with the findings that isolated ARSA has a minimal association with chromosomal abnormalities, making NIPT an efficient diagnostic option of first choice. In contrast, invasive testing remains essential for niARSA, especially when additional sonographic markers or structural abnormalities are present (1,2,8). Studies suggest that invasive procedures provide important insights into genetic and structural risk factors that support prenatal counseling and delivery planning (3,8).

The results confirm that ARSA, especially niARSA, should be considered as a marker of high clinical relevance in prenatal medicine. The strong correlation between niARSA and chromosomal abnormalities requires a detailed evaluation of coexisting sonographic markers and structural defects as well as other anomalies (3,8,10).

Although this study provides a robust analysis of ARSA, its retrospective design and single-center nature may limit its generalizability. Future multicenter, prospective studies are needed to validate these results and examine the long-term neonatal outcomes associated with ARSA (2,11).

CONCLUSION

ARSA is a valuable prenatal marker, with isolated cases generally associated with favorable outcomes and non-isolated cases associated with significant chromosomal and structural abnormalities. The distinction between iARSA and niARSA is crucial for appropriate prenatal screening and neonatal care. While non-invasive prenatal testing effectively rules out chromosomal abnormalities in iARSA, invasive methods remain essential in niARSA to ensure a comprehensive evaluation. The role of ARSA in prenatal diagnosis underscores its importance for personalized and multidisciplinary fetal care.

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REFERENCES

1. Annetta R, Nisbet D, O'Mahony E, Palma-Dias R. Aberrant right subclavian artery: embryology, prenatal diagnosis and clinical significance. *Ultrasound*. 2022;30:284-91.
2. Luo T, Liu S, Ran S, et al. Associated congenital anomalies and genetic anomalies in fetuses with isolated and non-isolated aberrant right subclavian artery. *J Matern Fetal Neonatal Med*. 2023;36:2211705.
3. Saraç T, Erzincan SG, Uygur L, et al. Isolated aberrant right subclavian artery: should invasive intervention be recommended in the era of noninvasive prenatal tests?. *J Ist Faculty Med*. 2023;86:37-43.
4. Morlando M, Morelli C, Del Gaizo F, et al. Aberrant right subclavian artery: the association with chromosomal defects and the related post-natal outcomes in a third level referral centre. *J Obstet Gynaecol*. 2022;42:239-43.
5. Aygün EG, Sarı U, Pata Ö, Dilek TUK. Isolated aberrant subclavian artery diagnosed in the second trimester examination: how should we approach? *Dicle Med J*. 2022;49:119-24.
6. Scala C, Leone Roberti Maggiore U, Candiani M, et al. Aberrant right subclavian artery in fetuses with Down syndrome: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2015;46:266-76.
7. Borenstein M, Minekawa R, Zidere V, et al. Aberrant right subclavian artery at 16 to 23 + 6 weeks of gestation: a marker for chromosomal abnormality. *Ultrasound Obstet Gynecol*. 2010;36:548-52.
8. De León-Luis J, Gámez F, Bravo C, et al. Second-trimester fetal aberrant right subclavian artery: original study, systematic review and meta-analysis of performance in detection of Down syndrome. *Ultrasound Obstet Gynecol*. 2014;44:147-53.
9. Nedelcu AH, Lupu A, Moraru MC, et al. Morphological aspects of the aberrant right subclavian artery-a systematic review of the literature. *J Pers Med*. 2024;14:335.
10. Özkan S, Aksan A, Fıratlıgil FB, et al. Persistent right umbilical vein: clinical outcomes and prognostic factors in prenatal diagnosis. *South Clin Istanbul Eurasia*. 2024;35:359-63.
11. Ranzini AC, Hyman F, Jamaer E, van Mieghem T. Aberrant right subclavian artery: correlation between fetal and neonatal abnormalities and abnormal genetic screening or testing. *J Ultrasound Med*. 2017;36:785-90.



Assessment of Symptom Burden Using the ESAS in Patients with Hypercapnic Respiratory Failure Receiving Noninvasive Mechanical Ventilation

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Abstract

Aim: The success of noninvasive mechanical ventilation (NIV), which is used in the treatment of hypercapnic respiratory failure (HRF), largely depends on patient adherence. One of the key components of adherence is effective symptom control. Therefore, it is recommended that symptoms other than dyspnea be systematically assessed in patients requiring NIV. This study was designed to evaluate the symptom burden of such patients using the Edmonton Symptom Assessment Scale (ESAS).

Material and Method: This study, conducted between January 2025 and March 2025, included patients undergoing NIV. The demographic characteristics and comorbidities of the patients were assessed. Symptoms and their severity were evaluated using the ESAS. Additionally, patients were divided into two groups: those with prior NIV experience and those undergoing NIV for the first time, and their symptom burden was analyzed accordingly.

Results: The mean age of the patients included in the study was 69±12 years, with 68.4% being male. According to the ESAS results, the most frequently reported symptoms were dyspnea (6.21±1.05), overall well-being (5.65±2.49), and fatigue (5.03±1.74). When comparing symptom burden based on NIV experience, dyspnea scores were significantly higher in patients with prior NIV use ($p<0.001$), whereas abdominal bloating and drowsiness were more pronounced in first-time NIV users ($p<0.001$, $p=0.049$). Gender-based analysis revealed that pain scores were significantly higher in female patients compared to males ($p=0.030$). Regarding age groups, older patients exhibited more pronounced dyspnea and appetite loss, while younger patients had higher scores for pain, anxiety, and overall well-being ($p<0.05$).

Conclusion: This study demonstrated that symptom burden is significant in patients undergoing NIV and that age, gender, and prior NIV experience influence symptom presentation. These findings highlight the importance of comprehensive assessment approaches to personalize symptom management and enhance patient adherence.

Keywords: Edmonton Symptom Assessment Scale, noninvasive mechanical ventilation, compliance, adherence

INTRODUCTION

Respiratory failure is a severe clinical condition frequently encountered in intensive care units and significantly impacts patients' quality of life (1). To provide respiratory support in these patients, noninvasive mechanical positive pressure ventilation (NIV) can be administered (2). While the effectiveness of NIV largely depends on patient adherence to treatment, the emergence of various symptoms during the application process can negatively affect treatment outcomes (3). During NIV, patients may experience not only physical discomforts such as facial discomfort due to the mask, pressure ulcers, dry mouth, nasal congestion,

headache, and ear pain but also psychosocial symptoms such as dyspnea, fatigue, depression, and anxiety (4). This highlights the importance of symptom management and the necessity of systematically screening for other symptoms.

The Edmonton Symptom Assessment Scale (ESAS) was developed to objectively and systematically evaluate symptom burden. Initially designed for use in cancer patients, it is now widely utilized in various patient populations (5-7). ESAS allows patients to rate their symptoms on a scale from 0 to 10, enabling the identification of the most burdensome symptoms.

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This study was designed to evaluate the most common symptoms and the severity of these symptoms in patients undergoing NIV in the intensive care unit due to hypercapnic respiratory failure (HRF) using ESAS. Additionally, it aimed to determine the relationship between these symptoms and prior NIV use, as well as patients' demographic characteristics.

MATERIAL AND METHOD

This prospective study was conducted between January and March 2025 in the Pulmonary Diseases Intensive Care Unit of our hospital on patients undergoing NIV due to HRF. The study was approved by the Clinical Research Ethics Committee of Ankara Atatürk Sanatorium Training and Research Hospital on January 22, 2025 (Approval No: 212) and conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The medical treatment of the patients was planned based on national and international guidelines. NIV was primarily administered using an oronasal mask.

Initially, the overall symptom profile identified by the ESAS was described for the entire patient population. Subsequently, the relationships between symptom scores and variables such as age, gender, and previous NIV experience were statistically analyzed.

Data Collection Method

In the study, the patients' age, gender, concomitant diseases and other demographic characteristics were examined in detail. The most frequently observed symptoms in patients undergoing NIV and their severity were assessed using the ESAS. ESAS data were collected through a survey-based method.

ESAS is a validated tool designed to measure symptom burden, rating symptom severity on a scale from 0 to 10. The scale evaluates nine core symptoms: pain, fatigue, nausea, depression, anxiety, appetite loss, sleep disorder, dyspnea, and overall well-being. Additionally, the "other symptoms" section of the ESAS questionnaire allows patients to report any additional predominant symptoms they experience. In this study, dry mouth and abdominal bloating were the most frequently reported additional symptoms. Through this structured survey approach, patients' symptoms and their severity were systematically evaluated.

Patient Selection

This study was designed to include patients who received NIV due to hypercapnic respiratory failure ($pCO_2 > 45$ mmHg) secondary to a chronic obstructive pulmonary disease (COPD) exacerbation during the specified period.

Patients with prior use of NIV at home were classified as the "previous NIV experience" group, while those who had never used NIV before were considered the "no prior NIV experience" group.

After assessing the symptom burden in the included patients, they were divided into two groups based on NIV usage: patients who had previously used NIV (previous NIV

Users) and patients who were undergoing NIV for the first time (First-time NIV Users). Based on this classification, potential differences between symptom burdens and symptom profiles of the two groups were comparatively assessed.

Inclusion Criteria:

- Patients diagnosed with HRF in the emergency department and subsequently treated with NIV in the intensive care unit,
- Patients with hypercapnic respiratory failure secondary to COPD exacerbation,
- Patients aged 18 years or older,
- Patients who provided informed consent and agreed to participate in the study.

Exclusion Criteria:

- Patients with hypercapnic respiratory failure due to causes other than COPD exacerbation,
- Patients who did not agree to participate in the study,
- Patients with incomplete data,
- Patients younger than 18 years old,
- Patients diagnosed with hypoxic respiratory failure,
- Patients with a history of any malignancy,
- Patients unable to provide reliable data due to dementia or cognitive impairment,
- Patients with communication barriers or inability to cooperate.

Statistical Analysis

The data obtained in the study were analyzed using the SPSS 27.0 statistical software. Descriptive statistics were presented as mean $\pm$ standard deviation (Mean $\pm$ SD). The normality of data distribution was assessed using the Kolmogorov-Smirnov test and histogram-graph methods. For comparisons between groups, the independent samples t-test was used for parametric data, while the Mann-Whitney U test was applied for non-parametric data. Categorical variables were analyzed using the Chi-square (χ^2) test. To evaluate the effects of age, gender, and prior NIV experience on symptom scores, Mann-Whitney U analysis was performed. In all analyses, a p-value < 0.05 was considered statistically significant.

RESULTS

A total of 136 patients were included in the study. The mean age of the patients was 69 ± 12 years, and 68.4% of the participants were male. At least one comorbidity was present in 87.5% ($n=119$) of the patients, with COPD being the most common comorbidity, observed in 64% ($n=87$) of cases.

Analysis of the ESAS scores revealed that the most prominent symptoms were dyspnea (6.21 ± 1.05), overall well-being (5.65 ± 2.49), and fatigue (5.03 ± 1.74). A summary of the ESAS results for the study population is presented in Table 1.

The patients included in the study were divided into two groups based on their NIV experience, and their ESAS scores were compared. A statistically significant difference was observed in dyspnea ($p<0.001$), drowsiness ($p=0.049$), and abdominal bloating ($p<0.001$) scores. Dyspnea scores were found to be higher in patients with

prior NIV experience, whereas drowsiness and abdominal bloating were more pronounced in first-time NIV users. No significant difference was detected between the two groups in terms of other symptoms ($p>0.05$). The symptom scores based on NIV experience are presented in Table 1.

Table 1. Edmonton Symptom Assessment Scale (ESAS) results of the study population and comparison based on prior NIV experience				
Symptom	All patients (N=136) Mean±SD	Previous NIV users (N=73) Mean±SD	First-time NIV users (N=63) Mean±SD	p-value
Pain	2.12±1.59	1.89±1.62	2.39±1.54	0.057
Fatigue	5.03±1.74	4.86±1.85	5.24±1.61	0.108
Nausea	0.82±0.30	0.84±0.57	0.79±0.16	0.482
Depressive feeling	2.05±1.10	1.88±1.11	2.25±1.08	0.138
Anxiety	2.57±1.77	2.38±1.83	2.79±1.71	0.138
Drowsiness	2.04±0.94	1.88±1.08	2.23±0.75	0.049
Loss of appetite	1.12±0.81	1.36±1.05	0.84±0.45	0.402
General well-being	5.65±2.49	5.50±1.54	5.82±1.44	0.399
Dyspnea	6.90±1.15	7.62±0.77	6.06±0.94	<0.001
Dry mouth	2.60±1.49	2.33±1.44	2.90±1.53	0.253
Abdominal bloating	4.43±1.70	3.63±1.58	5.35±1.34	<0.001

The symptoms of the patients included in the study were analyzed based on gender. The pain score was found to be 1.92±0.56 in male patients and 2.53±0.60 in female patients, with a statistically significant difference between the two groups ($p=0.030$).

The patients were divided into two groups based on the median age of 69 years as a reference. A statistically significant difference was observed between the two groups in terms of pain ($p=0.030$), nausea ($p=0.035$),

anxiety ($p=0.033$), overall well-being ($p=0.014$), dyspnea ($p=0.023$), and loss of appetite ($p<0.001$) scores. Pain, anxiety, and overall well-being scores were found to be higher in younger patients, whereas dyspnea and loss of appetite were more pronounced in older patients. No significant difference was detected between the groups for other symptoms ($p>0.05$). The symptom scores of the included patients based on age groups are presented in Table 2.

Table 2. Edmonton Symptom Assessment Scale (ESAS) results based on the age groups of the patients			
Symptom	≤69 years (N=62) Mean±SD	>69 years (N=75) Mean±SD	p-value
Pain	2.39±1.54	1.89±1.62	0.030
Fatigue	5.24±1.61	4.86±1.85	0.108
Nausea	0.79±0.17	0.84±0.57	0.035
Depressive feeling	2.27±1.09	1.88±1.11	0.109
Anxiety	2.81±1.73	2.38±1.82	0.033
Insomnia	2.23±0.75	1.88±1.08	0.064
Loss of appetite	0.85±0.45	1.36±1.05	<0.001
General well-being	5.83±2.46	5.50±2.54	0.014
Dyspnea	6.06±0.95	7.62±0.77	0.023
Dry mouth	3.95±1.52	3.32±1.44	0.618
Abdominal bloating	5.37±1.34	3.63±1.58	0.095

To evaluate the relationship between age and symptoms, univariate and multivariate logistic regression analyses were performed for each symptom with age as the independent variable. According to the results of the multivariate analysis, the appetite loss score was found to be significantly

and positively associated with age (HR: 1.576; 95% CI: 1.170–2.124; $p=0.003$). In addition, the dyspnea score was negatively associated with age. No significant associations were observed between age and the other symptoms. These results are summarized in Table 3.

Table 3. Evaluation of the relationship between age and symptoms using logistic regression analysis

Symptom	Univariate logistic regression		Multivariate logistic regression	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Pain	1.286 (1.023–1.616)	0.031	1.084 (0.817–1.439)	0.576
Fatigue	1.154 (0.945–1.410)	0.161	–	–
Nausea	1.045 (0.815–1.338)	0.730	–	–
Depressive feeling	1.043 (0.886–1.227)	0.614	–	–
Anxiety	1.123 (0.989–1.276)	0.073	0.926 (0.744–1.152)	0.489
Insomnia	1.107 (0.922–1.324)	0.278	–	–
Loss of appetite	1.452 (1.122–1.879)	0.005	1.576 (1.170–2.124)	0.003
General well-being	1.203 (1.042–1.389)	0.012	1.180 (0.932–1.494)	0.169
Dyspnea	0.703 (0.517–0.956)	0.025	0.587 (0.402–0.858)	0.006
Dry mouth	1.041 (0.908–1.193)	0.563	–	–
Abdominal bloating	1.195 (0.974–1.466)	0.088	1.077 (0.845–1.372)	0.551

DISCUSSION

In this study, a high overall symptom burden was observed among patients receiving NIV. Using the ESAS, we evaluated whether symptom burden differed according to clinical variables such as age, gender, and prior NIV experience. According to the findings, the most frequently reported symptoms were dyspnea, impaired well-being, and fatigue. The results indicate that symptom burden is substantial in patients undergoing NIV and that age, gender, and previous NIV experience significantly influence symptom profiles. These findings highlight the need for individualized symptom management strategies and underscore the importance of closely monitoring symptom burden to improve patient adherence to NIV.

In patients with advanced respiratory disease, severe dyspnea is often the predominant symptom; however, additional symptoms are frequently reported (8). In addition to dyspnea, various symptoms such as pain, fatigue, dry mouth, cough, depression, and anxiety have been documented in this patient population (9,10). This underscores the necessity of systematically evaluating a broader range of symptoms rather than solely focusing on dyspnea (11). In our study, although dyspnea was the most prominent complaint, symptoms such as fatigue, overall well-being, dry mouth, and anxiety were also commonly observed. These findings highlight the importance of a multidimensional approach to symptom management.

Rantala et al. reported that symptoms such as dyspnea, dry mouth, and loss of appetite were prominent in patients with chronic respiratory failure and that these symptoms varied depending on the underlying etiology of the disease (8). In the present study, patient symptoms were compared based on prior NIV experience. Our findings demonstrated that first-time NIV users exhibited lower dyspnea scores but experienced significantly higher levels of abdominal bloating. This observation suggests that patients who are unfamiliar with NIV may be more prone to developing abdominal discomfort. These results underscore the

necessity of implementing individualized approaches in symptom management.

Several studies have demonstrated that women have a higher perception of pain and are more susceptible to chronic pain syndromes compared to men (12). It has been suggested that the increased frequency and severity of pain reported by female patients may be associated with the interaction of hormonal, genetic, neurophysiological, and psychosocial factors (13). Consistent with these findings, our study also revealed that female patients had higher pain scores than their male counterparts. This finding suggests that pain perception may be more pronounced in women during the NIV process and underscores the need to consider gender-specific differences in symptom management strategies.

Significant differences in symptom profiles may be observed between older and younger patient groups (14). In the study by Johannessen et al., symptoms such as dyspnea, appetite loss, and constipation were more prominent in older patients, whereas younger patients more frequently reported fatigue, nausea, and anxiety (15). In our study, according to multivariate logistic regression analysis, appetite loss was significantly more common in older patients, while dyspnea scores were higher among younger individuals. These findings suggest that symptom perception and physiological responses may differ across age groups. The higher prevalence of appetite loss in older adults may be attributed to more common nutritional issues in this population, whereas the heightened sensitivity to dyspnea in younger patients may explain their higher scores. In conclusion, the impact of age-related physiological and psychological changes on symptom burden should be considered, and symptom management should be tailored to the specific needs of each age group.

This study has several limitations. First, it was conducted as a single-center study with a limited sample size. Additionally, the follow-up period and long-term clinical outcomes of the patients could not be evaluated. The

fact that data were obtained from a single center limits the generalizability of the results to broader patient populations. Moreover, the use of subjective assessment tools such as ESAS carries the risk of measurement bias due to patient perception variability.

CONCLUSION

This study demonstrated that symptom burden is significant in patients undergoing NIV and that age, gender, and prior NIV experience influence symptom profiles. Specifically, certain symptoms were found to be more pronounced in women, elderly patients, and first-time NIV users. These findings highlight the importance of comprehensive assessment approaches to personalize symptom management and enhance patient adherence. Future multicenter studies may contribute to the development of more comprehensive strategies for optimizing symptom management in patients receiving NIV.

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REFERENCES

- Villgran VD, Lyons C, Nasrullah A, et al. Acute respiratory failure. Crit Care Nurs Q. 2022;45:233-47.
- Munshi L, Mancebo J, Brochard LJ. Noninvasive respiratory support for adults with acute respiratory failure. N Engl J Med. 2022;387:1688-98.
- Yıldız M, Çelik D, Akoğlu F, et al. Structured practices increasing patient compliance to noninvasive mechanical ventilation therapy: example of best practice. Anatolian Curr Med J. 2022;4:126-32.
- Çelik D, Yıldız M, Kurt HG, Saymaz ZT. Do high PaCO₂ levels during discharge from the hospital predict medium-term mortality in chronic respiratory failure patients without domiciliary non-invasive mechanical ventilator?. J Med Palliat Care. 2022;3:135-41.
- Traldi Macedo L, Gomes Bastos Fernandes L, Palmeira HM, et al. Assessment of symptom intensity and psychological well-being of patients with advanced cancer undergoing palliative care in a Brazilian public hospital: a cross-sectional study. Palliat Support Care. 2023;21:651-7.
- Bandieri E, Banchelli F, Borelli E, et al. Edmonton symptom assessment system global distress score and overall survival among patients with advanced cancer receiving early palliative care. BMJ Support Palliat Care. 2024;13:e735-6.
- Mehrotra R, Davison SN, Farrington K, et al. Managing the symptom burden associated with maintenance dialysis: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2023;104:441-54.
- Rantala HA, Leivo-Korpela S, Lehtimäki L, Lehto JT. Assessing symptom burden and depression in subjects with chronic respiratory insufficiency. J Palliat Care. 2022;37:134-41.
- Antoniou SA, Apostol A, Boiculese LV. Extra-respiratory symptoms in patients hospitalized for a COPD exacerbation: prevalence, clinical burden and their impact on functional status. Clin Respir J. 2019;13:735-40.
- Carvajalino S, Reigada C, Johnson MJ, et al. Symptom prevalence of patients with fibrotic interstitial lung disease: a systematic literature review. BMC Pulm Med. 2018;18:78.
- Patel AR, Patel AR, Singh S, et al. Global initiative for chronic obstructive lung disease: the changes made. Cureus. 2019;11:e4985.
- Pieretti S, Di Giannuario A, Di Giovannandrea R, et al. Gender differences in pain and its relief. Ann Ist Super Sanita. 2016;52:184-9.
- Athnaiel O, Cantillo S, Paredes S, Knezevic NN. The role of sex hormones in pain-related conditions. Int J Mol Sci. 2023;24:1866.
- Gaudernack HE, Hareide MM, Miaskowski C, et al. Symptom experience of older oncology patients with low versus high levels of multimorbidity prior to chemotherapy. Eur J Oncol Nurs. 2021;54:102029.
- Johannessen MS, Miaskowski C, Kleven AG, et al. Age-related differences in the occurrence, severity, and distress of symptoms in older patients at the initiation of chemotherapy. BMC Geriatr. 2023;23:481.



Adverse Events of Eye Disorders Related to the Use of Vortioxetine: A Disproportionality Analysis

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Abstract

Aim: The present study aims to evaluate the potential risk of ocular adverse events with vortioxetine use by analyzing real-world adverse events reported in the U.S. Food and Drug Administration's Adverse Event Reporting System (FAERS) database.

Material and Method: The OpenVigil 2.1-MedDRA-v24 disproportionality analysis software package, including the Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR) algorithms, was used to determine the potential risk of ocular adverse events associated with vortioxetine and to determine signal strength. Ocular adverse event reports related to the generic name vortioxetine as the primary suspect in the FAERS database between 16 May 2014 and 30 September 2024 were included in this study. Risk signal strength for ROR and PRR were classified as low, medium and strong in line with the signal intensity.

Results: Twenty-nine 'preferred terms' with 3 or more reports were included in this study. Given the results of the disproportionality analysis, 5 adverse events with potential positive signals were found. These were halo vision (ROR=8.205, PRR=8.202; medium signal), angle-closure glaucoma (ROR=5.646, PRR=5.642; medium signal), blepharospasm (ROR=3.408, PRR=3.406; weak signal), oculogyric crisis (ROR=2.394, PRR=2.393; weak signal), and blurred vision (ROR=2.023, PRR=2.011; weak signal).

Conclusion: The disproportionality analysis conducted on the FAERS database revealed possible adverse events associated with vortioxetine in eye disorders and not documented in the drug's package insert (except for angle-closure glaucoma). In conclusion, these findings indicate that continued post-marketing surveillance plays a decisive role in signaling potential new ocular adverse drug events.

Keywords: Vortioxetine, adverse event, eye disorders, disproportionality analysis

INTRODUCTION

Vortioxetine is a new antidepressant with a unique profile as it is an atypical (multimodal) serotonergic agent (1). It is a second-generation antidepressant approved by the regulatory agencies in America and Europe (2). The marketing authorization for this medicine was approved by the U.S. Food and Drug Administration (FDA) on 30 September 2013 and by the European Medicines Agency (EMA) on 18 December 2013.

Efficacy and tolerability of vortioxetine have been demonstrated in studies (2). The Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guideline recommends vortioxetine, a relatively new antidepressant, as one of the first-line treatments for major depressive disorders due to its unique pharmacodynamic

mechanisms and efficacy (3). Therefore, its scientific popularity tends to increase (4).

However, since vortioxetine is a relatively new drug, its safety profile is not clear yet. There are limited adverse drug events (ADEs) data for recently approved antidepressant agents such as vortioxetine. Adverse events (AEs) of vortioxetine also differ from conventional antidepressants, with a low incidence of sexual dysfunction, weight gain, or cardiovascular changes (5). Gastrointestinal symptoms such as nausea and vomiting ranked first among the major AEs associated with the use of new-generation antidepressant drugs, while ophthalmic conditions such as glaucoma and cataract ranked seventeenth (6).

AEs are defined as medically undesirable occurrences resulting from the use of a pharmaceutical product. ADEs

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are prevalent and represent a substantial healthcare burden. The most comprehensive database of ADEs is that of the U.S. Food and Drug Administration's Adverse Event Reporting System (FAERS) (7). The FAERS database is a publicly accessible collection of ADE reports submitted voluntarily by healthcare professionals, patients, and pharmaceutical companies. The database reflects real-world occurrences of ADEs (8). The database includes patient information, adverse reaction data, drug utilization details, report sources, drug indications, and patient outcomes (9).

The FAERS database codes all adverse events using preferred terms (PTs) from the Medical Dictionary of Regulatory Activities (MedDRA). Disproportionality analysis of the data obtained from large databases of spontaneous AE reporting systems such as FAERS has been an important method for drug safety monitoring (10,11). Regarding the pharmacovigilance, proportional reporting ratio (PRR) (12) and reporting odds ratio (ROR) (13) are the most popular methodologies utilized for the detection of ADE signals. The FAERS database contains reports that are either duplicate or incomplete. Consequently, data mining tools such as OpenVigil are employed. OpenVigil, a web interface for the analysis of spontaneous or systematic collections of treatments (drugs) and observed AEs (adverse effects of drugs) (14), is a tool used when analyzing the pharmacovigilance data that calculates ROR and PRR values.

The present study aims to investigate the post-marketing safety profile of vortioxetine by performing a disproportionality analysis for vortioxetine and ocular ADEs using the FAERS database.

MATERIAL AND METHOD

Data Source and Collection

Adverse drug reactions reported in the public version of the FAERS database were used in this observational, retrospective pharmacovigilance study. The present study used OpenVigil 2.1-MedDRA-v24 to query the FAERS database. OpenVigil 2.1 is a software tool designed for the specific purpose of data extraction, cleaning, mining and analysis of AE data from the FAERS database. Ocular adverse event reports for the generic name 'vortioxetine', 'vortioxetine hydrobromide' and 'vortioxetine dl-lactate' submitted between 16 May 2014 and 30 September 2024 were selected and included in this study. The present study included reports of adverse reactions where the reporter indicated vortioxetine as 'Primary Suspect'. Ocular adverse events in the FAERS database were individually inquired by using the OpenVigil analysis tool. The relationship between drug and adverse events was analyzed by choosing 'Frequency' as the analysis method and 'Entire Cases' as the case type on the inquiry tab of this tool.

Data Analysis

A disproportionality analysis was performed using OpenVigil version 2.1. PRR and ROR were employed to

detect safety signals. All algorithms are based on 2x2 contingency tables. In this study, PTs with a reported frequency of ≥ 3 were selected for the initial screening procedure. The risk signal strength assessment criteria for ROR and PRR were signal intensity (assessment criteria) classification as weak ($2 < \text{ROR or PRR} \leq 10$), medium ($10 < \text{ROR or PRR} \leq 50$) and strong ($\text{ROR or PRR} > 50$) (15). If signals met the criteria of both methods, they were classified as positive signals. It is widely accepted that a chi-square value exceeding 4 is statistically significant (<https://openvigil.sourceforge.net/>). The analysis was performed using Microsoft Excel 2024 software.

The human-related datasets used in this study are publicly available for any research program. Patient consent was not obtained in this study because of the nature of the data source. This research did not require ethics committee approval since the authors had no knowledge of data collection or the participants in the present study.

RESULTS

ADE Reports and Clinical Information

A total of 29,661,136 ADE reports were recorded in the FAERS database until 30 September 2024. There were 15,448 ADE reports incorporating vortioxetine as the main suspect drug. Of these reports, 771 cases were related to eye disorders. There were more females (430 cases, 55.8%) than males (143 cases, 18.5%), most cases were submitted in 2024 (232 cases, 30%), and the predominant reporting country was USA (428 cases, 55.5%). In 46.3% of cases, the age of the case was not specified, and most cases with age information (42.8%) were aged between 18 and 64 (as shown in Table 1).

Signal Strength Analysis of Vortioxetine-Related Eye Disorder AEs

There were 29 PTs with 3 or more eye disorder reports associated with vortioxetine and 399 reports related to these PTs. The most reported PTs were vision blurred ($n=129$), visual impairment ($n=44$), and eye pain ($n=36$).

In this study, ROR and PRR were used to analyze ADE signals, and 5 potential positive signals were detected between 16 May 2014 and 31 September 2024. Angle-closure glaucoma (8 reports; $\text{ROR}=5.646$, 95% CI 2.818 - 11.311; $\text{PRR}=5.642$, 95% CI 2.818 - 11.298) and halo vision (4 reports; $\text{ROR}=8.205$, 95% CI 3.068 - 21.938; $\text{PRR}=8.202$, 95% CI 3.068 - 21.923) had a medium signal strength, whereas vision blurred (129 reports; $\text{ROR}=2.023$, 95% CI 1.701 - 2.407; $\text{PRR}=2.011$, 95% CI 1.694 - 2.388), blepharospasm (8 reports; $\text{ROR}=3.408$, 95% CI 1.702 - 6.823; $\text{PRR}=3.406$, 95% CI 1.702 - 6.816), and oculogyric crisis (3 reports; $\text{ROR}=2.394$, 95% CI 0.771 - 7.431; $\text{PRR}=2.393$, 95% CI 0.771 - 7.428) had a weak signal strength.

The observed frequency of eye pain ($\text{ROR}=1.51$, $\text{PRR}=1.508$, $\chi^2=5.668$) was statistically significantly higher than the expected frequency but did not meet the assessment criteria for signal intensity in this study. PTs related to eye disorders are presented in Table 2.

Table 1. Basic information on ocular adverse event reports related to vortioxetine*

Category		Number of cases (n)	Percentage (%)
Gender	Male	143	18.5
	Women	430	55.8
	Unknown	198	3.7
Age (years)	<18	11	1.4
	18-64	330	42.8
	65-84	71	9.2
	≥85	2	0.3
	Missing	357	46.3
Report year	2014	17	2.2
	2015	47	6.1
	2016	47	6.1
	2017	133	17.6
	2018	96	12.5
	2019	73	9.5
	2020	57	7.4
	2021	78	10.1
	2022	84	10.9
	2023	94	12.2
	2024	232	30.0
Reported countries	United States of America (USA)	428	55.5
	Non-USA	343	44.5

*FDA Adverse Event Reporting System (FAERS) Public Dashboard was used when preparing this table

Table 2. Signal detection results of ocular adverse event reports related to vortioxetine

PTs	Reports	ROR (95% CI)	PRR (95% CI)	χ ²
Vision blurred	129	2.023 (1.701-2.407)	2.011 (1.694-2.388)	64.857
Visual impairment	44	0.714 (0.531-0.961)	0.715 (0.533-0.961)	4.722
Eye pain	36	1.51 (1.088-2.095)	1.508 (1.088-2.09)	5.668
Eye swelling	18	1.086 (0.684-1.724)	1.085 (0.684-1.723)	0.051
Dry eye	13	0.63 (0.366-1.085)	0.63 (0.366-1.085)	2.465
Glaucoma	13	1.47 (0.853-2.531)	1.47 (0.853-2.534)	1.509
Diplopia	11	0.953 (0.528-1.722)	0.953 (0.528-1.721)	0.0
Mydriasis	11	1.701 (0.941-3.074)	1.7 (0.942-3.071)	2.509
Ocular hyperaemia	11	0.512 (0.283-0.925)	0.512 (0.284-0.925)	4.635
Eye pruritus	9	0.616 (0.32-1.183)	0.616 (0.32-1.183)	1.795
Photophobia	8	1.003 (0.502-2.007)	1.003 (0.502-2.006)	0.028
Blepharospasm	8	3.408 (1.702-6.823)	3.406 (1.702-6.816)	11.266
Angle-closure glaucoma	8	5.646 (2.818-11.311)	5.642 (2.818-11.298)	25.968
Eye disorder	8	0.502 (0.251-1.004)	0.502 (0.251-1.004)	3.469
Ocular discomfort	6	1.403 (0.63-3.126)	1.403 (0.63-3.124)	0.35
Blindness	6	0.291 (0.131-0.647)	0.291 (0.131-0.648)	9.679
Lacrimation increased	6	0.454 (0.204-1.011)	0.455 (0.204-1.012)	3.403
Cataract	6	0.244 (0.109-0.543)	0.244 (0.11-0.543)	13.329
Eye haemorrhage	6	0.935 (0.42-2.082)	0.935 (0.42-2.081)	0.001
Miosis	5	1.338 (0.557-3.217)	1.338 (0.557-3.215)	0.155
Eye irritation	5	0.205 (0.085-0.492)	0.205 (0.085-0.492)	14.664
Photopsia	5	1.709 (0.711-4.108)	1.708 (0.711-4.106)	0.844
Vitreous floaters	4	0.897 (0.336-2.39)	0.897 (0.336-2.389)	0.0
Halo vision	4	8.205 (3.068-21.94)	8.202 (3.068-21.923)	18.475
Macular degeneration	4	0.764 (0.287-2.037)	0.764 (0.287-2.036)	0.103
Blindness transient	4	1.102 (0.414-2.939)	1.102 (0.414-2.938)	0.005
Retinal haemorrhage	4	1.165 (0.437-3.107)	1.165 (0.437-3.105)	0.001
Eyelid oedema	4	0.739 (0.277-1.97)	0.739 (0.277-1.97)	0.153
Oculogyric crisis	3	2.394 (0.771-7.431)	2.393 (0.771-7.428)	1.236

PTs: preferred terms, ROR: reporting odds ratio, PRR: proportional reporting ratio; χ², Chi-Squared with Yates' correction

DISCUSSION

Drug use is based on a risk-benefit profile. As new medicines are constantly being developed, the physician must stay up to date with potential AEs (16). If all parties (ophthalmologists, psychiatrists, and patients) are aware of the adverse effects of medication, most severe and irreversible eye damage can be avoided. All psychotropic drugs can potentially cause ocular adverse effects such as eyelid and keratoconjunctival disorders, uveal diseases, cataract/pigmentary deposits in the cornea and lens, angle-closure glaucoma, and retinopathy (17). There are very few studies evaluating the ocular adverse effects of medicines. This study provides an assessment of the evidence regarding possible ocular adverse reactions thought to be caused by vortioxetine used in psychiatric treatment.

In the present study, the angle-closure glaucoma (ROR=5.646, PRR=5.642) was found to have a weak signal strength. Considering a study on the FAERS database, drug-induced glaucoma can be caused by drugs such as sulfonamides like topiramate which are well known to cause this adverse effect, as well as lesser-known drugs such as olanzapine and ranibizumab. Of all the drugs associated with angle-closure glaucoma in this study, tropicamide (18 reports; ROR=167.95, PRR=164.263) and acetazolamide (51 reports; ROR=114.782, PRR=113.088) were determined to be the statistically most significant ones (18). In a previous literature review, antidepressants were considered one of the drug classes known to increase the risk of angle-closure glaucoma (19). A study carried out on selective serotonin reuptake inhibitors (SSRIs) provided evidence of an association between various SSRI antidepressants and acute angle-closure glaucoma, particularly within the first week of starting treatment (OR=5.8, 95% CI 1.89 - 17.9) (20). There are two main risk factors for angle-closure glaucoma: anatomically narrow angles and the use of medications that affect intra-ocular pressure (21). The significantly higher incidence of vision disturbances leading to signal formation and eye pain compared to other drugs may be because it is one of the symptoms of acute angle-closure glaucoma.

Blurred vision and halo vision are visual disturbances that can be seen as drug adverse effects (22). Vortioxetine was associated with a lower risk of short-term blurred vision than placebo (OR=0.43; 95% CI 0.19-0.96; p-value=0.04) in a study of neurological adverse effects of antidepressants (23). In the present study, blurred vision (ROR=2.023, PRR=2.011) had a weak signal strength, whereas halo vision (ROR=8.205, PRR=8.202) had a medium signal strength. Considering the comparison between severe and non-severe groups for ocular adverse events associated with a group of drugs and blurred vision was found to be significantly higher in the severe patient group (24). As determined in this study, vision changes that occur as a drug adverse effect can be considered as a factor in determining the course of the disease.

Blepharospasm is one of the possible/rare adverse effects of antidepressants (25). In the present blepharospasm had 8 reports (ROR=3.408, PRR=3.406) and a weak signal strength. A similar FAERS disproportionality analysis study reported 172 reports for blepharospasm in adverse events of atypical antipsychotics associated with ocular neuromuscular disorders, and 54 of them reported strong signal for aripiprazole (26). In a case report, discontinuing psychotropic medication ameliorated blepharospasm in 67% of patients (27). As can be seen in these studies, blepharospasm caused by the drugs used in psychiatry and the recovery of blepharospasm upon discontinuation of those drugs indicate the importance of evaluating adverse events in patients follow-up.

Especially the use of antipsychotic drugs (e.g. neuroleptic drugs) is a risk factor for oculogyric crisis. Therefore, it is important to determine the causative drug for the diagnosis of drug-induced oculogyric crisis (28). In the present study, the oculogyric crisis had 3 reports (ROR=2.394, PRR=2.393) and a weak signal strength. In a FAERS database study comparable the present study, cariprazine used in the treatment of schizophrenia was found to have a high risk of causing possible oculogyric crisis (12 reports; ROR=45.95, PRR=45.88) (29).

In the package insert of for vortioxetine, the manufacturer only mentioned angle-closure glaucoma as an ocular adverse event (30). In November 2017, there were additions and/or revisions to the product information of vortioxetine regarding angle-closure glaucoma. In other words, this change was included in the product information approximately 4 years after the product was released (31). AEs associated with blurred vision, blepharospasm, halo vision, and oculogyric crisis are not explicitly mentioned in the product information, indicating the presence of novel ADE signals. In late 2013, vortioxetine was introduced to the market, and it was determined in the present study carried out 10 years after the introduction to the market that there may be various possible adverse effects on eyes.

Study Limitations

This research has several limitations. The study was limited to AEs in which vortioxetine was the primary suspect. Information on concomitant drug use, reporter type, drug indication, and outcome were not included in this study because of lack of data or inaccessibility. A weakness of the study is that in the spontaneous reports in the FAERS database, some case reporters were not healthcare professionals and self-identified the primary suspected drugs. Due to the nature of the study, a causal relationship between AEs and drugs could not be established. OpenVigil lacks information on the effect of comorbidity, dose and duration of use on the occurrence of AEs. Despite these limitations inherent in clinical trials, spontaneous reporting systems are valuable because they allow large amounts of data to be used for the safety

assessment of suspected AEs. It is recommended that future prospective studies be conducted to validate the findings of this investigation.

CONCLUSION

Patients are exposed to new and sometimes unexpected toxicities when using new-generation antidepressants prescribed by psychiatrists. Rare ocular adverse events may develop during antidepressant treatment. Ophthalmologists should be aware of such ophthalmic adverse events and their potential severity for better management and diagnosis, both in daily practice and clinical trials.

In the present study, FAERS disproportionality analysis was performed to investigate vortioxetine-related AEs and to identify possible ocular AE signals. The results achieved in this study provide an important reference point to ensure the safe use of vortioxetine in the treatment of depression. The available evidence obtained in this study suggests that initial and follow-up ophthalmic consultations may be necessary for patients receiving vortioxetine due to the risk of blepharospasm, blurred vision, angle-closure glaucoma, oculogyric crisis, halo vision, etc. Moreover, these results highlight the importance of ongoing post-marketing surveillance to detect potential new ADEs.

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REFERENCES

- Bang-Andersen B, Ruhland T, Jørgensen M, et al. Discovery of 1- [2- (2,4-Dimethylphenylsulfanyl) phenyl] piperazine (Lu AA21004): a novel multimodal compound for the treatment of major depressive disorder. *J Med Chem*. 2011;54:3206-21.
- Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet*. 2018;391:1357-66.
- Lam RW, Kennedy SH, Adams C, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults: Réseau canadien pour les traitements de l'humeur et de l'anxiété (CANMAT) 2023: Mise à jour des lignes directrices cliniques pour la prise en charge du trouble dépressif majeur chez les adultes. *Can J Psychiatry*. 2024;69:641-87.
- Tran BX, Ha GH, Vu GT, et al. Indices of change, expectations, and popularity of biological treatments for major depressive disorder between 1988 and 2017: a scientometric analysis. *Int J Environ Res Public Health*. 2019;16:2255.
- Salagre E, Grande I, Solé B, et al. Vortioxetina: una nueva alternativa en el trastorno depresivo mayor. *Rev Psiquiatr Salud Ment*. 2018;11:48-59.
- Carvalho AF, Sharma MS, Brunoni AR, et al. The safety, tolerability and risks associated with the use of newer generation antidepressant drugs: a critical review of the literature. *Psychother Psychosom*. 2016;85:270-88.
- Kommu S, Carter C, Whitfield P. Adverse drug reactions. 2024 Jan 10. In: *StatPearls* [Internet].
- Wu SN, Huang C, Wang YQ, et al. Adverse events of topical ocular prostaglandin medications for glaucoma treatment: a pharmacovigilance study based on the FAERS database. *Ther Adv Drug Saf*. 2024;15:20420986241285930.
- Food and Drug Administration. FDA Adverse Event Reporting System (FAERS) Public Dashboard. <https://www.fda.gov/drugs/fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard> access date 06.01.2025.
- Salvo F, Raschi E, Moretti U, et al. Pharmacological prioritisation of signals of disproportionate reporting: proposal of an algorithm and pilot evaluation. *Eur J Clin Pharmacol*. 2014;70:617-25.
- Davis SE, Zabotka L, Desai RJ, et al. Use of electronic health record data for drug safety signal identification: a scoping review. *Drug Saf*. 2023;46:725-42.
- Evans SJW, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. *Pharmacoepidemiol Drug Saf*. 2001;10:483-6.
- van Puijenbroek EP, Bate A, Leufkens HGM, et al. A comparison of measures of disproportionality for signal detection in spontaneous reporting systems for adverse drug reactions. *Pharmacoepidemiol Drug Saf*. 2002;11:3-10.
- Böhm R, von Hehn L, Herdegen T, et al. OpenVigil FDA – inspection of U.S. American adverse drug events pharmacovigilance data and novel clinical applications. *PLoS One*. 2016;11:e0157753.
- Pan Y, Wang Y, Zheng Y, et al. A disproportionality analysis of FDA adverse event reporting system (FAERS) events for ticagrelor. *Front Pharmacol*. 2024;15:1251961.
- Pula JH, Kao AM, Kattah JC. Neuro-ophthalmologic side-effects of systemic medications. *Curr Opin Ophthalmol*. 2013;24:540-9.
- Richa S, Yazbek JC. Ocular adverse effects of common psychotropic agents. *CNS Drugs*. 2010;24:501-26.
- Aftab OM, Khan H, Khouri AS. Blind spots in therapy: unveiling drug-induced angle-closure glaucoma through a national analysis. *Ophthalmol Glaucoma*. 2024;7:485-90.
- Wu A, Khawaja AP, Pasquale LR, Stein JD. A review of systemic medications that may modulate the risk of glaucoma. *Eye (Lond)*. 2020;34:12-28.
- Kirkham J, Seitz D. Evidence of ocular side effects of SSRIs and new warnings. *Evidence Based Mental Health*. 2017;20:27.
- Tripathi RC, Tripathi BJ, Haggerty C. Drug-induced glaucomas. *Drug Saf*. 2003;26:749-67.

22. Huillard O, Bakalian S, Levy C, et al. Ocular adverse events of molecularly targeted agents approved in solid tumours: a systematic review. *Eur J Cancer*. 2014;50:638-48.
23. Zhou Q, Li X, Yang D, et al. A comprehensive review and meta-analysis of neurological side effects related to second-generation antidepressants in individuals with major depressive disorder. *Behavioural Brain Research*. 2023;447:114431.
24. Mao K, Chen P, Sun H, et al. Ocular adverse events associated with antibody-drug conjugates in oncology: a pharmacovigilance study based on FDA adverse event reporting system (FAERS). *Front Pharmacol*. 2024;15:1425617.
25. Syed MF, Rehmani A, Yang M. Ocular side effects of common systemic medications and systemic side effects of ocular medications. *Med Clin North Am*. 2021;105:425-44.
26. Mu C, Chen L. Characteristics of eye disorders induced by atypical antipsychotics: a real-world study from 2016 to 2022 based on food and drug administration adverse event reporting system. *Front Psychiatry*. 2024;15:1322939.
27. Yuko Emoto. Twelve cases of drug-induced blepharospasm improved within 2 months of psychotropic cessation. *Drug Healthc Patient Saf*. 2011;3:9-14.
28. Mahal P, Suthar N, Nebhinani N. Spotlight on oculoerythric crisis: a review. *Indian J Psychol Med*. 2021;43:5-9.
29. Zhu H, Qu Y, Du Z, et al. Mining and analysis of adverse event signals of Cariprazine based on the real-world data of FAERS database. *J Affect Disord*. 2024;347:45-50.
30. U. S. Food and Drug Administration (FDA). Takeda Pharmaceuticals America, Inc. 2021 Trintellix® Full Prescription Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/204447s021s022lbl.pdf access date 05.01.2025.
31. Food and Drug Administration (FDA). Safety-related Labeling Changes Approved by FDA Center for Drug Evaluation and Research (CDER). <https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges/index.cfm?event=searchdetail.page&DrugNameID=381> access date 05.01.2025.



COVID-19 Anxiety and Eating Behaviors Among Patients Attending the Emergency Department: A Cross-Sectional Study

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Abstract

Aim: This study aimed to examine the relationship between COVID-19 anxiety and food cravings among adults and to identify the factors influencing this relationship.

Material and Method: This descriptive and cross-sectional study collected data from 265 individuals who agreed to participate between November 2021 and February 2022. Data collection tools included the Sociodemographic Data Form, the COVID-19 Anxiety Scale (CAS), and the Food Craving Questionnaire (FCQT-R). Analyses included means, standard deviations, percentages, independent t-tests for comparisons between groups, one-way ANOVA for comparisons among more than two groups, Pearson correlation analysis to determine relationships among scales, and linear regression analysis.

Results: The mean COVID-19 Anxiety Scale score was 3.63 ± 3.06 , while the mean Food Craving Questionnaire score was 37.64 ± 10.62 . A positive, moderate, and significant correlation was found between COVID-19 anxiety and food craving levels ($r = .368$, $p < .001$). Additionally, COVID-19 anxiety accounted for 12.8% of the variance in food craving levels ($R^2 = 0.128$, $F = 38.43$, $p < .001$).

Conclusion: The study revealed that certain sociodemographic characteristics, including age, marital status, and education level, significantly influenced COVID-19 anxiety and food cravings, and an increase in COVID-19 anxiety was associated with an increase in food cravings.

Keywords: COVID-19 anxiety, food cravings, emergency department

INTRODUCTION

The COVID-19 pandemic has had significant and enduring effects on health, economy, and social life globally since 2020. This process has substantially impacted individuals' mental health, leading to notable increases in anxiety and stress levels (1). Studies have shown that anxiety and depression rates worldwide have increased by more than 25% since the onset of the pandemic, highlighting the significant psychological burden imposed on individuals during this challenging period (2). This increase highlights the psychological burden imposed on individuals during this challenging period.

Anxiety is a complex condition that profoundly affects individuals' daily lives, thoughts, and behaviors (3). It is

particularly detrimental to mental health in environments dominated by uncertainty and fear, such as during a pandemic (4). Research indicates that the causes of anxiety experienced by individuals post-COVID-19 include fear of contracting the virus, concerns about losing loved ones, difficulties accessing healthcare services, financial struggles, and job losses, all of which have negatively impacted individuals' mental health. Quarantine measures and the loneliness caused by social isolation have also been identified as major contributors to heightened anxiety levels (5). The effects of the COVID-19 pandemic have been experienced differently across all age groups. Social determinants such as quarantine, social isolation, and income loss have significantly increased anxiety levels in every age group (6). Studies have found that adolescents

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faced heightened anxiety due to uncertainty about their future during the pandemic (7). A global study revealed that the prevalence of depression and anxiety symptoms during COVID-19 doubled among children and adolescents compared to pre-pandemic estimates (8). Meanwhile, in older age groups, factors such as the increased risk of illness and the presence of chronic health conditions were identified as significant contributors to COVID-19-related anxiety (9). It has been reported that approximately 65% of older adults experienced an increase in anxiety levels during the pandemic (10).

During the pandemic, individuals sought various coping mechanisms to manage increased stress and uncertainty. Among these, eating behaviors have often become a tool for stress management, with unhealthy coping strategies such as emotional eating emerging prominently. The literature suggests that during periods of anxiety, the body requires more calories to meet its energy needs, which is considered a factor that triggers food cravings (10-13). Stress- and anxiety-induced eating behaviors may provide temporary relief but can have long-term adverse effects on physical and psychological health. While anxiety triggers overeating or unhealthy eating habits in some individuals, it can lead to loss of appetite and reluctance to eat in others (14). Factors such as personality traits, emotional states, anxiety levels, general health status, stress-coping skills, and psychological resilience play a determining role in this variability (15-17). In this context, examining the psychological and physiological effects of COVID-19 anxiety on food cravings is an important subject.

The uncertainty created by the pandemic, prolonged quarantine periods, social isolation, and changes in social determinants of health, such as income and job losses, have also led to significant alterations in eating attitudes (18-20). Understanding the relationship between anxiety and eating behaviors is essential for protecting mental health and maintaining healthy eating habits, especially during crisis periods like pandemics. Studies in the literature generally evaluate pandemic-related anxiety using tools such as the Beck Anxiety Inventory, which measure general anxiety. However, studies specific to COVID-19 anxiety have primarily focused on concepts like hopelessness, sleep problems, and psychological resilience (21-26). Furthermore, existing literature has identified that COVID-19 anxiety triggers emotional eating (27,28). However, studies specifically examining its effects on food cravings remain scarce. Therefore, this study aims to investigate the relationship between COVID-19 anxiety and food cravings in adults, as well as the factors influencing this relationship.

Research Questions

- What are the levels of COVID-19 anxiety and food cravings among individuals?
- How do individuals' sociodemographic characteristics affect COVID-19 anxiety levels and food cravings?
- Is COVID-19 anxiety a predictor of food cravings?

MATERIAL AND METHOD

Study Type

This study was designed as a descriptive, cross-sectional research project.

Study Setting

The research was conducted between November 2021 and February 2022 in the emergency department of a district state hospital. Data were collected from individuals attending the outpatient clinic.

Population and Sample

The study sample was determined based on a previous study by Dalmaz and Şahin, using the G-Power 3.1.9.2 software. With a confidence interval of 80%, a sampling error of $\pm 5\%$, and an effect size of 0.35, the required sample size was calculated as 208 participants. However, the study was completed with 265 patients. The sample consisted of patients directed to the "green zone" by the admissions unit and those who remained in this zone after examination. Relevant scales and forms were administered in an unused clinic room after the completion of discharge procedures.

Data Collection Tool

The Sociodemographic Data Form, consisting of 9 questions, was used to collect demographic information about individuals, the COVID-19 Anxiety Scale (CAS) was applied to assess COVID-19-related anxiety, and the Food Craving Questionnaire (FCQT-R) was used to determine food cravings.

Sociodemographic Data Form: Created by the researchers, this form collected information on participants' age, gender, education level, marital status, parental status, employment status, and history of COVID-19 infection.

COVID-19 Anxiety Scale (CAS): Developed by Lee to measure anxiety levels related to COVID-19 during the pandemic, the scale's Turkish validity and reliability were established by Biçer et al. (29). The scale consists of 5 items scored on a scale from 0 ("never") to 4 ("almost every day"), with total scores ranging from 0 to 20. Higher scores indicate greater levels of COVID-19-related anxiety. The scale does not include any subscales. The Cronbach's alpha reliability coefficient was reported as 0.83 in the Turkish adaptation and calculated as 0.79 in this study.

Food Craving Questionnaire (FCQT-R): Originally developed by Cepeda-Benito et al. (2000) and revised into a short form (15 items) by Meule et al. (2014), the Turkish validity and reliability study was conducted by Traş and Gökçen (2021) (30). The 6-point Likert scale ranges from 15 to 90, with higher scores indicating higher food cravings. The scale consists of two subscales; preoccupation with eating thoughts and loss of control over eating. The Cronbach's alpha reliability coefficient was reported as 0.94 in the Turkish version and calculated as 0.87 in this study.

Data Collection

During data collection, pandemic-related guidelines were strictly followed, and factors that could compromise the reliability of the study were identified. Exclusion criteria (e.g., patients admitted with a COVID-19 pre-diagnosis, those with mental retardation or acute psychosis) were determined in collaboration with the unit's chief physician. After providing verbal information about the study, verbal consent was obtained from participants, and the scales were administered sequentially by the researcher. Due to restrictions on research permissions during the pandemic and to minimize risks to patients' health, the study was conducted only in the institution where one of the researchers was employed.

Data Analysis

The dependent variables of the study were COVID-19 anxiety and food craving levels, while independent variables included sociodemographic data (age, gender, education level, marital status, parental status, employment status, and history of COVID-19 infection). Data was processed and analyzed using IBM SPSS Statistics 23. Descriptive statistics included frequency (n) and percentage (%) for categorical variables and mean±standard deviation for continuous variables. Normality of continuous data was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For group comparisons, independent samples t-tests and one-way ANOVA were used for normally distributed data. Pearson correlation analysis evaluated relationships between scales, and multiple linear regression was used to assess predictors. Results were interpreted at a 95% confidence level with a significance threshold of $p < 0.05$.

Ethical Considerations

Prior to the study, ethical approval was obtained from the Ege University Medical Research Ethics Committee (dated 29.07.2021, Decision No: 21-7.1T/13), the Scientific Research Platform of the Ministry of Health (dated 15.01.2021, Decision No: T02-26-58), and the institution where the research was conducted. The study was carried out in accordance with ethical principles for research and publication.

RESULTS

It was determined that 25.7% of the individuals participating in the study were aged 55 and above, 50.9% were female, 71.7% were married, 43% had primary school education, 61.1% lived with their families, 61.9% were employed, 53.6% had children and 60% had previously contracted COVID-19 (Table 1).

Table 1. Socio-demographic characteristics of the participants (n=265)

Socio-demographic characteristics	n	%
Age		
24≥	31	11.7
25-34	53	20.0
35-44	57	21.5
45-54	56	21.1
55≤	68	25.7
Gender		
Male	130	49.1
Female	135	50.9
Marital status		
Married	190	71.7
Single	65	28.3
Education status		
Literate	47	17.8
Primary education	114	43.0
High school	71	26.8
University	33	12.5
With whom they live		
Single	72	27.2
Family	162	61.1
Roommate	31	11.7
Employment status		
Working	164	61.9
Not working	101	38.1
Parental status		
Yes	142	53.6
No	123	46.4
History of COVID-19		
Yes	105	40.0
No	159	60.0
Presence of chronic disease		
Yes	86	32.5
No	179	67.5
TOTAL	265	100

The mean scores for participants' CAS and FCQT-R are presented in Table 2. Accordingly, the mean score for CAS is 3.63 ± 3.06 , the mean score for FCQT-R is 37.64 ± 10.62 , the mean score for the "Preoccupation with Thoughts of Eating" subscale is 23.18 ± 7.89 , and the mean score for another "Preoccupation with Thoughts of Eating" subscale is 19.12 ± 7.12 (Table 2).

Table 2. Participants' mean scores for the "COVID-19 Anxiety Scale" and "Food Craving Scale" (n=265)

Scales	Points available	Score received	$\bar{X} \pm SD$
COVID-19 Anxiety Scale (CAS)	0-20	1-14	3.63 ± 3.06
Food Craving Questionnaire (FCQT-R)	0-90	6-69	37.64 ± 10.62
Preoccupation with eating thoughts	0-54	2-39	23.18 ± 7.89
Loss of control over eating	0-36	1-31	19.12 ± 7.12

$\bar{X}$ =mean, SD=standart deviation

The variations in the mean scores of CAS and FCQT-R based on socio-demographic variables are presented in Table 3. Accordingly, it was determined that the variables of age, education, and the presence of chronic diseases created a significant difference among groups for CAS. Post-hoc multiple comparisons conducted to identify the source of this difference revealed that CAS scores increased across all groups as age increased, whereas CAS scores statistically decreased across all groups as education level increased ($p < .05$).

When examining participants' FCQT-R scores, it was found that age and marital status significantly differed among groups. Post-hoc multiple comparisons conducted to determine the source of this difference for the age variable showed that participants aged 24 and below had statistically higher FCQT-R scores compared to participants in other age groups. Regarding marital status, single participants were observed to have higher FCQT-R scores compared to married participants ($p < .05$) (Table 3).

Table 3. Mean Scores of the "COVID-19 Anxiety Scale" and "Food Craving Scale" according to participants' socio-demographic characteristics (n=185)

Socio-demographic characteristics	COVID-19 Anxiety Scale	Test/p	Food Craving Questionnaire	Test/p
Age				
24≥ ^a	1.51±3.25	F=15.53 p=.001*	47.23±16.52a	F=2.52 p=.042*
25-34 ^b	1.69±3.17		38.3±11.58b	
35-44 ^c	3.32±2.63		36.75±7.81b	
45-54 ^d	3.51±2.02		37.37±10.03b	
55≤ ^e	3.83±2.79		37.48±12.03b	
Gender				
Male	3.32±3.13	t=-.76	37.21±10.24	t=-1.58
Woman	3.58±2.97	p=.442	39.34±11.63	p=.114
Marital status				
Married	3.47±2.84	t=1.94	37.45±10.1	t=-2.34
Single	2.54±3.64	p=.53	41.47±13.28	p=.02*
Education status				
Literate	4.19±2.78	F=7.07 p=.001*	40.14±11.78	F=1.02 p=.382
Primary education	4.03±2.77		38.71±11.05	
High school	2.74±3.04		37.26±11.09	
University	1.84±3.51		36.42±9.33	
Employment status				
Working	3.43±3.19	t=-.105	38.78±11.41	t=1.03
Not working	3.47±2.77	p=.916	37.36±10.18	p=.318
Parental status				
Yes	3.57±3.14	t=.729	38.28±10.61	t=-.006
No	3.29±2.95	p=.466	37.75±11.42	p=.876
History of COVID-19				
Yes	3.53±3.02	t=.404	38.18±11.52	t=-.358
No	3.37±3.05	p=.685	39.24±10.4	p=.721
Presence of chronic disease				
Yes	3.22±3.13	t=2.45	38.18±11.52	t=-.358
No	2.25±3.63	p=.032	39.24±10.4	p=.721
With whom they live				
Single	3.79±3.14	F=1.72 p=.181	38.33±11.1	F=.499 p=.608
Family	3.45±3.01		37.93±10.83	
Roommate	3.58±2.93		40.1±11.85	

F: One-Way Analysis of Variance (ANOVA), t: T-Test, *For data sets with $n < 30$, normality was tested using the Shapiro-Wilk test, $a < b < c < d$; according to the Bonferroni test, there is a statistically significant difference for CAS, $a > b$ according to the Bonferroni test, there is a statistically significant difference for FCQT-R * $p < .05$

“The results of the Pearson correlation analysis between the COVID-19 Anxiety Scale and the Food Craving Scale are presented in Table 4. Accordingly, a positive, significant, and moderate-level correlation was found between the level of COVID-19 anxiety and food craving ($r=.368$, $p<.001$). Additionally, significant positive correlations were identified with the subscales: preoccupation with food ($r=.315$, $p<.01$), loss of control ($r=.342$, $p<.01$), and emotional craving ($r=.389$, $p<.001$) (Table 4).

Table 4. The relationship between COVID-19 anxiety and food craving (Pearson correlation analysis) (n=185)		
Variable		CAS
FCQT-R 1		
Preoccupation with	r	.368
Eating thoughts	p	.000*
FCQT-R 2		
Loss of control	r	.292
Over eating	p	.000*
FCQT-R total	r	.357
	p	.000*
CAS total	r	1
	p	.000*
*CAS: COVID-19 Anxiety Scale, FCQT-R: Food Craving Questionnaire** The correlation is significant at the .001 level		

COVID-19 anxiety significantly predicts food craving at an advanced level ($\beta=.357$, $t=6.2$, $p<.001$). Additionally, COVID-19 anxiety explains a significant portion of the variance in food craving levels (12.8%) ($R^2=.128$, $F=38.43$, $p<.001$) (Table 5).

Table 5. Predictive effect of COVID-19 anxiety on food craving (Results of simple linear regression analysis) (n=185)							
Variable	N	B	SS	β	t	F	p
CAS*	2655	1.25	.203	.357	6.2	38.43	.000**
R ² =0.128							
*CAS: COVID-19 Anxiety Scale, **p<.001, dependent variable: Eating Desire Scale							

DISCUSSION

The pandemic has caused significant health, economic, and social uncertainties globally, resulting in notable changes in individuals' mental health. During this period, marked by heightened concerns about health, social isolation, and uncertainty, eating behavior has been framed as an emotional response directly associated with anxiety and uncertainty. In this context, the present study primarily examined the variability of COVID-19 anxiety and food cravings based on socio-demographic characteristics and subsequently investigated the relationship between COVID-19 anxiety and eating behaviors.

Among socio-demographic factors, variables such as age, education level, and the presence of chronic diseases were found to create significant differences in COVID-19 anxiety levels across groups. Older individuals, those

with lower education levels, and those with chronic illnesses were found to have higher levels of COVID-19 anxiety. Notably, age significantly influenced participants' COVID-19 anxiety levels ($p<.001$). As age increased, anxiety levels also rose, indicating that older individuals experienced greater anxiety concerning the pandemic. Considering that advanced age and chronic illnesses are established risk factors for COVID-19, these findings align with existing literature (2). Additionally, education level significantly affected participants' anxiety levels. Individuals with lower education levels reported higher anxiety. It can be suggested that educated individuals, with greater access to information and awareness about health precautions during the pandemic, are better equipped to manage anxiety. This finding aligns with previous studies emphasizing the critical role of education in managing stress, fear, and anxiety (31-33).

When examining the variability of food cravings based on socio-demographic factors, it was found that individuals under the age of 24 and single participants had higher food cravings. This finding corresponds with existing literature, which suggests that loneliness and emotional stress can trigger eating behaviors. Single individuals may lack family-based social support, making it more challenging to cope with stress and potentially leading to behaviors such as emotional eating (34,35). Young individuals, particularly during the pandemic, may be more inclined toward emotional eating as a means of coping with uncertainty and anxiety. Factors such as being more influenced by social media and peer pressure could exacerbate stress, contributing to emotional eating behaviors (36,37).

Regarding the relationship between COVID-19 anxiety and food cravings, which was one of the primary aims of this study, a moderate positive correlation was identified between the two variables. Specifically, as COVID-19 anxiety increased, food cravings also increased. Furthermore, COVID-19 anxiety was found to have a significant predictive effect on food cravings, explaining 12.8% of the variance ($R^2=.128$, $F=38.43$, $p<.001$). This relationship highlights that food cravings, often considered an ineffective coping strategy, became more prominent during the pandemic as individuals struggled to manage stress and anxiety. Individuals who faced difficulties coping with the uncertainty and fear associated with the pandemic may have turned to overeating or emotional eating as a coping mechanism. Existing literature supports the notion that COVID-19 anxiety influences food cravings. Factors such as increased time spent at home, decreased physical activity levels, and limited social support during the pandemic may have led individuals to turn to eating behaviors as a way to suppress or cope with negative emotions (18). A meta-analysis conducted by Chang et al. revealed significant changes in body weight and body mass index (BMI) among school-aged children and adolescents during quarantine periods (38). Similarly, another meta-analysis by Anderson et al. identified significant increases in weight gain and obesity prevalence among both children and adults during the COVID-19 pandemic (39). Therefore, it can be argued that the findings of this study are consistent with those of

related meta-analyses. Importantly, it should be noted that while eating behaviors or thoughts may provide temporary relief in the short term, they could further harm individuals' emotional well-being in the long term. The findings of this study highlight the necessity of guiding individuals toward more functional coping strategies during stressful processes like the pandemic.

Limitations and Strengths

This study has some limitations that should be considered. The cross-sectional design prevents establishing causal relationships between COVID-19 anxiety and food cravings. Self-reported data may also introduce biases, such as overreporting or underreporting behaviors. Additionally, the sample may not fully represent all demographics, limiting the generalizability of findings. Cultural and regional differences in pandemic experiences, which could influence anxiety and eating behaviors, were not specifically addressed. Future studies should aim to overcome these limitations for a more comprehensive understanding.

CONCLUSION

The findings of the study indicate that COVID-19 anxiety increases individuals' food cravings, which emerged as an ineffective method of coping with stress and uncertainty. Additionally, socio-demographic factors were found to significantly affect both COVID-19 anxiety and food cravings. Specifically, age, education level, and the presence of chronic diseases significantly influenced anxiety levels, while younger individuals and single participants were found to have higher food cravings. These findings contribute to our understanding of the relationship between emotional and psychological well-being and eating behaviors during societal crises like the pandemic. Based on the study findings, healthcare providers are encouraged to implement strategies that address the mental health challenges heightened by the pandemic. Programs focusing on mindfulness-based stress management and emotion regulation can help individuals develop healthier coping mechanisms. Additionally, psychosocial support services should be tailored to high-risk groups, including older adults, individuals with chronic illnesses, and those with lower education levels, to mitigate anxiety and promote resilience. Training healthcare providers in managing pandemic-related mental health issues and promoting community-based interventions, such as awareness campaigns and nutritional counseling, can further support mental well-being. Strengthening health policies to improve access to mental health services and adopting a multidisciplinary approach are critical steps to addressing the psychological and behavioral impacts of the pandemic effectively.

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REFERENCES

1. Manchia M, Gathier AW, Yapici-Eser H, et al. The impact of the prolonged COVID-19 pandemic on stress resilience and mental health: a critical review across waves. *Eur Neuropsychopharmacol.* 2022;55:22-83.
2. Jordan RE, Adab P, Cheng KK. COVID-19: risk factors for severe disease and death. *BMJ.* 2020;368:m1198.
3. Craske MG, Rauch SL, Ursano R, et al. What is an anxiety disorder? *Focus (Am Psychiatr Publ).* 2011;9:369-88.
4. Pfefferbaum B, North CS. Mental Health and the COVID-19 Pandemic. *N Engl J Med.* 2020;383:510-2.
5. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet.* 2020;395:912-20.
6. Koçak O, Koçak ÖE, Younis MZ. The psychological consequences of COVID-19 fear and the moderator effects of individuals' underlying illness and witnessing infected friends and family. *Int J Environ Res Public Health.* 2021;18:1836.
7. Kaplan V, Kürümlüoğlu R, Bütün B. The effect of the quarantine process due to the COVID-19 pandemic on adolescents' future expectations and anxiety levels. *Journal of Child and Development.* 2021;4:12-23.
8. Racine N, McArthur BA, Cooke JE, et al. Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: a meta-analysis. *JAMA Pediatr.* 2021;175:1142-50.
9. Qiu J, Shen B, Zhao M, et al. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations. *Gen Psychiatr.* 2020;33:e100213. Erratum in: *Gen Psychiatr.* 2020;33:e100213corr1.
10. Gosselin P, Castonguay C, Goyette M, et al. Anxiety among older adults during the COVID-19 pandemic. *J Anxiety Disord.* 2022;92:102633.
11. Nutley SK, Falise AM, Henderson R, et al. Impact of the COVID-19 pandemic on disordered eating behavior: qualitative analysis of social media posts. *JMIR Ment Health.* 2021;8:e26011.
12. van der Kooij MA. The impact of chronic stress on energy metabolism. *Mol Cell Neurosci.* 2020;107:103525.
13. Block JP, He Y, Zaslavsky AM, et al. Psychosocial stress and change in weight among US adults. *Am J Epidemiol.* 2009;170:181-92.
14. Chankasingh K, Booth A, Albert A, et al. Coping during the COVID-19 pandemic: a mixed methods approach to understand how social factors influence coping ability. *Heliyon.* 2022;8:e10904.
15. Tınmazoğlu E, Doksat NG. Relationship between emotional eating and big five personality characteristics and mood disorder symptoms. *Manas Journal of Social Studies.* 2020;9:34-46.
16. Robert M, Shankland R, Bellicha A, et al. Associations between resilience and food intake are mediated by emotional eating in the NutriNet-Santé Study. *J Nutr.* 2022;152:1907-15.

17. Reents J, Seidel AK, Wiesner CD, Pedersen A. The effect of hunger and satiety on mood-related food craving. *Front Psychol.* 2020;11:568908.
18. Garipoğlu G, Bozar N. Changes in dietary habits of individuals in social isolation during the COVID-19 pandemic. *Pearson Journal.* 2020;6:100-13.
19. Cipolla C, Curatola A, Ferretti S, et al. Eating habits and lifestyle in children with obesity during the COVID-19 lockdown: a survey in an Italian center. *Acta Biomed.* 2021;92:e2021196.
20. O'Connor S, Bélanger-Gravel A, iCARE study team. Social determinants of long-term reported changes in physical activity and healthy eating during the COVID-19 pandemic in Canada: Multiple cross-sectional surveys analysis from the iCARE study. *Appl Physiol Nutr Metab.* 2023;49:179-89.
21. Özmen S, Ocakdan UB. Examination of the effect of death anxiety level of nurses on psychological resilience during the COVID-19 pandemic. *Süleyman Demirel University Visionary Journal.* 2022;13:1224-36.
22. İri NiÖ, Korkmaz F. The Effect of individuals' coronavirus anxiety levels on their psychological resilience. *GUJHS.* 2021;10:769-71.
23. Yeşilyaprak T, Özsoy H, Korkmaz FD. Determining the relationship between anxiety, psychological resilience and perceived social support levels of surgical nurses in the COVID-19 period. *Hemşirelik Bilimi Dergisi.* 2023;6:18-25.
24. Yılmaz Z, İstemihan F, Arayıcı S, et al. The investigation of anxiety and hopelessness among individuals throughout COVID-19 outbreak. *Kriz Dergisi.* 2020;28:135-50.
25. Şahin B, Önal BS, Hoşoğlu E. Anxiety levels and sleep disturbance in children of healthcare workers with COVID-19. *Türk J Child Adolesc Ment Health.* 2021;28:41-8.
26. Erdoğan Y, Koçoğlu F, Sevim C. An investigation of the psychosocial and demographic determinants of anxiety and hopelessness during COVID-19 pandemic. *Turkish J Clin Psy.* 2020;23:24-37.
27. Bermanian M, Mæland S, Blomhoff R, et al. Emotional eating in relation to worries and psychological distress amid the COVID-19 pandemic: A population-based survey on adults in Norway. *Int J Environ Res Public Health.* 2021;18:130.
28. Güner Ö, Aydın A. Determining the relationship between anxiety levels, stress coping styles, and emotional eating of women in the COVID-19 pandemic. *Arch Psychiatr Nurs.* 2022;41:241-7.
29. Biçer İ, Çakmak C, Demir H, Kurt ME. Coronavirus Anxiety Scale: Turkish validity and reliability study. *Anatol Clin.* 2020;25:216-25.
30. Traş Z, Gökçen G. Adaptation of the short version of the Food Cravings Questionnaire—trait to Turkish culture: a study of validity and reliability. *Ahmet Keleşoğlu Faculty of Education Journal.* 2021;3:200-15.
31. Türk A, Şahan H, Engin E. The relationship between fear of COVID-19 and satisfaction with life in patients admitted to the emergency department. *EHD.* 2023;16:447-59.
32. Joannès C, Redmond NM, Kelly-Irving M, et al. The level of education is associated with an anxiety-depressive state among men and women—findings from France during the first quarter of the COVID-19 pandemic. *BMC Public Health.* 2023;23:1405.
33. Ostberg V, Åhlén J, Brodin Låftman S. Educational attainment and symptoms of anxiety and depression in young adulthood. *Eur J Public Health.* 2023;33:ckad160-1578.
34. Huang Y, Su X, Si M, et al. The impacts of coping style and perceived social support on the mental health of undergraduate students during the early phases of the COVID-19 pandemic in China: A multicenter survey. *BMC Psychiatry.* 2021;21:530.
35. Yıldız K, Dirik D. The role of perceived self-efficacy in the relationship between perceived social support and ways of coping. *SPORMETRE.* 2019;17:132-44.
36. Suhag K, Rauniyar S. Social media effects regarding eating disorders and body image in young adolescents. *Cureus.* 2024;16:e58674.
37. Filippone L, Shankland R, Hallez Q. The relationships between social media exposure, food craving, cognitive impulsivity, and cognitive restraint. *J Eat Disord.* 2022;10:184.
38. Chang TH, Chen YC, Chen WY, et al. Weight gain associated with COVID-19 lockdown in children and adolescents: a systematic review and meta-analysis. *Nutrients.* 2021;13:3668.
39. Anderson LN, Yoshida-Montezuma Y, Dewart N, et al. Obesity and weight change during the COVID-19 pandemic in children and adults: A systematic review and meta-analysis. *Obes Rev.* 2023;24:e13550.



Relationship Between *Helicobacter pylori* and Blood Groups

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Abstract

Aim: It was aimed to see the relationship between *Helicobacter pylori* (*H. pylori*), a bacterium that settles in various parts of the stomach and duodenum, and blood groups and its distribution among blood groups.

Material and Method: A retrospective analysis was conducted on 285 patients who underwent *H. pylori* testing between 2020 and 2022. Data on patients' age, sex, *H. pylori* test results, and blood types were collected. Student's t-test was used for age comparisons and chi-square was used for gender distribution. Blood group distributions were expressed as percentages.

Results: In the study, it was determined that 70% of *H. pylori* positive patients were female and 30% were male. The *H. pylori* negative individuals were reported as 21.4% male and 78.6% female and no significant difference was found in terms of gender. When age groups were analysed, *H. pylori* positive patients were found to be 53.5±15.8 years old and negative patients were found to be 52.4±15.8 years old and no significance was found ($p=0.57$). Among the patients with *H. pylori*, 10.9% were in group AB, 13.6% in group B, 37.3% in group O and 38.2% in group A. Furthermore, there is no significant distinction between negative patients and the opposite groups ($p=0.242$).

Conclusion: The findings suggest that *H. pylori* infection is more frequently observed in individuals with blood groups A and O, indicating that these blood types may be associated with a higher susceptibility to the infection.

Keywords: *H. pylori*, blood groups, blood group A, blood group O

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a notable stomach pathogen, characterized by its S-shaped, short spiral, or gull-wing morphology. It is a motile, non-spore-forming, capsule-free, microaerophilic, Gram-negative bacillus. Scientific studies have proven that *H. pylori* infection is associated with many serious gastric diseases ranging from duodenal ulcer to gastric adenocarcinoma (1).

H. pylori infections are generally contracted throughout childhood, with many strains potentially colonizing the stomach during this time. Children of infected mothers are approximately five times more likely to get *H. pylori* infections than those of uninfected mothers, with familial transmission, especially from mother to child, being prevalent (2).

H. pylori, a pathogen particular to humans, can be transferred by fecal contact, contaminated food and

water, saliva, or medical devices utilized in endoscopic procedures. Ongoing colonization in dental plaques is seen as a source of endogenous infection (3). About half of the world's population is infected with *H. pylori*. The prevalence ranges from 70% to 90% in impoverished nations and from 25% to 50% in developed countries (4).

A study in Brazil revealed a correlation between ABO blood groups and infections from Gram-negative bacilli in patients having upper gastrointestinal endoscopy (5). Although certain investigations indicated no correlation between blood groups and *H. pylori*, new study has demonstrated that persons with blood group O exhibit increased susceptibility to *H. pylori* colonization in the stomach epithelium (6).

In this study, we aimed to determine the possible distribution between *H. pylori* infection and blood groups and which blood group is more common.

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MATERIAL AND METHOD

Ethical approval was secured from the Ordu University ethics committee prior to the commencement of the project. A retrospective review was conducted on patients who had *H. pylori* testing from 2020 to 2022. The study comprised 285 patients with both *H. pylori* test findings and documented blood group information.

The patients' age, gender, chronic disease history, *H. pylori* test outcomes, and blood group information were documented. Patients with solely blood group data or alone *H. pylori* test findings were excluded from the analysis. Group comparisons were conducted with Student's T-test and the chi-square test. Numerical data were presented as mean $\pm$ standard deviation (SD), while categorical variables were represented as percentages.

This study was approved by Ordu University Clinical

Research Ethics Committee with decision number 107 on 14.04.2023.

RESULTS

The study included 285 patients and 38% (110) of them were found to be positive for *H. pylori*. Of the positive patients, 70% (77) were reported as female and 30% (33) were reported as male. Among the negative patients, 78.6% women and 21.4% men were found to be negative and no significant difference was found between gender and *H. pylori* (p=0.120).

The age of *H. pylori* positive patients was 53.5 $\pm$ 15.8 years, and the age of *H. pylori* negative patients was 53.05 $\pm$ 15.9 years, and these differences were not considered significant (p=0.817). No statistical significance was found for chronic diseases (Table 1).

Table 1. Comparison of age, gender and chronic diseases of patients with <i>H. pylori</i> positive and negative groups			
	<i>H. pylori</i> positive n=110	<i>H. pylori</i> negative n=175	p
Age, year	53.5 $\pm$ 15.8	53.05 $\pm$ 15.9	0.817
Gender n (%)			
Male	33 (30)	37 (21.4)	0.120
Female	77 (70)	138 (78.6)	
Hypertension, n (%)			
Yes	57 (51.8)	81 (46.6)	0.397
No	53 (48.2)	93 (53.4)	
Diabetes mellitus, n (%)			
Yes	56 (50.9)	84 (48.3)	0.715
No	54 (49.1)	90 (51.7)	
Coronary artery disease, n (%)			
Yes	5 (4.5)	10 (5.7)	0.789
No	105 (95.5)	164 (94.3)	
Cerebrovascular accident, n (%)			
Yes	0	2 (1.2)	0.523
No	110 (100)	171 (98.8)	
Heart failure, n (%)			
Yes	3 (2.7)	4 (2.3)	1
No	107 (97.3)	169 (97.7)	

When blood groups were analysed, 37.3% of *H. pylori* positive patients belonged to group O and 38.2% to group A.

There was also no significant difference between negative patients and the opposite groups (p=0.242) (Table 2).

Table 2. Comparison of <i>H. pylori</i> positive and negative groups in terms of blood groups			
	<i>H. pylori</i> positive n=110	<i>H. pylori</i> negative n=175	p
A blood group, n (%)	41 (37.3)	55 (31.4)	0.242
O blood group, n (%)	42 (38.2)	71 (40.6)	
B blood group, n (%)	15 (13.6)	37 (21.1)	
AB blood group, n (%)	12 (10.9)	12 (6.9)	

DISCUSSION

The findings of our study show that *H. pylori* infection is more common in individuals with A and O blood groups. It was determined that 38.2% of the patients with *H. pylori* infection had blood group A and 37.3% had blood group O. This finding was supported by previous studies showing the distance the link between *H. pylori* and blood classification systems.

Boren et al. reported that Lewis and H blood group antigens have a binding function of transmission of *H. pylori* to human gastric mucosa. In this study, the majority of the people with *H. pylori* receptor were individuals with blood group O. They reported that most of the *H. pylori* positive individuals had O blood group (7). In addition, it has also been suggested that blood group A and B antigens may prevent the binding of *H. pylori* and the economic risk may be lower in these groups (8). Mentis et al. reported in a study that individuals with duodenal ulcer belonged mostly to group O, which may be related with *H. pylori* (9).

Similarly, in another success, it was stated that Lewis B antigen showed weak binding of *H. pylori* to the gastric epithelium with AB blood group records and the risk of disease was lower in individuals with AB blood groups (10). In another development, *H. pylori* positivity was analysed according to blood groups and it was reported that gastric and duodenal ulcers were associated with A blood type (11).

However, Konur and co-workers investigated whether there was a relationship between *H. pylori* and blood groups and found no significant relationship between the blood classification system and *H. pylori* (12). Similarly, Şenkaynağı and other scientists did not find a significant relationship between *H. pylori* infection and blood groups and found that the distribution of infection among blood groups was similar. This suggests that *H. pylori* infection may be related not only with blood group, but also with other symptoms, especially environmental and genetic variables (13).

Nalbant and Aydın examined whether there is a relationship between *H. pylori* infection and vitamin D, blood groups and hemogram parameters and found that the highest rate of blood group A was 49%, but there was no relationship between *H. pylori* positivity and blood groups (14). In another study conducted by Önder et al. no significant difference was found between *H. pylori* positivity, Rh factor and gender and it was concluded that AB blood type may be less common in terms of *H. pylori* (15). In a different study, Sarıış and colleagues analysed whether there is a link between *H. pylori* found positive in gastroduodenal biopsy and ABO Rh blood groups as a result of retrospective examination of 1774 patient data and reported that *H. pylori*, which is common in many countries, was more common in the female sex, although no significant relationship could be found between *H. pylori* and blood and Rh groups (16). In the study conducted by Rizatto et al., although there

are limited number of studies on the relationship between ABO blood groups and precancerous gastric lesions, it was reported that the risk of precancerous gastric lesions was higher in *H. pylori* positive individuals with blood group A compared to those with blood group O. In addition, the risk of gastric cancer development in individuals with blood group A was found to be significantly higher than in individuals with other blood groups (17). However, in a different study conducted by Gisi and İspiroğlu, contrary to the findings of Rizatto et al. the rates of precancerous gastric lesions were found to be higher in individuals with B and AB blood groups, although not statistically significant. This finding may be related with the family tree and geography of the individuals included in the study (18). Tüzün et al. reported that they did not find any significance in the study in which *H. pylori* and blood group antigens were analysed, but they also reported that more comprehensive studies with a larger number of patients are needed (19).

CONCLUSION

This study shows that *H. pylori* infection may be more common in individuals with A and O blood groups. In particular, *H. pylori* infection was more common in blood group A with 38.2% and in blood group O with 37.3%. This finding supports the hypothesis that the risk of *H. pylori* infection may be related to blood groups. This study highlights the possible impact of blood types on susceptibility to *H. pylori* infection, while additional large-scale research is required. An enhanced comprehension of the influence of blood groups on infection susceptibility may aid in the formulation of novel preventative and therapeutic approaches to address *H. pylori*.

Understanding the interplay between genetic, environmental, and physiological factors will provide deeper insights into the pathogenesis of *H. pylori* and its clinical implications.

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REFERENCES

1. Marshall BJ. Helicobacter pylori. Am J Gastroenterol. 1994;89:S116-28.
2. Alarcon T, Martinez MJ, Urruzuno P, et al. Prevalence of CagA and VacA antibodies in children with H. pylori-associated peptic ulcer compared to prevalence in pediatric patients with active or nonactive chronic gastritis. Clin Diagn Lab Immunol. 2000;7:842-4.
3. Goosen C, Theron J, Ntsala M, et al. Evaluation of a novel heminested PCR assay based on the phosphoglucosamine mutase gene for detection of H. pylori in saliva and dental plaque. J Clin Microbiol. 2002;40:205-9.

4. Kayar Y, Pamukçu Ö, Eroğlu H, et al. Relationship between H. pylori Infections in diabetic patients and inflammations, metabolic syndrome and complications. *Int J Chronic Dis*. 2015;2015:290128.
5. de Mattos LC, Rodrigues Cintra J, Sanches FE, et al. ABO, Lewis, secretor and non-secretor phenotypes in patients infected or uninfected by the *Helicobacter pylori* bacillus. *Sao Paulo Med J*. 2002;120:55-8.
6. Henriksson K, Uribe A, Sandstedt B, Nord CE. H. pylori infection, ABO blood group, and effect of misoprostol on gastroduodenal mucosa in NSAID-treated patients with rheumatoid arthritis. *Dig Dis Sci*. 1993;38:1688-96.
7. Borcn T, Faik P, Roth KA, et al. Attachment of H. pylori to human gastric epithelium mediated by blood group antigens. *Science*. 1993;262:1892-5.
8. Reid ME, Bird GW. Associations between human red cell blood group antigens and disease. *Transfus Med Rev*. 1990;4:47-55.
9. Mentis A, Blackwell CC, Weir DM, et al. AB O blood group, secretuar status and detection of H. pylori among patients with gastric or duodenal ulcers. *Epidemiol Infect*. 1991;106:221-9.
10. Lindén S, Nordman H, Hedenbro J, et al. Strain-and blood group- dependent binding of H. pylori to human gastric MUC5AC glycoforms. *Gastroenterol*. 2002;123:1923-30. Erratum in: *Gastroenterology*. 2003;124:588.
11. Seyda T, Derya C, Fusun A, Meliha K. The relationship of H. pylori positivity with age, sex, and ABO/Rhesus blood groups in patients with gastrointestinal complaints in Turkey. *Helicobacter*. 2007;12:244-50.
12. Konür Ş, Kayar Y, Dertli R, et al. The relationship between H. pylori infection and blood group. *Van Med J*. 2020;27:514-9.
13. Şenkaynağı A, Yıldız M. The relationship among H. pylori positivity, acute phase reactants, blood groups and tumor markers in urea breathe test. *Middle Black Sea J Health Sci*. 2017;3:13-9.
14. Nalbant A, Aydın A. Association of H. pylori infection with vitamin D, hemogram parameters, and blood group. *Academic Journal of Gastroenterology*. 2017;16:01-5.
15. Önder T, Hasbal NB, Kahramanca Ş, Anuk T. The relationship between H. pylori infection and sex, blood groups and rhesus factor in patients with chronic gastritis. *İKSST Derg*. 2016;8:93-6.
16. Sarıış A, Torun C, Şeneldir H, Tuncer İ. The relationship between ABO/Rhesus blood group antigens with the presence of H. pylori in gastroduodenal biopsy-retrospective analyze of 1774 patient data. *Van Med J*. 2023;30:286-92.
17. Rizzato C, Kato I, Plummer M, et al. Risk of advanced gastric precancerous lesions in H. pylori infected subjects is influenced by ABO blood group and cagA status. *Int J Cancer*. 2013;133:315-22.
18. Gisi K, İspiroğlu M. Are ABO blood groups associated with premalignant gastric lesions and H. pylori?. *Laparosc Endosc Surg Sci*. 2022;29:1-5.
19. Tüzün A, Doğru T, Çetin C, et al. H. pylori Infection and blood group antigens. *Türkiye Klinikleri J Gastroenterohepatol*. 1998;9:113-6.



Efficacy Comparison of Transdermal Fentanyl and IV Morphine PCA in Post-orthopedic Surgery Pain: A Randomized Clinical Trial

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Abstract

Aim: Effective postoperative pain management is crucial for early mobilization and recovery in orthopedic surgery patients. While intravenous patient-controlled analgesia (IV-PCA) with morphine is widely used, it has limitations including IV access dependency and mobility restrictions. Transdermal fentanyl (TDF) patches have emerged as an alternative due to their long-lasting analgesic effects. This study compares their efficacies in managing postoperative pain following orthopedic surgeries and evaluates patient satisfaction levels.

Material and Method: This prospective, randomized, controlled, comparative study included 40 patients aged 20-65 years undergoing orthopedic surgery under general anesthesia between July-December 2010. Patients were randomized into Group TDF (n=20) and Group IV-PCA (n=20). Postoperative pain intensity quantification was performed utilizing standardized VAS methodology, while concurrent sedation depth monitoring employed RSS parameters throughout the initial 24-hour postoperative period. Additionally, hemodynamic parameters, rescue analgesia requirements, side effects, and satisfaction levels were monitored.

Results: Post-surgical nociceptive metrics demonstrated significant temporal reduction across both cohorts ($p<.001$). Beyond the initial 90-minute phase, IV-PCA administration achieved superior analgesic efficacy compared to transcutaneous delivery ($p<.001$). Sedation parameters and adverse event profiles maintained statistical equivalence between modalities ($p>.05$). Patient-reported satisfaction metrics indicated significant preference for automated morphine administration protocols ($p<.001$).

Conclusion: Despite providing adequate initial pain relief, TDF patches demonstrated lower efficacy compared to IV-PCA with morphine in managing postoperative pain and achieving patient satisfaction following orthopedic surgery. These findings suggest the need for careful consideration when selecting postoperative pain management strategies.

Keywords: Pain, postoperative, patient-controlled analgesia, fentanyl/therapeutic use

INTRODUCTION

Postoperative pain, which is common following orthopedic surgical procedures, hinders early mobilization and rehabilitation, increases the risk of immobility-related complications, and prolongs hospital stays (1). Contemporary postoperative analgesia encompasses multiple therapeutic approaches, with intravenous patient-controlled analgesia (IV-PCA) systems, healthcare provider-initiated parenteral administration, and intermittent intravenous bolus protocols representing the primary interventional strategies (1,2). Contemporary evidence indicates IV-PCA morphine administration maintains predominance in acute surgical pain management,

particularly for moderate to severe intensity cases requiring precise analgesic titration (3). However, it has been associated with significant limitations, including requiring IV access, specialized setup and supervision, risks of overdose, mobility restrictions, side effects, and system-related interruptions in pain control (1-3).

As an alternative, fentanyl offers several advantages in postoperative pain management, including high potency, a broad therapeutic window, and rapid onset of action. It is not only the mainstay of intraoperative analgesia during anesthesia induction. The pharmacological versatility of fentanyl manifests through diverse administration routes, encompassing transmembranous delivery platforms,

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sublingual applications, nasally-administered formulations, and transcutaneous drug delivery systems (1,4,5). Although transdermal fentanyl (TDF) patches are primarily used to manage cancer-related pain in patients who use chronic opioids, there is evidence that they are also effective in controlling chronic and acute postoperative pain (4).

Clinical investigations have established the therapeutic potential of transcutaneous fentanyl delivery systems in managing post-surgical nociception across multiple surgical disciplines, with documented efficacy in orthopedic interventions, abdominal procedures, and gynecological operations (1,6-10). However, most of the studies on the use of TDF patches conducted in Türkiye addressed its use in non-surgical conditions such as rib fractures and cancer pain (11,12).

In view of the foregoing, this study was conducted to address the said gap by comparatively evaluating the efficacies of TDF patches and IV-PCA with morphine in the management of postoperative pain after orthopedic surgeries and the satisfaction levels of patients with these analgesia methods.

MATERIAL AND METHOD

Study Design

We implemented a monocentric prospective clinical investigation utilizing a randomized controlled parallel-group methodology. Our research protocol received institutional ethics board authorization (Reference: 2, Authentication Date: 30.06.2010) and adhered to Declaration of Helsinki principles governing human subject research. All study participants provided documented voluntary informed consent prior to enrollment.

Population and Sample

The study population comprised consecutive patients aged 20 to 65 years who underwent orthopedic surgery under general anesthesia at the Operating Room of Pamukkale University Research and Training Hospital, Türkiye, between July and December 2010. The patients were evaluated for subjective pain severity one day before surgery using the visual analog scale (VAS) (13). The study's inclusion criteria were having a VAS score of ≥ 4 and grade I to III American Society of Anesthesiologists (ASA) physical status. Study exclusion encompassed: preoperative VAS < 4, ASA classification IV-V, renal/hepatic dysfunction, ischemic myocardial pathology, decompensated cardiac dysfunction alongside advanced respiratory insufficiency, documented opioid/fentanyl hypersensitivity, pre-existing psychiatric/dermatologic diagnoses, weight parameters outside 50-100kg range, substance dependence history, alongside non-general anesthetic protocols. We calculated that our sample should consist of at least 38 people, 19 patients in each group, in order to obtain the α value of 0.05 and power (1- β) of 0.80 as stated in the literature (10). Considering that some patients may drop out of the study, we included 40 patients in the sample.

We randomized the 40 patients into two groups, Group TDF and Group IV-PCA, using sealed envelopes.

Preoperative Assessments and Interventions

Patients' demographic and clinical characteristics, including age, gender, weight, ASA physical status grades, and underlying orthopedic disease for surgery, were prospectively recorded. Double blinding was not possible. Pain-trained nurses performed all assessments for sedation and pain severity.

Patients' VAS and Ramsay sedation scale (RSS) scores were recorded before anesthesia induction preoperatively (10). In VAS, patients are asked to rate their pain severity on a scale from 0 (no pain) to 10 (worst possible pain). RSS evaluation utilized a 6-tier classification system (14): Level 1 indicates consciousness with psychomotor agitation; Level 2 signifies alert status with appropriate orientation and composure; Level 3 represents wakeful state with command-response capacity; Level 4 denotes somnolence with preserved quick arousal to glabellar/auditory stimulation; Level 5 indicates delayed arousal response; Level 6 represents complete absence of stimulus response.

For TDF cohort participants, transdermal fentanyl delivery systems (Durogesic® 50µg/hr, Janssen Pharmaceutica) were positioned on thoracic anterolateral surfaces or upper limb regions 10 hours pre-anesthetic induction. The system provided continuous fentanyl administration at 50µg hourly intervals. Protocol excluded supplementary pre-surgical medications. Clinical monitoring encompassed potential adverse effects: gastrointestinal manifestations, cardiovascular alterations, respiratory compromise, and cutaneous reactions.

The patients included in Group PCA were given paracetamol (Perfalgan, 10 mg/ml, 100 ml vial, Bristol-Myers Squibb Inc., İstanbul, Türkiye) and pethidine HCl (Aldolan, 100 mg/2 ml, G.L. Pharma GmbH, Lannach, Austria) as required before they arrived in the operating room.

Intraoperative Assessments and Interventions

Following mandated pre-surgical fasting, comprehensive physiological surveillance was initiated utilizing multi-parameter monitoring systems: cardiac electrical activity registration, peripheral oxygen saturation quantification, oscillometric arterial pressure evaluation, and end-tidal CO₂ analysis. Propofol administration (1% solution, Fresenius Kabi) was quantitatively documented from anesthetic initiation through procedural completion. Airway management quality assessment employed the Cooper classification protocol (reference 15), stratifying intubation success into four categories: superior (8-9 points), adequate (6-7 points), suboptimal (3-5 points), and inadequate (0-2 points).

Emergence chronometry was calculated from anesthetic gas discontinuation to successful airway device removal. Extubation quality underwent standardized evaluation utilizing validated ordinal assessment methodology (15).

Postoperative Assessments and Interventions

Post-surgical transfer to acute recovery facilities was executed, with temporal documentation initiated upon patient arrival to establish reference baseline measurements.

Sedation quantification and pain assessment (both static and dynamic) utilizing RSS and VAS parameters were conducted at designated intervals: initial phase (30/60/90 minutes), intermediate phase (hours 2-8), and extended phase (hours 12-24). Concurrent adverse event documentation was maintained throughout these evaluation timepoints.

Among the patients in Group TDF, those with a VAS score of ≥ 4 at any of these time points were administered 1 g IV paracetamol (Perfalgan, 10 mg/ml, 100 ml vial). TDF patches were removed 24 hours after the surgery.

The patients in Group PCA were provided with a PCA device (Pain Management Provider, Abbott Laboratories, North Chicago, USA) with preset parameters for morphine administration (two mg of loading dose, basal infusion rate of 1 mg/hr, one mg with a 10-minute lockout, and a 4-hour maximum dosage of 25 mg) (Morphine HCl ampoule, 10 mg/ml, Galen, İstanbul, Türkiye). Patients with a VAS score of ≥ 4 at any of the said time points were administered additional rescue IV morphine HCl (1–2 mg). The total morphine dose received by each patient was recorded.

On the second postoperative day, a 4-point (excellent, good, moderate, and poor) Likert-type assessment tool was used to evaluate patients' satisfaction with the analgesia method (16).

Statistical Analysis

Primary endpoints comprised post-procedural RSS/VAS measurements, with patient satisfaction serving as secondary outcome parameter. Data underwent statistical evaluation utilizing contemporary analytical software (SPSS 17.0, Chicago). Quantitative variables received descriptive treatment through central tendency/dispersion metrics (mean $\pm$ SD), supplemented by range values for specific parameters (e.g., opioid consumption profiles). Categorical data underwent frequency distribution analysis with proportional representation. Distribution normality underwent Kolmogorov-Smirnov verification. Inter-group comparisons for normally-distributed parameters (demographic characteristics, procedural duration, anesthetic agent utilization, airway management metrics) employed independent t-test methodology.

Paired t-test was used to conduct subgroup analyses. In comparing the differences in categorical variables (gender, ASA classification, operation type, patient comfort levels, side effects including nausea, vomiting, and pruritus) between the groups, Pearson's chi-square test was used for 2x2 tables with expected cells of 5 or more, Fisher's exact test for 2x2 tables with expected cells of less than 5, and Fisher-Freeman-Halton test for RxC tables with expected cells of less than 5.

Longitudinal sedation/pain score trajectories underwent repeated-measures compositional analysis with temporal decomposition. Post-hoc multiple comparison procedures (Bonferroni-adjusted) identified specific temporal coordinates driving observed variations in static/dynamic pain metrics. Statistical inference employed alpha threshold of 0.05 for significance determination.

RESULTS

Comparative analysis revealed statistically equivalent demographic/clinical parameter distributions between cohorts ($p>0.05$; demographic metrics detailed in Table 1). The distribution of underlying orthopedic conditions was similar between both groups, with no statistically significant differences observed ($p=.999$). The pre-induction RSS score was significantly higher than the preoperative RSS score in Group TDF (1.05 ± 0.22 vs. 2.00 ± 0.00 , $p<.001$). The pre-induction RSS score was significantly lower than the preoperative RSS score in Group IV-PCA (1.50 ± 0.51 vs. 1.20 ± 0.41 , $p=.004$). Inter-group RSS differentials achieved statistical significance at pre-induction and pre-surgical timepoints ($p=.002$; $p<.001$). Both cohorts demonstrated significant pre-induction VAS reductions compared to pre-surgical measurements ($p=.024$; $p<.001$). VAS metrics exhibited statistical equivalence between groups at both evaluation points ($p>.05$; comprehensive data presented in Table 2).

Anesthetic agent requirements demonstrated significant inter-group variation: IV-PCA cohort exhibited elevated propofol consumption (187.0 ± 21.8 mg versus 125.0 ± 28.9 mg; $p<.001$). Emergence characteristics revealed superior extubation metrics in IV-PCA recipients (2.60 ± 1.19 versus 1.05 ± 0.22 ; $p<.001$), while TDF group demonstrated enhanced Cooper intubation parameters (8.60 ± 0.60 versus 7.05 ± 1.93 ; $p=.003$). Remaining intraoperative anesthetic variables maintained statistical equivalence between groups ($p>.05$; detailed in Table 3).

There were no significant differences in RSS scores assessed during the 24 hours after surgery within or between the groups ($p>.05$). On the other hand, there were significant differences in both resting and ambulatory VAS scores assessed during the 24 hours after surgery within both groups ($p<.001$).

Additionally, initial resting VAS scores assessed at the 30th, 60th, and 90th minutes were significantly higher in Group IV-PCA than in Group TDF (6.15 ± 1.23 vs. 4.70 ± 0.57 , 6.55 ± 1.39 vs. 3.55 ± 0.51 , and 3.55 ± 0.89 vs. 3.10 ± 0.31 ; $p<.05$ for all cases). While the ambulatory VAS score assessed at the 30th minute was significantly higher in Group IV-PCA than in Group TDF ($p<.001$), there was no significant difference between the groups in VAS score assessed at the 60th and 90th minutes ($p>.05$). Nociceptive assessment revealed temporal variations: while early post-surgical phase (<90 minutes) demonstrated comparable VAS metrics, subsequent evaluations (hours 2-24) consistently indicated superior analgesic efficacy in IV-PCA cohort for

both static/dynamic pain parameters ($p<.05$ universally; comprehensive data in Table 4).

Bonferroni posthoc analyses revealed that resting VAS values, which were initially significantly higher in Group IV-PCA than in Group TDF, significantly decreased in Group IV-PCA from the postoperative 30th minute onward ($p<.001$). Bonferroni posthoc analyses revealed that resting VAS values, which were initially significantly lower in Group TDF than in Group IV-PCA, minimally decreased in Group TDF after the postoperative 90th- minute and even slightly elevated from the postoperative 4th hour onward. Ambulatory VAS scores, which were initially significantly higher in Group IV-PCA than in Group TDF, rapidly declined from the postoperative 60th minute onward in Group IV-PCA ($p<.001$). Despite significantly lower initial ambulatory VAS scores in Group TDF than in Group IV-PCA, ambulatory VAS scores slowly declined in Group TDF over the course of postoperative 24 hours. The most pronounced declines in resting and ambulatory VAS scores occurred within the

first 90 minutes postoperatively in both groups. However, while the resting and ambulatory VAS scores continued to decline in Group IV-PCA from the postoperative 2nd hour onward, they plateaued in Group TDF (Table 5).

Adverse event profiles maintained statistical equivalence across treatment modalities ($p>.05$).

Morphine consumption peaked at the postoperative 8th hour in Group IV-PCA (24.00 ± 4.81 mg) and then gradually declined. In Group TDF, the rescue paracetamol requirement significantly decreased over the course of the postoperative 24 hours (from 100% in the postoperative 4th hour to 35% in the postoperative 24th hour) (Table 6).

There was a significant difference in patient satisfaction between the groups ($p<.001$). Of the 20 patients, 14 (70.0%) expressed excellent satisfaction in Group IV-PCA, compared to only 1 (5.0%) in Group TDF. Most patients in Group TDF expressed moderate ($n=10$, 50%) and good ($n=8$, 40.0%) satisfaction (Table 7).

Table 1. Demographic and clinical characteristics of the study groups			
	Group TDF (n=20)	Group PCA (n=20)	p
Age (years)†	45.0±13.9	41.4±13.4	.416*
Weight (kg)†	74.9±13.2	76.4±12.4	.713*
Sex‡			
Female	8 (40.0)	6 (30.0)	.507**
Male	12 (60.0)	14 (70.0)	
ASA physical status‡			
I	12 (60.0)	10 (50.0)	.806**
II	7 (35.0)	9 (45.0)	
III	1 (5.0)	1 (5.0)	
Operation time (min)†	179.5±68.3	174.0±85.7	.824*
Underlying disease‡			
Symptomatic hip osteoarthritis	6 (30.0)	7 (35.0)	.999**
Femur fracture	5 (25.0)	4 (20.0)	
Humerus fracture	3 (15.0)	3 (15.0)	
Tibia fracture	3 (15.0)	3 (15.0)	
Forearm fracture	2 (10.0)	2 (10.0)	
Rotator cuff tear	1 (5.0)	1 (5.0)	
†: mean±standard deviation, ‡: n (%); *: Independent Samples T-test, **: Pearson Chi-Square/Fisher Freeman Halton test; TDF: transdermal fentanyl, PCA: patient-controlled analgesia, ASA: American Society of Anesthesiologists			

Table 2. Preoperative and preinduction RSS and VAS scores			
	Group TDF (n=20)	Group PCA (n=20)	p *
RSS†			
Preoperative evaluation	1.05±0.22	1.50±0.51	.002
Pre-induction of anesthesia	2.00±0.00	1.20±0.41	<.001
p**	p<.001	.004	
VAS†			
Preoperative evaluation	5.10±0.97	4.85±0.93	.391
Pre-induction of anesthesia	3.85±0.99	4.15±1.09	.590
p**	.024	<.001	
†: mean±standard deviation, *: Independent Samples t test, **: Paired t test; RSS: Ramsay sedation score, VAS: visual analog scale, TDF: transdermal fentanyl, PCA: patient-controlled analgesia			

Table 3. Comparison of intraoperative anesthesia-related parameters between the groups

	Group TDF (n=20)	Group PCA (n=20)	p *
Propofol (mg) [†]	125.0±28.9	187.0±21.8	<.001*
Cooper intubation score [†]	8.60±0.60	7.05±1.93	.003*
Atropin use [‡]	1 (5)	0 (0)	.152**
Duration of extubation (min) [†]	5.60±2.98	5.50±2.44	.945*
Extubation quality [†]	1.05±0.22	2.60±1.19	<.001*

†: mean±standard deviation, ‡: n (%), *: Independent Samples t test, **: Pearson Chi-Square/Fisher Freeman Halton test, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 4. Intra- and inter-group comparisons of the RSS and VAS scores during the postoperative 24 hours between the groups

	Group TDF (n=20)	Group PCA (n=20)	p *
RSS[†]			
30th min	1.65±0.93	1.70±0.98	.914
60th min	1.85±0.88	1.65±0.81	.427
90th min	1.95±0.22	1.95±0.69	.653
2nd hour	2.00±0.00	1.95±0.22	.317
4th hour	2.00±0.00	2.00±0.32	.999
8th hour	2.10±0.31	2.05±0.39	.671
12th hour	2.10±0.45	2.10±0.45	.999
16th hour	2.15±0.37	2.00±0.32	.179
20th hour	2.10±0.31	2.00±0.32	.323
24th hour	2.05±0.22	2.05±0.39	.979
p**	.128	.837	
Resting VAS[†]			
30th min	4.70±0.57	6.15±1.23	<.001
60th min	3.55±0.51	4.65±1.39	.004
90th min	3.10±0.31	3.55±0.89	.037
2nd hour	3.05±0.22	2.65±0.67	.011
4th hour	3.70±0.87	2.45±0.69	<.001
8th hour	3.90±0.85	2.10±0.45	<.001
12th hour	3.55±0.51	1.90±0.45	<.001
16th hour	3.45±0.51	1.80±0.41	<.001
20th hour	3.25±0.44	1.55±0.51	<.001
24th hour	3.25±0.64	1.40±0.50	<.001
p**	<.001	<.001	
Ambulatory VAS[†]			
30th min	6.50±0.83	8.45±1.43	<.001
60th min	6.25±1.07	6.80±1.88	.257
90th min	5.40±0.88	5.75±1.83	.754
2nd hour	5.25±0.72	4.35±0.93	.002
4th hour	5.20±0.70	4.20±1.01	.001
8th hour	5.05±0.51	3.60±1.00	<.001
12th hour	4.80±0.77	3.00±0.56	<.001
16th hour	4.70±0.57	2.75±0.55	<.001
20th hour	4.45±0.69	2.75±0.55	<.001
24th hour	4.15±0.49	2.50±0.51	<.001
p**	<.001	<.001	

†: mean±standard deviation, *: Independent Samples t test, **: Paired t test; RSS: Ramsay sedation score, VAS: visual analog scale, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 5. Bonferroni corrected post-hoc analysis of resting and ambulatory VAS scores during the postoperative 24 hours

Time 1	Time 2	Resting VAS		Ambulatory VAS	
		Group TDF	Group PCA	Group TDF	Group PCA
		p (Bonferroni)	p (Bonferroni)	p (Bonferroni)	p (Bonferroni))
30th min	60th min	.154	.053	.154	.004
30th min	90th min	<.001	.002	<.001	.007
30th min	2nd hour	<.001	<.001	<.001	<.001
30th min	4th hour	<.001	<.001	<.001	<.001
30th min	8th hour	<.001	<.001	<.001	<.001
30th min	12th hour	<.001	<.001	<.001	<.001
30th min	16th hour	<.001	<.001	<.001	<.001
30th min	20th hour	<.001	<.001	<.001	<.001
30th min	24th hour	<.001	<.001	<.001	<.001
60th min	90th min	.013	.126	.013	.126
60th min	2nd hour	<.001	.005	<.001	.005
60th min	4th hour	<.001	<.001	<.001	<.001
60th min	8th hour	<.001	<.001	<.001	<.001
60th min	12th hour	<.001	<.001	<.001	<.001
60th min	16th hour	<.001	<.001	<.001	<.001
60th min	20th hour	<.001	<.001	<.001	<.001
60th min	24th hour	<.001	<.001	<.001	<.001
90th min	2nd hour	.002	.231	.002	.231
90th min	4th hour	<.001	<.001	<.001	<.001
90th min	8th hour	<.001	<.001	<.001	<.001
90th min	12th hour	<.001	<.001	<.001	<.001
90th min	16th hour	<.001	<.001	<.001	<.001
90th min	20th hour	<.001	<.001	<.001	<.001
90th min	24th hour	<.001	<.001	<.001	<.001

VAS: visual analog scale, TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 6. Use of postoperative rescue morphine and paracetamol in Groups PCA and TDF

Time	Group PCA (n=20)		Group TDF (n=20)
	Morphine (mg)		Paracetamol
	Mean±SD	Min-max	n (%)
4th hour	20.25±5.27	10-28	20 (100.0)
8th hour	24.00±4.81	16-30	15 (75.0)
12th hour	20.10±5.86	6-30	11 (55.0)
16th hour	13.50±6.71	4-24	10 (50.0)
20th hour	8.40±6.31	4-28	5 (25.0)
24th hour	7.70±6.91	4-32	7 (35.0)

TDF: transdermal fentanyl, PCA: patient-controlled analgesia

Table 7. Results of the questionnaire for patient satisfaction regarding analgesia methods

Patient satisfaction	Group TDF (n=20)	Group PCA (n=20)	p
Excellent	1 (5.0)	14 (70.0)	<.001
Good	8 (40.0)	5 (25.0)	
Moderate	10 (50.0)	1 (5.0)	
Poor	1 (5.0)	0 (0.0)	

‡: n (%); Fisher Freeman Halton test; TDF: transdermal fentanyl, PCA: patient-controlled analgesia

DISCUSSION

Our investigation revealed distinctive temporal efficacy patterns between transcutaneous fentanyl delivery and automated morphine administration systems. Initial post-surgical phase demonstrated superior nociceptive control with TDF implementation (static measurements through 90 minutes; dynamic assessments within 30 minutes). However, subsequent temporal analysis indicated sustained analgesic superiority in IV-PCA cohort, commencing at post-procedural hour 2 and maintaining throughout the observational period. This pharmacodynamic evolution suggests differential therapeutic profiles: TDF systems exhibit enhanced immediate post-surgical efficacy, while automated morphine delivery protocols demonstrate superior sustained analgesia throughout the critical 24-hour recovery phase in orthopedic interventions.

Findings in the literature regarding the comparison of TDF patches with IV-PCA are conflicting, particularly in the context of orthopedic surgeries. These discrepancies in the findings of relevant studies may be due to differences between the studies' methodologies, TDF doses, timing of application, and patient characteristics. In one of these studies, Ebrahimzadeh et al. (5) found no significant difference between TDF patches and IV-PCA with morphine in terms of pain severity and patient satisfaction scores after orthopedic surgeries, even though they applied a lower dose of TDF (25 µg/hour) compared to the 50 µg/hour dose we applied. Similarly, in a study where TDF doses (12.5-25 µg/h) were titrated according to patient age to minimize the side effects while maintaining efficacy, Hall et al. (1) found no significant difference between TDF patches and IV-PCA with morphine in terms of analgesic efficacy, patient discharge times, and side effects in patients undergoing total knee replacement.

Contrasting observations were reported by Minville and colleagues (10), who demonstrated superior analgesic outcomes with prophylactic transcutaneous fentanyl administration in total hip arthroplasty patients, evidenced by reduced nociceptive scores and diminished opioid requirements compared to morphine-based IV-PCA protocols. The fact that they did not use preventive analgesia or premedication before surgery in the IV-PCA group may have had an impact on their findings. In comparison, even though our timing of TDF patch application was consistent with that of Minville et al. (10), we did not observe the prolonged pain-reducing effects of TDF patches Minville et al. did. Although the surgical distributions of our study groups were similar, differences in the underlying diseases may have caused our results to differ from those of Minville et al.

Several other studies investigating the effect of TDF patches on pain relief and total rescue morphine consumption during the first 48 to 72 hours after total

knee arthroplasty have reported that using TDF patches in combination with PCA reduced postoperative pain and adjunctive morphine consumption (9,13). On the other hand, other studies found no significant benefit of TDF patches over placebo patches in patients undergoing forefoot surgery or surgical repair of hip fractures (7,8). Inconsistent findings in the literature regarding the efficacy of TDF patches suggest that significant analgesic benefits from TDF patches may not be obtained in certain surgical contexts or patient groups, emphasizing the importance of tailoring analgesic strategies to specific surgical procedures and patient needs.

Findings in the literature on the efficacy of TDF patches in the context of abdominal surgeries are also inconsistent. Transcutaneous fentanyl delivery systems demonstrated enhanced nociceptive control following gynecologic procedures, however, analgesic efficacy data remains heterogeneous for general abdominal surgical interventions (6,17,18). In one study, although the pain scores of the TDF patch group at certain time points within 36 hours postoperatively were found to be slightly higher than those of the placebo group, it was concluded that TDF patch applications were safe and effective in analgesia after laparotomy, since the mean pain severity score of the TDF patch group was significantly lower than that of the placebo group (18,19). In contrast, Jang et al. (6) found that TDF patches had no advantage over IV fentanyl in reducing pain scores or rescue analgesic use after laparoscopic cholecystectomy. These findings underscore the need to address the heterogeneity in patient characteristics and variations in TDF doses and application protocols between studies. In sum, the findings of this study, together with literature findings, suggest that TDF patches may offer specific advantages in selected scenarios but do not provide consistent superiority over IV-PCA in orthopedic surgeries in particular.

Our findings should be interpreted in the context of contemporary multimodal analgesia approaches. In current clinical practice, postoperative pain management typically employs multiple analgesic modalities rather than relying on a single method. While TDF may not be as effective as IV-PCA, it could be considered as part of a multimodal approach that doesn't restrict patient mobility. However, when developing multimodal analgesia protocols, thorough understanding of the efficacy and safety profile of each component remains essential.

Prospective, large-scale studies that account for confounding factors are needed to understand better the efficacy and relative advantages of TDF patches versus IV-PCA for postoperative pain management. Future studies should explore the potential of individualized analgesic strategies, integrating patient-specific factors such as age, weight, comorbidities, and surgical context in

order to optimize the efficacy and safety of TDF patches. Comparative studies examining the cost-effectiveness, ease of use, and long-term outcomes of TDF patches versus IV-PCA could provide valuable insights into their relative advantages and limitations in postoperative pain management.

Limitations of the Study

A notable methodological constraint emerged from restricted participant numbers, potentially limiting comprehensive characterization of analgesic response variability, particularly within demographically or clinically-defined subpopulations. Secondly, the use of fixed-dose (50 µg/h) TDF patches did not allow for taking individual factors such as body weight, age, and comorbidities into account, and therefore, not all patients received the optimal dose. Additionally, the single-center design and limited sample size restrict the generalizability of our findings. Thirdly, long-term postoperative pain or patient-reported outcomes beyond the initial 24-hour period were not assessed. Future studies should employ individualized TDF dosing, larger patient populations, and multi-center designs.

CONCLUSION

In conclusion, despite enhanced initial analgesic efficacy, TDF systems demonstrated suboptimal pain control compared to IV-PCA morphine delivery in the management of post-orthopedic surgical pain. These findings suggest that the selection of analgesic methods for postoperative pain management should consider patient characteristics, surgical type, and pain severity, with emphasis on developing individualized treatment approaches. Future studies should be conducted in larger patient populations, with individualized dosing regimens, and multi-center designs.

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Ethical approval: The research protocol was approved by the Clinical Research Ethics Committee of Pamukkale University Faculty of Medicine (Reference Number: 2, Approval Date: 30.06.2010). The study was conducted in accordance with the principles outlined in the Declaration of Helsinki for research involving human participants. Written informed consent was obtained from all participants prior to their enrollment in the study.

REFERENCES

- Hall MJ, Dixon SM, Bracey M, et al. A randomized controlled trial of postoperative analgesia following total knee replacement: transdermal Fentanyl patches versus patient controlled analgesia (PCA). *Eur J Orthop Surg Traumatol*. 2015;25:1073-9.
- Hartrick CT, Bourne MH, Gargiulo K, et al. Fentanyl iontophoretic transdermal system for acute-pain management after orthopedic surgery: a comparative study with morphine intravenous patient-controlled analgesia. *Reg Anesth Pain Med*. 2006;31:546-54.
- Langford RM, Chang KY, Ding L, Abraham J. Comparison of fentanyl iontophoretic transdermal system and routine care with morphine intravenous patient-controlled analgesia in the management of early postoperative mobilisation: results from a randomised study. *Br J Pain*. 2016;10:198-208.
- Kaye AD, Menard BL, Ehrhardt KP, et al. Consensus Perioperative Management Best Practices for Patients on Transdermal Fentanyl Patches Undergoing Surgery. *Curr Pain Headache Rep*. 2019;23:50.
- Ebrahimzadeh MH, Mousavi SK, Ashraf H, et al. Transdermal fentanyl patches versus patient-controlled intravenous morphine analgesia for postoperative pain management. *Iran Red Crescent Med J*. 2014;16:e11502.
- Jang JS, Hwang SM, Kwon Y, et al. Is the transdermal fentanyl patch an efficient way to achieve acute postoperative pain control? A randomized controlled trial. *Medicine (United States)*. 2018;97:e13768.
- Merivirta R, Pitkänen M, Alanen J, et al. Postoperative pain management with transdermal fentanyl after forefoot surgery: A randomized, placebo-controlled study. *J Pain Res*. 2015;8:39-45.
- Labmayr V, Rief M, Reinbacher P, et al. Simplified pain management including fentanyl TTS in PACU patients with hip fracture surgery to improve patients' well-being: a double-blind randomized trial. *J Perianesth Nurs*. 2024;39:461-7.
- Sathitkarnmanee T, Tribuddharat S, Noiphitak K, et al. Transdermal fentanyl patch for postoperative analgesia in total knee arthroplasty: A randomized double-blind controlled trial. *J Pain Res*. 2014;7:449-54.
- Minville V, Lubrano V, Bounes V, et al. Postoperative analgesia after total hip arthroplasty: patient-controlled analgesia versus transdermal fentanyl patch. *J Clin Anesth*. 2008;20:280-3.
- Solak O, Öz G, Kokulu S, et al. The effectiveness of transdermal opioid in the management multiple rib fractures: Randomized clinical trial. *Balkan Med J*. 2013;30:277-81.
- Kömürcü Ş, Turhal S, Altundag K, et al. Safety and efficacy of transdermal fentanyl in patients with cancer pain: phase IV, Turkish oncology group trial. *Eur J Cancer Care (Engl)*. 2007;16:67-73.
- Abrisham SMJ, Ghahramani R, Heiranizadeh N, et al. Reduced morphine consumption and pain severity with transdermal fentanyl patches following total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc*. 2014;22:1580-4.
- Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with alphaxalone-alphadolone. *Br Med J*. 1974;2:656-9.
- Cooper R, Mirakhor RK, Clarke RSJ, Boules Z. Comparison of intubating conditions after administration of org 9426 (rocuronium) and suxamethonium. *Br J Anaesth*. 1992;69:269-73.

16. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg*. 2010;111:120-8.
17. Myles PS, Williams DL, Hendrata M, et al. Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients. *Br J Anaesth*. 2000;84:6-10.
18. Broome IJ, Wright BM, Bower S, Reilly CS. Postoperative analgesia with transdermal fentanyl following lower abdominal surgery. *Anaesthesia*. 1995;50:300-3.
19. Hosseini H, Kargar S, Shiryazdi SM, et al. Fentanyl transdermal patch (Durogesic® D-TRANS) for post abdominal laparotomy analgesia: a double blind randomized study. *Minerva Chir*. 2015;70:401-8.



Gender Disparities in Decision-Making and Outcomes in Lumbar Spine Surgery: A Retrospective Analysis

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Abstract

Aim: The objective of this study is to explore gender differences in decision-making and outcomes in lumbar spine surgery.

Material and Method: In this retrospective analysis, 74 patients (42 women and 32 men) who had lumbar spine surgery at İstinye University's Gaziosmanpaşa Hospital between January 2023 and April 2024 were included. Sociodemographics, surgical choices, comorbidities, and medication use were among the data gathered; these were examined to find variations.

Results: Women were more likely to attend appointments with family members and to have surgery at their initial consultation. In addition, women were more likely than men to have smoked, had had previous surgery, and used antidepressants. In terms of surgical operations, stabilizing procedures were more commonly assigned to women. Additionally, compared to patients with only a primary school education, those with better educational backgrounds—especially those who have graduated from university—tended to make judgments faster. Preoperative discomfort and impairment were higher among women, according to the results.

Conclusion: Comorbidities, gender, and educational background have a big influence on lumbar spine surgical decision-making and results. By addressing these issues in therapeutic settings, it may be possible to improve patient care and lessen treatment and recovery inequities.

Keywords: Gender disparities, lumbar spine surgery, decision-making, patient outcomes, educational status

INTRODUCTION

Gender disparities have affected medical procedures at a spectrum of specialties, as well as any area of life. Prior studies have found that women were less likely to receive diagnostic angiography than men, even after considering confounding factors (1). Despite advanced outreach of medical procedures in the modern world, these discrepancies remain. The underutilization of diagnostic procedures still causes higher mortality and morbidity rates for women across many fields (2). Atypical symptomatology, as well as implicit gender biases, can

lead to incorrect diagnosis and delayed true diagnosis in women (3). This bias and disparities have been seen in multiple specialties including endocrinology, immunology, cardiology, (1,3-5). Similar results have been observed in spine surgery in previous studies as well. Reports indicate women are less likely to receive surgical intervention than men for spinal conditions. According to a systematic review by Mobbs et al. (6), women are more prone to have wound-related complications, and men tend to have more medical complications and mortality following spinal surgery. These reports underscore the importance of addressing gender biases in any clinical setting. Our study

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aims to examine the role of gender in the decision-making process for lumbar spine surgery and analyze the impact of gender factors throughout the stages before, during, and after surgical interventions. Additionally, it remains unclear how gender differences influence doctors' recommendations for surgical interventions and patient preferences. Furthermore, this study seeks to reveal how gender affects surgical decisions, postoperative recovery processes, and patient satisfaction in lumbar spine surgery. Key factors influencing surgical decisions may include patient expectations, the surgeon's clinical approach, and gender-based biases. Notably, it is believed that female patients may experience lower rates of surgical decision-making, whereas males may be directed toward surgical intervention more rapidly. The goal is to present the impact of these differences on patient outcomes using scientific data. The results may enhance the understanding of gender-related clinical differences in lumbar spine surgery and contribute to the development of strategies aimed at improving surgical processes.

MATERIAL AND METHOD

Following the Institutional Review Board's approval, a retrospective patient archive search was conducted for patients undergoing lumbar spinal surgery at İstinye University, Gaziosmanpaşa Hospital, in the Department of Neurosurgery between January 1, 2023, and April 1, 2024. Institutional review board approval was obtained from İstinye University, Faculty of Medicine (Protocol No: 24-215, 22.11.2024).

Inclusion criteria were as follows: 1) patient age 18 years or older, 2) has a diagnosis requiring a lumbar spinal surgery, 3) literate educational status, and 4) has signed the informed consent for participation. Patients were excluded if, 1) with a history of lumbar spinal trauma, 2) malignancy at the lumbar spine, 3) patients age <18 years.

Data Collection

Patients' data were collected from individual patient records, including demographic data (age, gender), Marital Status (Married, Single), Educational level (Primary, High school, University), Type of Surgery (MicroDiscectomy, Posterior Stabilization), Acceptance of Surgery at the first consultation, Attendance to first consultation alone or with a relative, Later attendance (Alone or with a relative), Attendance to more than two consultations, the Time difference between first consultation and the preoperative anesthesia planning, Patients clinical Status at the first consultation (Presence of Neurologic Deficits, Presence of Comorbidities, History of Previous Surgery, History of Previous Spine Surgery), Patients perspective on surgery postoperatively (Failed, Successful), Delay of surgery due to anti-platelet therapy, Smoking history, Antidepressant use. The given variables were compared between two genders and surgical procedural types.

Statistical Analysis

Statistical analyses were conducted using the SPSS (version 22.0, SPSS Inc., Chicago, IL, USA). Continuous variables were reported as means and standard deviations, while the Categorical variables were dichotomized and presented as percentages and frequencies. Shapiro-Wilk test was used to assess the normality and a p value of <0.05 was considered statistically significant.

RESULTS

The study included 42 women with an average age of 50.36 ± 13.29 and 32 men with an average age of 46.00 ± 14.90 . The comparison of the patients' sociodemographic characteristics by gender is provided in Table 1. The educational status and type of surgery of the groups were statistically significantly different ($p < 0.001$). The number of women who accepted surgery at the first consultation, visited more than twice, later came with a first-degree relative, had a surgical history, smoking history, and used antidepressants was statistically significantly higher than men ($p < 0.05$). The duration between the first consultation and anesthesia preparation was similar for women and men ($p = 0.272$, Table 1).

According to the educational status, the duration between the first consultation and anesthesia preparation differed between the patients ($p = 0.05$). Patients with only primary school education (8.55 ± 8.11 days) had a longer duration between the first consultation and anesthesia preparation compared to high school graduates (4.33 ± 6.34 days) ($p = 0.004$) and university graduates (4.71 ± 9.20 days) ($p = 0.007$). There was no difference between high school and university graduates ($p = 0.939$). Patients who used antidepressants (11.31 ± 8.90 days) had a longer duration between the first consultation and anesthesia preparation compared to those who did not use antidepressants (4.66 ± 7.26 days) ($p = 0.003$). The duration between the first consultation and anesthesia preparation was similar for patients who had previous surgeries (7.08 ± 7.26 days) and those who had not (5.56 ± 8.50 days) ($p = 0.445$).

In the disc surgery group, 19 (43.2%) women and 25 (56.8%) men were included, while in the stabilization surgery group, 23 (76.7%) women and 7 (23.3%) men were included. The number of patients who accepted disc surgery at the first consultation and came alone was higher compared to the stabilization surgery group ($p < 0.05$). In the stabilization surgery group, the number of patients who later came with a first-degree relative, visited more than twice, had comorbidities, were waiting due to antiplatelet use, and used antidepressants was statistically significantly higher compared to the disc surgery group ($p < 0.05$). The duration between the first consultation and anesthesia preparation was shorter in the disc surgery group ($p = 0.015$).

Table 1. Sociodemographic variables by gender

Variables	Female (n=42)	Male (n=32)	p-value
Age, years	50.36±13.29	46.00±14.90	0.189
Marital status			
Married	35 (83.3%)	23 (71.9%)	0.236
Single	7 (16.7%)	9 (28.1%)	
Educational status			
Primary school	25 (59.5%)	4 (12.5%)	<0.001
High school	5 (11.9%)	19 (59.4%)	
University	12 (28.6%)	9 (28.1%)	
Type of operation			
Disc surgery	19 (45.2%)	25 (78.1%)	0.004
Stabilization surgery	23 (54.8%)	7 (21.9%)	
Accepted surgery at first consultation	19 (45.2%)	23 (71.9%)	0.022
Came alone to first consultation	20 (47.6%)	20 (62.5%)	0.203
Later came with a first-degree relative	19 (45.2%)	6 (18.8%)	0.017
Attended more than two consultations	19 (45.2%)	5 (15.6%)	0.007
Time between first consultation and anesthesia preparation	7.00±7.39	4.91±8.86	0.272
Motor deficit	8 (19%)	6 (18.8%)	0.974
Comorbidity	22 (52.4%)	3 (9.4%)	<0.001
History of prior surgery	21 (50%)	6 (18.8%)	0.006
History of spinal surgery	10 (23.8%)	7 (21.9%)	0.845
History of unsuccessful surgery	6 (14.3%)	1 (3.1%)	0.104
Waited due to antiaggregant use	6 (14.3%)	1 (3.1%)	0.104
Smoking history	10 (23.8%)	25 (78.1%)	<0.001
Antidepressant use	13 (31%)	3 (9.4%)	0.025

DISCUSSION

Our study examined 42 women and 32 men, to assess gender differences in lumbar spinal surgery decision making. Between women and men, significant differences were seen in educational status and types of surgery these groups will be receiving. Based on our finding from our cohort, women were more likely to accept surgery during the first consultation, visit the clinic more than twice, attend the appointments with a relative, have a prior history of surgical history and smoking, and use antidepressants. Our findings align with previous studies in the literature where women often report worse preoperative pain, disability, health-related quality of Life (HRQL) compared to men, leading to more decisive decision (7-9).

Although there were no significant differences between preoperative counseling and the anesthesia appointment. Naturally, educational status affected the decision-making duration, where university graduate patients were faster to decide on surgery than the Primary school graduates. Moreover, increased education level possibly pushes those patients to do more self-research, leading to conclusions which might benefit the duration between consultation and preoperative anesthesia (8). Furthermore, the patients with an antidepressant use have significantly longer duration between consultation and preoperative anesthesia, this might be due to the increased incidence of anxiety

disorders within the population, leading to prolonged decision making presumably due to excessive thinking of all possible outcomes (9). Finally, there is also a possible link between smoking history and antidepressants use.

When compared between surgical procedures, there were more patients within the disc surgery group to accept surgery than the stabilization group; this was also seen attending alone rather than with a relative between the two groups. Furthermore, the duration between anesthesia and preoperative counselling was significantly shorter in the disc surgery group. This may be explained by the perception that stabilization surgeries are regarded as more aggressive in patients' minds than disc surgeries. In the stabilization group, patients tended to come more with their relatives, had comorbidities, visited the clinic more than twice, had been receiving antiplatelet therapy, which prolonged the preoperative period, and also had been using antidepressants more than the disc surgery group (8,9). Given the incidence and prevalence of coronary arterial disease, and risk of atherosclerosis in the Turkish population, it might be expected that comorbidities and antiplatelet use are juxtaposed within our cohort.

Furthermore, in the literature, several authors looked at both the preoperative patient symptomatology and postoperative reported outcomes. Maclean et al. (7) in their prospective study concluded that female patients

had worse preoperative clinical assessment, and selected healthcare resources. Furthermore, in their review they have concluded that female patients had worse postoperative disability and quality of life (10). Siccoli et al. (8) had consistent findings in their study as well, where female patients had more severe preoperative symptoms, and in the postoperative long-term follow-up as well. Störmqvist et al. (9) found that female patients had a higher rate of consumption of analgesics postoperatively, and a higher rate of postoperative pain, and less improvement in their quality of life, when compared to men and their preoperative status. In summary, existing literature provides some insights between two genders, where these results indicate that gender plays an important role in patient outcomes, and differences should be considered in both the preoperative and postoperative settings.

Our study has provided some valuable insights, however, not without limitations. Firstly, the relatively small sample size may limit the generalizability of our findings. A more diverse cohort with a widened age range, and socioeconomic background could provide more comprehensive results. Furthermore, retrospective single-center design of our study may limit our ability to draw natural conclusions and introduce selection biases. Lastly, our study had only two surgery types to compare, so we are limited and can not generalize our findings to a broader range of surgical interventions. Our cohort comprised a single culture background of patients, which is also a limitation and hinders our results from being applied to different cultural populations.

CONCLUSION

Our study underscores the importance of gender-bias in the preoperative decision-making setting. We have tried to explore how gender, educational status, various patient-centered variables such as smoking history, comorbidities, and medication use, such as antidepressants, influence the preoperative decision-making. We hope that physicians remind themselves of these gender differences during their approaches to patients to achieve a more favorable outcome. However, for greater applicability of our results, we need more prospective, multi-institutional, multi-cultural studies to achieve a greater perspective, across many cultural dimensions.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: Institutional review board approval was obtained from İstinye University, Faculty of Medicine (Protocol No: 24-215, 22.11.2024).

REFERENCES

1. Rathore SS, Chen J, Wang Y, et al. Sex differences in cardiac catheterization: the role of physician gender. *JAMA*. 2001;286:2849-56.
2. Spörri R, Joller N, Hilbi H, Oxenius A. A novel role for neutrophils as critical activators of NK cells. *J Immunol*. 2008;181:7121-30.
3. Skvortsova A, Meeuwis SH, Vos RC, et al. Implicit gender bias in the diagnosis and treatment of type 2 diabetes: a randomized online study. *Diabet Med*. 2023;40:e15087.
4. Sempere L, Bernabeu P, Cameo J, et al. Gender biases and diagnostic delay in inflammatory bowel disease: multicenter observational study. *Inflamm Bowel Dis*. 2023;29:1886-94.
5. Claréus B, Renström EA. Physicians' gender bias in the diagnostic assessment of medically unexplained symptoms and its effect on patient-physician relations. *Scand J Psychol*. 2019;60:338-47.
6. Seo W, Muroi S, Akiyama K, Taniuchi I. Distinct requirement of Runx complexes for TCR β enhancer activation at distinct developmental stages. *Sci Rep*. 2017;7:41351.
7. MacLean MA, Charest-Morin R, Stratton A, et al. Gender differences in spine surgery for degenerative lumbar disease: prospective cohort study. *J Neurosurg Spine*. 2024;42:24-32.
8. Siccoli A, Staartjes VE, de Wispelaere MP, Schröder ML. Gender differences in degenerative spine surgery: do female patients really fare worse?. *Eur Spine J*. 2018;27:2427-35.
9. Strömquist F, Strömquist B, Jönsson B, Karlsson MK. Gender differences in patients scheduled for lumbar disc herniation surgery: a National Register Study including 15,631 operations. *Eur Spine J*. 2016;25:162-7.
10. MacLean MA, Touchette CJ, Han JH, et al. Gender differences in the surgical management of lumbar degenerative disease: a scoping review. *J Neurosurg Spine*. 2020;32:799-816.



Efficacy of Endovenous Laser Ablation and Ultrasound-Guided Foam Sclerotherapy in Patients with Great Saphenous Vein and Perforating Vein Insufficiency

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Abstract

Aim: In this study, we aimed to investigate the efficacy of endovenous laser ablation (EVLA) and EVLA combined with ultrasound-guided foam sclerotherapy (UGFS) and outcomes of treatments in patients with great saphenous vein (GSV) and perforating vein (PV) insufficiency.

Material and Method: Patients underwent EVLA and EVLA+UGFS at the Interventional Radiology Department of a tertiary referral hospital over a 2-year period were retrospectively analysed. Lower limbs of patients were divided into 2 groups according to the treatment method: lower limbs underwent EVLA (group 1) and EVLA+UGFS (group 2). Before and after the procedures, GSVs and incompetent PVs were assessed by colour Doppler ultrasound. Chronic venous insufficiency symptoms (CVIS): pain, heaviness, night cramps, fatigue, itching, burning sensation, swelling, numbness, tingling and visual analogue scale (VAS) scores were assessed before and at 6 months after treatment.

Results: The study group included 29 female (69.1%) and 13 male (30.9%) patients with a mean age of 49.8 ± 12.5 years (range, 24-73 years). All treated GSVs and IPV were occluded at 6 months after procedures. Improvement in one or more CVIS was observed in all limbs. Full recovery in CVIS was 11/38 (28.9%) in group 1 and 2/9 (22.2%) in group 2. No significant difference was found between the two groups in the comparison of the percentage reduction in the rate of full recovery of symptoms ($p > 0.05$). The VAS scores were significantly decreased after procedures in group 1 and 2 ($p = 0.0001$ and 0.007 , respectively). The difference in the percentage decrease in VAS scores in the 6th month compared to before treatment was not statistically different between the two groups ($p > 0.05$).

Conclusion: EVLA and UGFS are highly effective and reliable treatments for GSV and PV insufficiency. EVLA+UGFS treatments provide similar improvements in CVIS in lower limbs with GSV and PV insufficiency. Patients with lower clinical severity, treatment only for GSV insufficiency may be considered instead of concomitant treatment of GSV insufficiency and PVI.

Keywords: Endovenous laser ablation, ultrasound-guided foam sclerotherapy, great saphenous vein, varicose vein, perforating vein insufficiency

INTRODUCTION

Chronic venous insufficiency (CVI) in the lower limbs affects a significant proportion of the world's population. CVI has a wide clinical spectrum. It can be asymptomatic or cause more serious symptoms and signs such as varicose veins, fatigue, heaviness, leg cramps and ulcers (1,2). Recent research has indicated that if patients with varicose veins are not treated, a significant proportion will experience a substantial decline in quality of life. Progressive fasciocutaneous deterioration may result in leg ulcers, superficial venous thrombosis and even

significant bleeding in varicose veins (3).

The symptoms of CVI in the lower extremities may be caused by insufficiency of the saphenous veins, deep veins, perforating veins (PV), or combinations of these venous insufficiencies (4). Previously, surgery was the standard method in the management of CVI. However, this has mostly been replaced by endovenous thermal ablation (EVTA), which has better results and fewer complications. Endovenous laser ablation (EVLA), one of the EVTA procedures, has comparable efficacy to surgery with lower complication rates and shorter recovery times in cases of

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great saphenous vein (GSV) insufficiency (1). Furthermore, conventional surgical procedures have been superseded by minimally invasive techniques in the treatment of perforating vein insufficiency (PVI) (5). Ultrasound-guided foam sclerotherapy (UGFS), as a minimally invasive technique for the treatment of PVI, offers several attractive features. The process is relatively straightforward and can be executed expeditiously (6).

There is no consensus for PVI treatment in patients with GSV and PV insufficiency with low clinical severity, and the question of whether perforator treatment can reduce the incidence of varicose vein recurrence is still controversial. Not enough data reported on improvement in symptoms of CVI after treatment (7).

The objective of the present retrospective study was to evaluate clinical outcomes of the treatment with EVLA and EVLA+UGFS and to determine the changes in chronic venous insufficiency symptoms (CVIS) at 6 months after procedure in patients with GSV and PV insufficiency.

MATERIAL AND METHOD

Study Populations and Design

This study retrospectively analyzed patients who underwent EVLA at the Interventional Radiology Department of a tertiary referral hospital over a 2-year period. Three patients who underwent EVLA for tributary vein insufficiency, venous anomaly and small saphenous vein insufficiency were excluded. Also, patients without PVI accompanying GSV insufficiency (n=48) and patients with incomplete hospital records (n=5) were excluded. In the final analysis, 47 lower limbs with GSV and PV insufficiency in 42 patients were included in the study (Figure 1). EVLA in one lower limb and EVLA+UGFS in the other lower limb was not performed in any of the patients in the study.

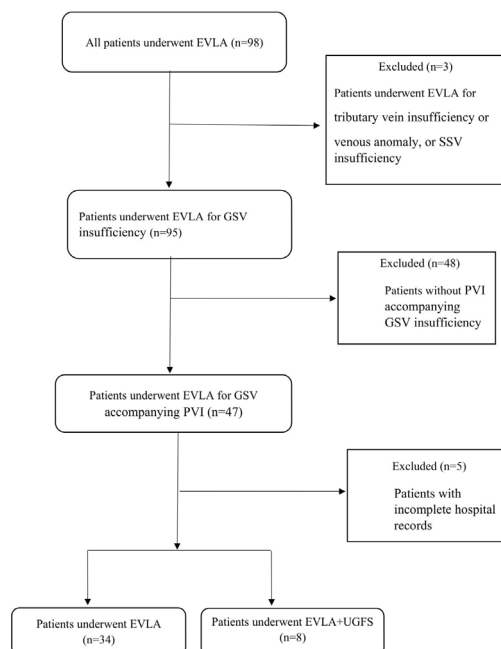


Figure 1. Derivation of the study population; EVLA: endovenous laser ablation, GSV: great saphenous vein, SSV: small saphenous vein, PVI: perforating vein insufficiency, UGFS: ultrasound-guided foam sclerotherapy

The present study has been conducted in accordance with the national regulations and institutional policies that are currently in force and it is consistent with the principles of the Helsinki Declaration. The study was approved by the Ethics Committee of the Faculty of Medicine at Pamukkale University (by decision no. 2013/10 dated 05/08/2013). The lower limbs of patients in the study group were divided into two groups: lower limbs underwent EVLA alone (group 1) and those underwent EVLA with UGFS (group 2). Group 1 consisted of 38 legs in 34 patients and group 2 consisted of 9 legs in 8 patients.

Patients were diagnosed by colour Doppler ultrasound (CDUS) using a 13-5 MHz and a 9-4 MHz multi-frequency linear transducer (Antares, Siemens Medical). All CDUS examinations were carried out by the same experienced radiologist before and after treatment. Clinical and CDUS examinations were performed in the standing position in all patients. Backflow duration ≥ 500 ms in GSV and the PV during the performance of compression or the Valsalva manoeuvre were considered to be pathological. The number of incompetent perforating veins (IPV), measurements of maximal diameters of IPVs were recorded before and after the treatment. The presence of new IPVs (competent before treatment but incompetent after procedure), partial or total thrombosis of IPVs diagnosed before treatment were also evaluated after the procedures.

EVLA was not performed in pregnant and lactating women and patients with deep venous insufficiency and/or thrombosis, prior varicose vein treatment, severe arterial insufficiency, a history of allergy to local anesthetic substances or sclerosing agents. Before the procedure, the patients were classified according to CEAP (Clinical, Etiologic, Anatomic, and Pathophysiologic) classification (8). The duration of the complaints and body mass index (BMI) were recorded. All patients were asked to rate their pain in their limbs using visual analogue scale (VAS). In the VAS scale, zero denotes the absence of pain, while ten represents the most intense pain imaginable. The VAS scores were assessed before the procedure and at 6 months after the procedure. Prior to all procedures, potential risks and benefits of the EVLA and UGFS was discussed with patients. Each patient gave informed consent. EVLA and UGFS were in accordance with the American Venous Forum Joint Statement reporting standards (8).

EVLA and UGFS Procedures

The EVLA and UGFS procedures were the same for all patients and applied by the same radiologist. The limbs were prepared in a sterile manner in supine position before the procedures and femoral nerve block was performed. All procedures in EVLA and UGFS were performed using 7-12 MHz multifrequency linear array probe (LOGIQ P5, GE Healthcare, Hertfordshire, UK). All EVLA procedures were performed with the same kit (Standard Procedure Kit with 4F 70 cm marked sheath, Vascular Solutions Inc, Sycamore Court, Minneapolis, USA). GSV was punctured either at the level of the knee or below the knee with a 21-gauge needle. A 4F catheter was inserted over

guidewire. A 600 μ m platinum-tipped laser fiber was inserted into the catheter with the wire tip 1 to 2 cm distal to the saphenofemoral junction. Tumescence anesthesia was applied around the GSV using normal saline (1000 cc), 2% prilocaine (20 cc) and 8.4% sodium bicarbonate and 1 mg adrenalin (Figure 2).



Figure 2. The administration of the tumescent anaesthesia

Laser system parameters (Gigaa 980 nm, Vari-Lase endovenous laser system, Vascular Solutions Inc., Sycamore Court, Minneapolis, USA) were: power, 10–20 W; pulse duration, 4–8 sec; and pulse interval, 1 sec. The amount of applied energy was set according to the diameter, depth, and localization of the vein (120–140 J/cm for the proximal part, 70–90 J/cm for the middle part, and 40–50 J/cm for the distal part of the GSV). Real-time ultrasound was used to visualise intravascular air bubbles during the procedure (Figure 3). The total amount of laser energy and the length of treated GSV were recorded.

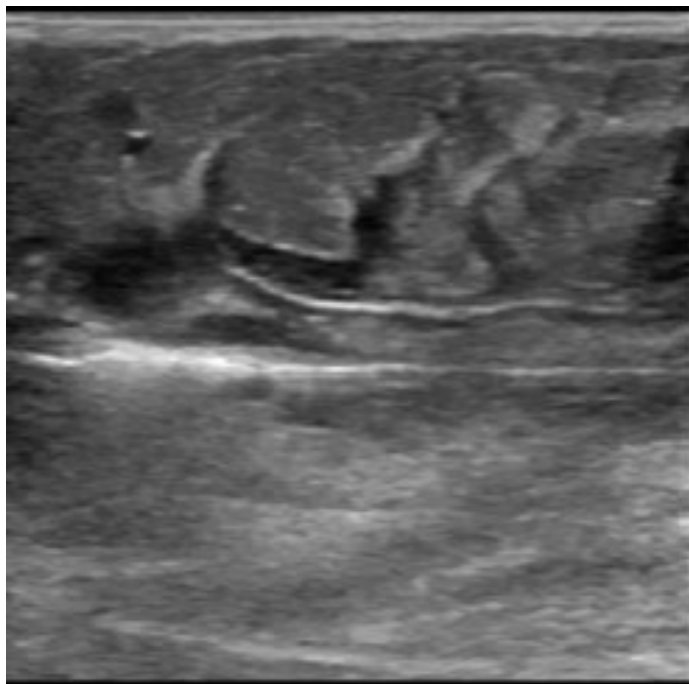


Figure 3. An ultrasound image of intravascular air bubbles

In UGFS procedure, IPVs were accessed under ultrasound guidance with 21G or 22G needles. A thick foam was produced by mixing 1–3% polidocanol solution (Aethoxysklerol, Cem Farma, Ankara, Türkiye) with air 1:4. When IPVs were filled with echogenic foam, before the sclerosing agent reached to the deep venous system, the injection was stopped. A maximum 4 mL sclerosing agent solution was used for each limb.

Follow-up appointments were scheduled for 1st week and on the 1st, 3rd and 6th months post-procedure, and depending on patient complaints thereafter. CDUS was used to evaluate all GSVs and IPVs in treated limbs. Newly developed PV and PVI and the diameters of them were recorded. The patients were again asked to rate their pain using the VAS.

No additional treatment was performed on the patients after procedures. Due to the complication guidelines of the Society of Interventional Radiology Standards of Practice Committee, minor complications were pain, ecchymosis, dysaesthesia, induration, haematoma and superficial thrombophlebitis. Deep vein thrombosis, pulmonary embolism and nerve injury as seen after EVLA were major complications. CVIS (heaviness, night cramp, fatigue, itchiness, burning, swelling, numbness, tingling) were classified as present/absent before the procedure and as full recovery, partial recovery, no change, and worsening at the 6th month after the procedure.

Statistical Analysis

The statistical analyses were conducted utilising SPSS version 18.0 for Windows. The expression of continuous variables is as follows: mean $\pm$ standard deviation or median (minimum-maximum). Categorical variables were expressed in quantitative terms as frequency and percentage. Comparison between independent groups was performed using the test of significance of difference between two means in parametric conditions and in non-parametric conditions by using the Mann-Whitney U test. For the comparison between dependent groups, Wilcoxon paired two-sample test was used. The comparison of qualitative data was conducted by employing the McNemar and Chi-square and tests. P values less than 0.05 were considered significant.

RESULTS

The study included 29 female (69.1%) and 13 male (30.9%) patients with a mean age of 49.8 $\pm$ 12.5 years (range, 24–73 years). The mean BMI of all patients was 29.75 $\pm$ 4.55 kg/m² (range, 23.2–46.1 kg/m²) and the main duration of symptoms in lower limbs was 9.77 $\pm$ 5.67 years (range, 2–26 years). There was no significant difference between patients in 2 groups in terms of age and BMI ($p>0.05$ for each). There was no statistical difference between the two groups in terms of duration of symptoms ($p>0.05$). Table 1 summarises the characteristics of patients and lower limbs in the study.

The mean length of treated GSV was 54.60±11.15 cm (range, 31-75 cm). The mean energy delivered in all limbs was 5755.34±894.53 J/limb (106.32±11.22 J/cm). There was no statistical difference between the two groups in terms of treated GSV length, energy delivered/limb and energy/cm (p>0.05, for all) (Table 1).

Table 1. The characteristics of the study population			
	Group 1 (n=38 limbs in 34 patients)	Group 2 (n=9 limbs in 8 patients)	Total (n=47 limbs in 42 patients)
Age (years), mean±SD, (range)	50.1±12.6 (24-73)	48.5±12.9 (28-65)	49.8±12.5 (24-73)
Female/male, n (%)	11 (32.4) / 23 (67.6)	2 (25) / 6 (75)	13 (31) / 29 (69)
BMI (kg/m ²) mean±SD, (range)	29.75±4.84 (23.2-46.1)	29.71±3.28 (26.2-34.5)	29.75±4.55 (23.2-46.1)
Duration of symptoms (years), mean±SD, (range)	10.16±6.00 (2-26)	8.11±3.82 (2-15)	9.77±5.67 (2-26)
Right/Left limb, n (%)	21 (55.3) / 17 (44.7)	8 (88.9) / 1(11.1)	29 (61.7) / 18 (38.3)
CEAP, n (%)			
C0	-	-	-
C1	1 (2.6)	-	1 (2.1)
C2	9 (23.7)	-	9 (19.2)
C3	13 (34.2)	6 (66.7)	19 (40.4)
C4	13 (34.2)	3 (33.3)	16 (34)
C5	2 (5.3)	-	2 (4.3)
C6	-	-	-
Length of ablated GSV (cm), mean±SD	54.84±10.07 (33-75)	53.56±13.56 (31-70)	54.60±11.15 (31-75)
Total energy (J)/limb, mean±SD	5786.24±902.94 (3960-7672)	5624.89±898.13 (4158-6904)	5755.34±894.53 (3960-7672)
Energy (J)/cm mean±SD	106.44±10.62 (85.07-137.90)	105.84±14.24 (93.68-134)	106.32±11.22 (85.07-137.90)
SD: standard deviation, BMI: body mass index, CEAP: clinical, etiologic, anatomic, and pathophysiologic, GSV: great saphenous vein; Continuous variables were presented as mean±standard deviation or median (interquartile range); Absolute variables were presented as number (%)			

Before treatment, pain was the most common complaint (100%). Burning sensation (38.3%) was the least common complaint. Frequency of fatigue was higher in group 1 than group 2 (p=0.003). The frequency of other CVISs were not significantly different in both groups before treatment (p>0.05, for all). The frequency of CVIS is shown in Table 2.

Table 2. The frequency of symptoms in lower limbs before treatment			
Symptom	Group 1 n (%)	Group 2 n (%)	Total n (%)
Pain	38 (100)	9 (100)	47 (100)
Heaviness	28 (73.7)	6 (66.7)	34 (72.3)
Night cramp	23 (60.5)	7 (77.8)	30 (63.8)
Fatigue	36 (94.7)	8 (88.9)	44 (93.6)
Itchiness	16 (42.1)	4 (44.4)	20 (42.6)
Burning sensation	14 (26.8)	4 (44.4)	18 (38.3)
Swelling	32 (84.2)	7 (77.8)	39 (83)
Numbness	21 (55.3)	5 (55.6)	26 (55.3)
Tingling	20 (52.6)	4 (44.4)	24 (51.1)

Initial technical successes were achieved in all EVLA processes. All concomitant UGFS were also technically successful in group 2. At 6 months after procedures, the diameter of the treated GSV was significantly reduced in both groups (Table 3) and all treated GSVs and PVI were completely occluded.

Table 3. The diameters of GSV before treatment and at 6th month after procedure in group 1 and 2

	Segment of GSV	Before treatment mean (mm)±SD	After procedure (6th month) mean (mm)±SD	p*
EVLA (n=38)	Proximal thigh	8.77±2.91	3.31±0.36	0.0001
	Mid thigh	7.47±2.16	3.08±0.40	0.0001
	Distal thigh	6.95±1.90	2.90±0.50	0.0001
	Proximal kruris	5.26±2.17	2.48±0.42	0.0001
	Distal kruris	3.24±0.95	2.13±0.28	0.0001
EVLA+UGFS (n=9)	Proximal thigh	7.16±2.57	3.31±0.53	0.008
	Mid thigh	6.97±1.92	3.00±0.27	0.008
	Distal thigh	6.88±2.43	2.80±0.34	0.008
	Proximal kruris	5.34±1.98	2.62±0.55	0.008
	Distal kruris	3.96±1.56	2.19±0.40	0.008
All lower limbs (n=47)	Proximal thigh	8.46±2.90	3.31±0.39	0.0001
	Mid thigh	7.37±2.10	3.07±0.38	0.0001
	Distal thigh	6.94±1.98	2.88±0.47	0.0001
	Proximal kruris	5.27±2.12	2.51±0.44	0.0001
	Distal kruris	3.38±1.11	2.14±0.30	0.0001

GSV: great saphenous vein, SD: standard deviation, EVLA: endovenous laser ablation, UGFS: ultrasound-guided foam sclerotherapy, p*: comparison of GSV diameter before treatment and at 6th month after procedure

Before procedures, 110 IPVs were detected in 47 limbs (93 IPVs in group 1 and 17 IPVs in group 2). The mean diameter of IPVs was 4.31±1.24 mm (range, 2.8-8.4 mm in group 1 and 5.32±1.86 mm (range, 3.2-10 mm) in group 2. At the 6th month, the mean diameter of IPVs was 4.70±1.33 mm in group 1 and 3.15±0.95 mm in group 2. The mean diameter of IPVs at 6th after procedure was higher in group 1 and lower in group 2 compared to before treatment (p<0.0001 for each). At 6th months after treatment there was one new IPV in group 1, however no new IPV was observed in group 2. At the 6th month, there were 28 PVs (mean diameter, 2.45±0.32 mm; range, 2.0-3.2 mm) in group 1 and

4 PVs (mean diameter, 2.28±0.17 mm; range, 2.1-2.5 mm) in group 2, which had no insufficiency but became visible compared to before procedure.

Improvement in at least 1 symptom was observed in all limbs in both groups. The proportion of extremities with full recovery in symptoms was 11/38 (28.9%) in group 1 and 2/9 (22.2%) in group 2. No significant difference was found between the two groups in the comparison of the percentage reduction in the rate of full recovery of symptoms (p>0.05). The changes in CVIS at the end of the 6th month is shown in Table 4.

Table 4. Changes in the symptoms at 6th month compared to before procedures

Symptom		Full Recovery n (%)	Partial recovery n (%)	No Change n (%)	Worsened n (%)
Pain	Group 1 (n=38)	14 (36.8)	22 (57.9)	2 (5.3)	-
	Group 2 (n=9)	6 (66.7)	3 (33.3)	-	-
Heaviness	Group 1 (n=28)	12 (42.9)	14 (50)	2 (7.1)	-
	Group 2 (n=6)	4 (66.6)	1 (16.7)	1 (16.7)	-
Night cramp	Group 1 (n=23)	11 (47.8)	1 (4.8)	1 (4.4)	-
	Group 2 (n=7)	5 (71.4)	2 (28.6)	-	-
Fatigue	Group 1 (n=36)	13 (36.1)	17 (47.2)	5 (13.9)	1 (2.8)
	Group 2 (n=8)	3 (37.5)	4 (50)	1 (12.5)	-
Itchiness	Group 1 (n=16)	6 (37.5)	7 (43.8)	2 (12.5)	1 (6.2)
	Group 2 (n=4)	3 (75)	1 (25)	-	-
Burning sensation	Group 1 (n=14)	7 (50)	3 (21.4)	3 (21.4)	1 (7.2)
	Group 2 (n=4)	2 (50)	1 (25)	1 (25)	-
Swelling	Group 1 (n=32)	14 (43.8)	13 (40.6)	4 (12.5)	1 (3.1)
	Group 2 (n=7)	3 (42.8)	2 (28.6)	1 (14.3)	1 (14.3)
Numbness	Group 1 (n=21)	10 (47.6)	6 (28.6)	3 (14.3)	2 (9.5)
	Group 2 (n=5)	2 (40)	1 (20)	1 (20)	1 (20)
Tingling	Group 1 (n=20)	8 (40)	11 (55)	1 (5)	-
	Group 2 (n=4)	2 (50)	2 (50)	-	-

Table 5 shows the major and minor complications in group 1 and 2. As a major complication, 1 patient in group 2 had thrombus in the popliteal vein. Thrombus was detected 1 week after procedure and popliteal vein was completely recanalized after acetylsalicylic acid

treatment at 1st follow-up. Other major complication was a second-degree skin burn occurred in the anteromedial aspect of the cruris in one limb in group 1. The energy applied to this limb was the highest as 137.9 J/cm.

Table 5. Major and minor complications in Group 1 and 2		
Complication	Group 1 (n=38)	Group 2 (n=9)
Deep vein thrombosis	-	1 (11.1%)
Skin burn	1 (2.6%)	-
Ecchymosis, tenderness	29 (76.3%)	4 (44.4%)
Increased pigmentation	11 (28.9%)	7 (77.8%)
Paresthesia	11 (28.9%)	4 (44.4%)
Thrombophlebitis	2 (5.3%)	1 (11.1%)

The most common minor symptom in all limbs after procedures was ecchymosis and tenderness (70.2%). Complete regression of ecchymosis was observed at 1st month in all limbs. Local thrombophlebitis developed as a result of thrombosis of varicose veins in three limbs (6.4%). Of the lower limbs with paresthesia (15/47, 31.9%), 10 were ablated to the ankle, 4 to the mid-crural region, and 1 to below the knee. Paresthesia was observed in only one limb (8.3%) where ablation was performed proximal to the cruris. The incidence of paresthesia was 4/12 (33.3%) and 10/23 (43.5%) in patients who underwent ablation to the mid-crural and ankle, respectively. At 6th month after procedures, increased pigmentation was found in 18 (38.3%) limbs. Increased pigmentation was found more in lower limbs that underwent EVLA+UGFS than those underwent EVLA alone (p=0.006). Other complication rates were similar for both groups (p>0.05).

After the treatment, the mean VAS scores improved significantly, falling from 6.13±1.12 (range, 4-8) before procedure to 2.21±1.02 (range, 0-5) at the end of 6th months in group 1 and from 6.33±1.32 (range, 4-8) to 2.11±0.60 (range, 1-3) in group 2 (p=0.0001 and 0.007, respectively). The difference in the percentage decrease in VAS scores at 6th month compared to before treatment was not statistically different between the two groups (p>0.05).

DISCUSSION

In this study, complete occlusion was observed in all veins treated with EVLA or EVLA+UGFS in lower limbs with GSV and PV insufficiency. EVLA and EVLA+UGFS treatments resulted in similar rates of significant improvement in CVISs. There was a significant decrease in VAS scores at 6 months postprocedure compared to before treatment with EVLA and EVLA+UGFS. However, there was no significant difference in the rate of decrease in VAS values between both groups. Major complications were low, and minor complications were high with EVLA and EVLA+UGFS treatments. The increase in pigmentation was found to be higher with EVLA+UGFS than with EVLA alone. Paresthesia was more common in cases where the distal parts of the GSV were also ablated in the crural region.

CVI is a progressive condition that requires public health consideration due to its extensive nature. The following risk factors have been identified as common to CVI: prolonged standing or sitting, venous thrombosis history, increasing age, pregnancy, family history of venous disease, smoking, obesity, history of trauma or surgery to the lower extremities (3,9). While patients with CVI may remain asymptomatic, others may experience localised discomfort. This may include pain, itching or throbbing around the affected veins. Untreated CVI can lead to the advancement of venous disease to a more severe stage, including symptoms such as fatigue, heaviness, and leg cramps. It is estimated that as many as 10% of adults suffering from CVI may eventually have progressive disease. It may include venous ulcers, thrombophlebitis or bleeding from varicosities (1,10). In our study, pain in all lower limbs was the most common symptom. Fatigue was the second most common symptom with a prevalence of 93.6%.

CVISs and varicose veins in limbs may be caused by insufficiency of the saphenous veins, deep veins, PVs, or a combination of these venous insufficiencies (4). PVI has been shown to be a contributing factor to the symptoms of advanced CVI. The majority of patients diagnosed with CVI can be treated with either the ablation of the axial veins or with compression therapy. However, this treatment is sometimes unsuccessful, and patients have been observed to suffer from recurrent varices. In this group, recalcitrant symptoms may be attributed to PVI. In patients with ulcers or a history of ulcers, treatment of PVIs can improve the rate of healing of the ulcer and prevent the recurrence of ulcers. A comprehensive meta-analysis of data derived from 20 trials has concluded that in patients diagnosed with PVI treated in CEAP C6 class, initial cure rates approached 90%, accompanied by a recurrence rate of only 13% (5,11).

The landscape for the treatment of symptomatic varicose veins has changed significantly. This is primarily attributable to the advent of minimally invasive endovascular procedures. Among these procedures, EVTA techniques, particularly EVLA and radiofrequency ablation, have emerged as first-line treatments (1,12). The

EVLA procedure entails the insertion of a laser fiber into the target vein, resulting in the emission of laser energy, which induces thermal damage within the vessel. The consequences include venous constriction, thrombosis and fibrosis (12). The utilisation of radial fibers and lasers characterised by higher wavelengths (1470-1940 nm) has been introduced for the promotion of uniform damage to the vein wall (13). An investigation into the frequently utilised parameters of EVLA (wavelength, administered energy) has demonstrated that these factors exert no influence on the success rates of treatment. The overall success rate of EVLA is found to be high (92%), even in the context of increasing follow-up periods (14). In our study, we used 980 nm wavelength and all GSVs treated with EVLA were thrombosed at the end of the 6th month. The findings of this study are consistent with the extant literature and lend further support to the high success rate of EVLA.

The diameter of GSVs decreases gradually within months following successful treatment with EVLA and the great majority (85%) become invisible on CDUS at the end of the first year (15). In the present study, thigh and crural GSV diameters were significantly reduced 6 months after EVLA compared to preprocedure.

Complications associated with EVLA are generally minor and major complications are uncommon. In the literature, the rate of deep venous thrombosis was reported to be 0-8%, paresthesia was reported to be 0-12%, and skin burn was reported to be 0-12% after EVLA (16). A review focusing on the complications of EVLA reported that the rate of ecchymosis and pain ranged 24-100% and superficial thrombophlebitis ranged 1- 22% (17). In the present study, partial thrombus was detected in one patient. Development of thrombus in this patient who underwent EVLA+UGFS was attributed to the sclerosing agent's leaking into the deep venous system through the PV. The other major complication was skin burn in one patient. The energy delivered to this patient was 137.9 J/cm, the highest value in the study. The rate of major complications in the present study was in line with that reported in the literature.

Superficial thrombophlebitis following EVLA was more common in large varicose veins and in the venous structures with impaired drainage due to ablation and it is reported nearly 5% (16). In the present study, superficial thrombophlebitis was detected due to thrombosis of the varicose veins in a total of 3 limbs (6.4%). The most common complication observed in the present study was ecchymosis and tenderness lasting for nearly 1-2 weeks in 70.2% (33/47) of the limbs. The rate of these minor complications in this study were consistent with the literature.

It has been reported that ablation of crural GSV has high risk for saphenous nerve injury and that temporary paresthesia frequently occurs due to the damage of the nerve (which has only sensorial branches in the crural segment) resulting from inserting vascular sheath or catheter, tumescent anesthesia or direct thermal effect.

Long lasting paresthesia can be seen by 0-10% (18). As a general agreement on minimizing the risk of postoperative nerve injury, it has been reported that preferably the inferior aspect of the knee joint is convenient for accessing and that accessing from a segment more inferior to the 1/3 proximal aspect of the cruris should be avoided (19). In the present study, paresthesia was observed in a total of 15 lower limbs (31.9%). The rate of paresthesia was higher in limbs exposed to ablation through the middle part of cruris and the ankle. The findings of the present study support the opinion that long-segment GSV ablation enhances the rates of nerve injury and paresthesia.

Current societal recommendations include perforator closure in CEAP C5-6 disease by traditional or minimally invasive techniques (5). However, there is no consensus for the treatment of PVI in patients with lower clinical severity and the question of whether or not perforator treatment can reduce the incidence of varicosity recurrence is still controversial (7). The seven-center retrospective cohort study confirmed that IPVs were important factors for recurrent varicose veins after EVTA (20). However, there are several reasons against definitive perforator transection. Firstly, treatment of GSV alone improves a significant proportion of IPVs; secondly, interruption of IPVs using a variety of techniques is associated with residual or 'missed' IPVs; finally, recurrence is often associated with progression of CVI, not just IPVs (21).

Traditional surgical techniques have been replaced by minimally invasive procedures for the treatment of PVI. UGFS is one of these effective techniques. It is technically simple and can be performed quickly. Also, it is less expensive than thermal ablation. Multiple IPVs and varicose veins can be treated with a single injection. Improvement in symptoms, as measured by venous clinical scores, was seen in patients with successfully treated IPV (6). In contemporary literature, completion rates of between 69% and 96% have been reported with UGFS. Patients with successful IPV thrombosis demonstrated high rates of ulcer healing (11). In the present study, all treated IPVs were occluded at 6 months post-procedure and the success rate of complete occlusion of IPVs was consistent with the literature.

The major complications associated with UGFS were reported to include anaphylactic reactions (although these were rare), deep venous thrombosis (1-3%), and stroke (0.01%). Other complications reported were superficial venous thrombosis (4.4%), tissue necrosis, oedema (0.5%), and nerve injury (0.2%). Among the cosmetic complications, newly developed telangiectasia was reported to be 15-24% (22). In this study, increased pigmentation was detected in 18 lower limbs (38.3%) after 6 months after treatment. Of these lower limbs, 7 (77.8%) were in group 2 and 11 were (28.9%) in group 1. A systematic review showed that the incidence of hyperpigmentation with sclerotherapy increased with higher concentrations of polidocanol. In addition, at polidocanol concentrations greater than 0.25%, more pigmentation was observed after sclerotherapy

of epifacial veins than intrafacial truncal veins (23). We believe that the relatively high concentration of polidocanol used in our study and the fact that polidocanol injected into the perforating veins passes into the superficial venous structures may explain why more pigmentation was observed in the second group.

In the present study, the decrease in VAS scores at 6 months post procedure was statistically significant for patients underwent EVLA alone and EVLA+UGFS ($p=0.0001$ and 0.007 , respectively). In the literature, it is reported that the maximum clinical benefit is seen in the first three to six months after EVTA. In addition, it is indicated that no clinical improvement has been seen after 6 months of treatment (24). Therefore, 6 months after treatment seemed to be the best time to assess clinical benefit after treatment. In this study, all limbs were clinically evaluated and CDUS examinations were performed at the end of 6th month following treatment. For this reason, we are of the opinion that there is sufficient data in our study to determine the changes in CVIS after the treatment.

Previous studies have compared the anatomic success rate and improvement in quality of life according to the type of EVTA. Not enough data has been reported for the improvement of CVIS and the rate of full recovery of CVIS is uncertain (25,26). In a study (27), involving a total of 174 patients, the changes in CVIS in patients underwent cyanoacrylate ablation+UGFS and EVLA+UGFS were evaluated. The most significant improvements reported were night cramps (94.7%), itching (93.8%), heaviness (85.2%), numbness (77.8%) and pain (60.9%). Also, the improvement rates for all symptoms were found to be similar in both groups. In our series, there was no statistically significant difference in the frequency of limbs with improvement in 1 or more symptoms and full recovery from all symptoms between the EVLA and EVLA+UGFS groups ($p>0.05$ for each). Also, there was no significant difference in the percentage decrease in VAS scores between the two groups after the procedure ($p>0.05$). For these reasons, we are in the opinion that there is no significant difference between EVLA and EVLA+UGFS treatment in terms of improvement of CVIS in limbs with GSV and PV insufficiency.

Thrombosis (blood clots) in the saphenous and varicose veins, as well as inflammation in the vessel wall and the structures around it, may cause an increase in CVIS in the early period after treatment of the saphenous vein (1). These complaints are mostly transient, and they can even be reduced by compression stockings and anti-inflammatory medications (27). In our study, the incidence of deterioration in symptoms post-treatment was found to be minimal (in 0 to 2 limbs with EVLA and 0-1 limbs with EVLA+UGFS). Our results are in line with the literature, but further research is needed to determine the cause of the worsening of symptoms.

Limitations of Study

There are some limitations of this study. It has a retrospective and single-center design. This methodological framework may be susceptible to selection bias, thereby restricting

the external validity of the findings. The 6th month post-procedure data may result in a relative lack of outcome measures. Moreover, the study's sample size is limited, which has the potential to compromise the statistical power and precision of the results.

CONCLUSION

EVLA and UGFS are highly effective and reliable treatments for GSV and PV insufficiency. They are associated with high patient satisfaction and low complication rates. EVLA alone and EVLA+UGFS treatments provide similar improvements in symptoms in patients with GSV and PV insufficiency. In this patient group with lower clinical severity, treatment only for GSV insufficiency may be considered instead of concomitant treatment of GSV insufficiency and PVI. However, large randomised trials comparing EVLA and EVLA+UGFS are needed in these patients.

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Ethical approval: The present study was approved by the Ethics Committee of the Faculty of Medicine at Pamukkale University (approval number: 2013/10; date of approval: 05/08/2013). The study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients during their period of hospitalisation.

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REFERENCES

1. Fayyaz F, Vaghani V, Ekhatior C, et al. Advancements in varicose vein treatment: anatomy, pathophysiology, minimally invasive techniques, sclerotherapy, patient satisfaction, and future directions. *Cureus*. 2024;16:e51990.
2. Ontario Health (Quality). Nonthermal endovenous procedures for varicose veins: a health technology assessment. *Ont Health Technol Assess Ser*. 2021;21:1-188.
3. Azar J, Rao A, Oropallo A. Chronic venous insufficiency: a comprehensive review of management. *J Wound Care*. 2022;31:510-9.
4. Whiteley MS. Current Best Practice in the Management of varicose veins. *Clin Cosmet Investig Dermatol*. 2022;15:567-83.
5. Hager ES, Washington C, Steinmetz A, et al. Factors that influence perforator vein closure rates using radiofrequency ablation, laser ablation, or foam sclerotherapy. *J Vasc Surg Venous Lymphat Disord*. 2016;4:51-6.
6. Masuda EM, Kessler DM, Lurie F, et al. The effect of ultrasound-guided sclerotherapy of incompetent perforator veins on venous clinical severity and disability scores. *J Vasc Surg* 2006;43:551-7.
7. Dillavou ED, Harlander-Locke M, Labropoulos N, et al. Current state of the treatment of perforating veins. *J Vasc Surg Venous Lymphat Disord*. 2016;4:131-5.

8. Gloviczki P, Lawrence PF, Wasan SM, et al. The 2022 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society clinical practice guidelines for the management of varicose veins of the lower extremities. Part I. Duplex Scanning and Treatment of Superficial Truncal Reflux: Endorsed by the Society for Vascular Medicine and the International Union of Phlebology. *J Vasc Surg Venous Lymphat Disord.* 2023;11:231-61. Erratum in: *J Vasc Surg Venous Lymphat Disord.* 2024;12:101719.
9. Fukaya E, Flores AM, Lindholm D, et al. Clinical and genetic determinants of varicose veins. *Circulation.* 2018;138:2869-80.
10. Piazza G. Varicose veins. *Circulation.* 2014;130:582-7.
11. Kiguchi MM, Hager ES, Winger DG, et al. Factors that influence perforator thrombosis and predict healing with perforator sclerotherapy for venous ulceration without axial reflux. *J Vasc Surg* 2014; 59:1368-76.
12. Gao RD, Qian SY, Wang HH, et al. Strategies and challenges in treatment of varicose veins and venous insufficiency. *World J Clin Cases.* 2022;10:5946-56.
13. Pavei P, Spreafico G, Bernardi E, et al. Favorable long-term results of endovenous laser ablation of great and small saphenous vein incompetence with a 1470-nm laser and radial fiber. *J Vasc Surg Venous Lymphat Disord.* 2021;9:352-60.
14. Malskat WS, Engels LK, Hollestein LM, et al. Commonly used endovenous laser ablation (EVLA) parameters do not influence efficacy: results of a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg.* 2019;58:230-42.
15. Theivacumar NS, Dellagrammaticas D, Darwood RJ, et al. Fate of the great saphenous vein following endovenous laser ablation: does re- canalisation mean recurrence?. *Eur J Vasc Endovasc Surg.* 2008;36:211-5.
16. Khilnani NM, Grassi CJ, Kundu S, et al; Cardiovascular Interventional Radiological Society of Europe, American College of Phlebology, and Society of Interventional Radiology Standards of Practice Committees. Multi-society consensus quality improvement guidelines for the treatment of lower-extremity superficial venous insufficiency with endovenous thermal ablation from the Society of Interventional Radiology, Cardiovascular Interventional Radiological Society of Europe, American College of Phlebology and Canadian Interventional Radiology Association. *J Vasc Interv Radiol.* 2010; 21:14- 31.
17. Van den Bos RR, Neumann M, De Roos KP, et al. Endovenous laser ablation induced complications: review of the literature and new cases. *Dermatol Surg.* 2009;35:1206-14.
18. Vaz C, Matos A, de Pereira MSC, et al. Iatrogenic complications following laser ablation of varicose Veins: In Rutherford's Vascular Surgery. Philadelphia: Saunders Elsevier 2010:871-88.
19. Sanioglu S, Yerebakan H, Ozgen A, et al. Mid-calf level as a puncture site is not safe enough for thermal ablation of the small saphenous vein. *SAGE Open Med.* 2017;5:2050312117731474.
20. Bush RG, Bush P, Flanagan J, et al. Factors associated with recurrence of varicose veins after thermal ablation: results of the recurrent veins after thermal ablation study. *Scientific World J.* 2014;2014:505843.
21. Shi H, Liu X, Lu M, et al. The effect of endovenous laser ablation of incompetent perforating veins and the great saphenous vein in patients with primary venous disease. *Eur J Vasc Endovasc Surg.* 2015;49:574-80.
22. Cavezzi A, Parsi K. Complications of foam sclerotherapy. *Phlebology.* 2012;27:46-51.
23. Bossart S, Daneluzzi C, Cazzaniga S, et al. Skin hyperpigmentation after sclerotherapy with polidocanol: a systematic review. *J Eur Acad Dermatol Venereol* 2023;37:274-83.
24. Yilmaz S, Ceken K, Alparslan A, et al. Endovenous laser ablation for saphenous vein insufficiency: immediate and short-term results of our first 60 procedures. *Diagn Interv Radiol.* 2007;13:156-63.
25. Vourliotakis G, Sahsamanis G, Evagelidis P, et al. Endovascular laser treatment of incompetent saphenous veins using the 1470 nm diode laser and radial fiber. *Ann Med Surg.* 2018;25:12-6.
26. Yie K. Symptom improvement after cyanoacrylate glue adhesion and endovenous laser ablation in low-grade CEAP clinical classes. *J Vasc Surg Venous Lymphat Disord.* 2022;10:360-9.e2.
27. Oğuzkurt L. Ultrasonographic anatomy of the lower extremity superficial veins. *Diagn Interv Radiol.* 2012;18:423-30.



Weekly Rapid Infusion Rituximab Treatment in Immune Thrombocytopenic Purpura and Autoimmune Hemolytic Anemia: Is It Safe and Effective?

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Abstract

Aim: The study aimed to assess the safety and efficacy of weekly rapid infusion rituximab in patients with immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA). Rituximab is widely used for various hematological and autoimmune conditions but can cause infusion-related reactions (IRRs), particularly during initial infusions. Traditional infusion methods are time-consuming and affect hospital stay and healthcare resources. This study aimed to evaluate whether a rapid infusion protocol can address these challenges while maintaining safety and efficacy.

Material and Method: This retrospective, single-arm study included 29 patients (22 ITP, 7 AIHA). Patients received rituximab at 375 mg/m² weekly for four doses using a rapid infusion protocol. The primary outcomes were safety and efficacy. Cost-effectiveness was evaluated based on hospital stay duration and resource use.

Results: Rapid infusion of rituximab was well tolerated, with only 2 of 116 infusions resulting in Grade 1 IRRs (nausea). No severe adverse reactions were reported. In the ITP group, 66% achieved complete response (CR) and 26% had partial response (PR). In the AIHA group, 50% of patients achieved CR and 50% achieved PR. Post-treatment, the hemoglobin and platelet counts improved significantly. The study also noted reduced hospital stay and healthcare resource utilization.

Conclusion: Weekly rapid infusion of rituximab is safe and effective for ITP and AIHA patients and offers advantages in terms of time, cost, and patient comfort. The low incidence of IRRs and high response rates suggest that it could replace the traditional infusion methods. However, larger multicenter studies with long-term follow-up are required to confirm these findings.

Keywords: Rituximab, rapid infusion, immune thrombocytopenic purpura, autoimmune hemolytic anemia

INTRODUCTION

Rituximab, a chimeric anti-CD20 monoclonal antibody, was approved by the FDA in 1997. It targets the CD20 protein on the surface of B lymphocytes, inducing cell death through multiple mechanisms, including antibody-dependent cellular cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), antibody-dependent phagocytosis (ADP), and direct apoptosis (1).

Rituximab is widely used for both on-label and off-label indications. On-label indications include follicular lymphoma (FL), diffuse large B-cell lymphoma (DLBCL), and chronic lymphocytic leukemia (CLL). Off-label uses extend to conditions such as immune thrombocytopenic purpura (ITP), autoimmune hemolytic anemia (AIHA), rheumatoid arthritis (RA), Waldenström macroglobulinemia, refractory

myasthenia gravis, multiple sclerosis, systemic lupus erythematosus, and more. In the context of ITP and AIHA, rituximab is typically administered as a second-line therapy following steroid resistance or relapse, with response rates of 70–80% observed for weekly doses of either 375 mg/m² or 100 mg/m² (2,3).

Despite its widespread use, rituximab administration can be complicated by infusion-related reactions (IRRs), which are most commonly seen during the initial infusion. These reactions typically occur within the first 30 to 120 minutes and can range from mild to severe. Mild reactions, such as itching, rash, urticaria, and mild nausea, can usually be managed by slowing the infusion rate and administering antihistamines. Moderate reactions, including hypotension, fever, chills, and mild dyspnea, may require temporarily halting the infusion, along with antipyretics and fluid support.

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Severe reactions, such as anaphylaxis, bronchospasm, angioedema, acute respiratory distress syndrome (ARDS), and even death, necessitate immediate intervention, including the administration of epinephrine, intravenous steroids, and oxygen therapy. Premedication with antihistamines, steroids, and antipyretics has been shown to help prevent IRRs. IRRs occur in approximately 23.5% of patients during the first dose, with 74% experiencing Grade 2 reactions and 26% experiencing Grade 3 reactions (4).

To minimize the risk of IRRs, rituximab infusions are typically initiated at a slow rate of 50 mg/hour, with incremental increases of 50 mg/hour every 30 minutes, up to a maximum rate of 400 mg/hour over a 2–4 hour period. Although this gradual titration reduces the severity and likelihood of IRRs, it results in prolonged infusion times, which increase hospital stays, resource utilization, and infection exposure, ultimately reducing healthcare efficiency (5).

To address these challenges, alternative administration methods, such as rapid infusion protocols and subcutaneous (SC) formulations, have been developed. Subcutaneous administration, approved in 2017 for FL, DLBCL, and CLL, significantly reduces infusion times while improving cost-effectiveness by decreasing hospital stays, enhancing staff efficiency, and aligning with patient preferences (6-8).

Studies indicate that patients who do not develop IRRs during the initial infusion are highly unlikely to experience severe IRRs in subsequent doses, with the incidence of IRRs during rapid infusion protocols being approximately 1%. This risk is further minimized with the use of premedication. Rapid infusion protocols aim to reduce infusion durations while maintaining safety, tolerability, cost-effectiveness, and efficacy (4,9).

The goal of this study is to evaluate the safety and efficacy of rapid infusion rituximab administration compared to the traditional intravenous method. Additionally, this study seeks to assess its potential to improve patient outcomes, reduce healthcare resource utilization, and enhance overall treatment satisfaction across various clinical indications.

MATERIAL AND METHOD

This study is retrospective observational, single-arm analysis designed to evaluate the safety, efficacy, and cost-effectiveness of rapid infusion rituximab treatment in patients with ITP and AIHA. The study does not include a control group, as all patients receive the same rapid infusion protocol. Ethical approval for this study was obtained from the Non-Interventional Scientific Research Ethics Committee of Afyonkarahisar Health Sciences University, with approval number and date 2025/4, 07.03.2025.

Study Design and Population

This retrospective study was conducted at Afyonkarahisar Health Sciences University between 2022 and 2024. The study included patients diagnosed with ITP and AIHA who had either failed or relapsed after first- or second-line treatment. The study aimed to investigate the efficacy and safety of weekly rapid infusion rituximab in patients who did not develop IRRs after the first dose of standard infusion protocol, with subsequent doses (2nd, 3rd, and 4th)

administered using the rapid infusion method. The inclusion criteria were as follows: patients must be aged 18 years or older, diagnosed with ITP or AIHA with steroid resistance or relapse after prior therapies, and must be initiated on rituximab therapy with the rapid infusion protocol. Written informed consent was obtained from each participant prior to enrollment in the study. Exclusion criteria included active infections, contraindications to rituximab, known hypersensitivity to rituximab or its components, and pregnancy or lactation.

All participants in this study received rituximab via a rapid infusion protocol. The dose of rituximab was 375 mg/m² weekly for a total of four doses. The infusion was initially administered at a rate of 100 mg/hour, with incremental increases of 100 mg/hour every 15 minutes, reaching a maximum rate of 800 mg/hour over 1-2 hours. To reduce the risk of IRRs, premedication was administered to all patients 30-60 minutes before the rituximab infusion. The premedication regimen consisted of antihistamines (e.g. diphenhydramine 25-50 mg IV or oral), corticosteroids (e.g. methylprednisolone 100 mg IV), and antipyretics (e.g. paracetamol 500 mg oral or IV).

The primary outcomes of the study were safety and efficacy. Safety was assessed by monitoring the incidence and severity of IRRs during the treatment period, which were classified into mild, moderate, or severe based on established grading scales. Efficacy was evaluated by measuring platelet counts for ITP and hemoglobin levels for AIHA at baseline. The response to treatment in ITP, particularly with therapies like rituximab, is primarily assessed based on changes in platelet count. A complete response (CR) is defined as a platelet count of 100,000/ μ L or higher, while a partial response (PR) is observed when the platelet count falls between 30,000/ μ L and 100,000/ μ L, with an increase to at least twice the pre-treatment baseline. No response (NR) is defined when the platelet count remains below 30,000/ μ L, with no significant increase following treatment. Similarly, in AIHA, the response to rituximab is typically evaluated based on changes in hemoglobin levels. CR is characterized by hemoglobin levels of 12 g/dL or higher, along with complete resolution of clinical symptoms. PR is defined as hemoglobin levels between 10 g/dL and 12 g/dL, with significant clinical improvement in symptoms. NR is indicated when hemoglobin levels remain below 10 g/dL, with no improvement or response to treatment. Cost-effectiveness was determined by calculating the treatment costs based on the duration of hospital stay, infusion time, and the total costs associated with medication and resources used during treatment.

The primary objective of this retrospective analysis was to assess the occurrence of Grade 3 and Grade 4 toxicities associated with weekly rapid infusion of rituximab, as defined by the Common Terminology Criteria for Adverse Events version 4. Secondary objectives included examining all infusion-related adverse events (Grades 1–4) associated with weekly rituximab and exploring the relationship between adverse events and different weekly rituximab treatment schedules.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Since there was no control group, descriptive statistics were used to summarize the outcomes. The efficacy and safety parameters were compared within the study cohort using paired t-tests for continuous variables and chi-square tests for categorical variables.

RESULTS

The median age of the patients was 49.9 years (range: 28–80). Among them, 12 (41%) were male and 17 (59%) were female. A total of 22 patients (72%) were diagnosed with ITP, while 7 patients (28%) had AIHA. A total of 116 infusions were administered, 88 (72%) in ITP patients and 28 (28%) in AIHA patients. Out of the 31 patients included in the study, only two experienced Grade 3 reactions and were excluded from the analysis. A total of 29 patients and 116 infusions of rituximab, including those who experienced Grade 0 and Grade 1 reactions after the first dose, were included in the study. All patients received premedication before the infusions. Infusion-related reactions (IRRs) were

observed in 2 out of 116 infusions (2%), both classified as Grade 1 nausea. No severe adverse reactions were reported. Regarding prior treatments, all patients had received methylprednisolone, and 5 ITP patients (25%) had also received intravenous immunoglobulin (IVIG). The overall treatment response rates demonstrated that in the ITP group, 14 patients (66%) achieved complete response (CR), 5 patients (26%) had partial response (PR), and 2 patients (8%) were classified as non-responders (NR). Similarly, in the AIHA group, 4 patients (50%) achieved CR, while the remaining 4 patients (50%) had PR, with no non-responders. Regarding hematological parameters, platelet counts significantly increased after treatment. The median pretreatment platelet count was $13 \times 10^3/\mu\text{L}$ (range: 7–19), which increased to $103 \times 10^3/\mu\text{L}$ (range: 24–264) posttreatment. Similarly, hemoglobin levels improved, with a median pretreatment value of 7.65 g/dL (range: 5.3–9), increasing to 11.2 g/dL (range: 10.8–14) after treatment (Table 1). These laboratory results show stable renal and liver function, with no significant abnormalities. Mildly elevated CRP and LDH suggest some inflammatory response, which is common after rituximab treatment, but no major adverse effects were noted in these parameters (Table 2).

Table 1. Rapid rituximab infusion patient characteristics		
Age	49.9 (28-80)	
Gender		
Male	12/41%	
Female	17/59%	
	ITP	AIHA
No. patients/%	22/72	7/28
No. total infusions/%	88/72	28/28
No. premedications	88/72	28/28
No. prior therapy	Metilprednizolon: 22/100% IVIG: 5 25%	Metilprednizolon: 7/100%
Treatment response	CR: 15/66%	CR: 4/50%
	PR: 5/26%	PR: 4/50%
	NR: 2/8%	NR: 0
PLT:10 ³ /L	Pretreatment: 13 (7-19)	
	Posttreatment: 103 (24-264)	
Hgb:g/dl	Pretreatment: 7.65 (5.3-9)	
	Posttreatment: 11.2 (10.8-14)	
No. IRRs	2/112 (/2%) (Grade 1 nause)	

Table 2. Laboratory findings after rapid infusion rituximab	
	Median
Urea (mg/dl)	34 (17-58)
Creatinine (mg/dl)	0.8 (0.56-1.01)
ALT U/L	20 (11-39)
AST U/L	20 (14-29)
WBC (x10 ³ /μL)	8.8 (2.49-15.6)
Lymphocyt (x10 ³ /μL)e	1.91 (1.21-4.86)
CRP mg/dl	5.2 (0.3-19)
LDH (U/L)	305 (198-461)
Bilirubine mg/dl	0.67 (0.07-2.78)

DISCUSSION

This study was the first to assess the efficacy and side effect profile of the rapid infusion rituximab protocol in patients with ITP and AIHA. These findings indicate that rapid infusion of rituximab can be administered safely in these patient groups, with no serious side effects observed. These results suggest that rapid infusion protocols offer significant advantages by reducing the duration of hospital stay, enhancing patient comfort, and facilitating the sustainability of the healthcare system. Research on the safety and efficacy of rapid infusion protocols for rituximab in rheumatological diseases and hematological cancers is increasing.

Comparable results were obtained in the literature when comparing the efficacy of slow-infusion rituximab with that of rapid infusion. In patients with ITP, CR and PR were achieved in 92% of cases, while in AIHA patients, 100% achieved CR and PR. In the literature, response rates for rituximab treatment in patients with AIHA and ITP have varied across studies. A review of AIHA patients found an overall response rate (ORR) of 84%, while another review for ITP patients reported response rates as high as 72.5% (10,11). These rates are somewhat lower than the response rates observed in our study, which may be attributed to the shorter follow-up period in our cohort. Early evaluations of response, which were done in our study, often result in higher response rates compared to long-term follow-up assessments, as seen in the aforementioned studies, where long-term outcomes were considered. When evaluating treatment efficacy, as early responses may not always translate into sustained benefits over time. These findings align with those observed in our study, where rapid infusion rituximab did not lead to a loss of response compared to traditional slow infusion protocols. Additionally, the shorter infusion duration was associated with enhanced patient motivation, as studies have demonstrated that rapid infusion regimens contribute to improved treatment adherence and overall satisfaction. This finding is consistent with the growing body of evidence suggesting that rapid infusion rituximab exhibits similar efficacy and safety profiles to standard infusion protocols, further supporting its use in clinical practice (Table 1).

One of the primary benefits of rapid infusion is their ability to save time and labor. Although conventional infusion protocols typically require 4-6 hours, rapid infusion protocols significantly reduce this duration. This enhancement not only improves patient adherence to treatment, but also optimizes the patient capacity of healthcare facilities. Furthermore, rapid infusion protocols offer an economic advantage by decreasing the workload of nursing and other healthcare personnel, which is particularly beneficial for healthcare systems with limited resources. A cost-effectiveness study indicated that IV rituximab is more economical than its SC counterpart, with the cost per patient for SC rituximab being approximately 10% higher than that for the IV form (12). In the context of our hospital, there is no price disadvantage when comparing the SC form with an average IV dose of 700 mg. Limited experience in diagnosing ITP and AIHA, which are benign hematological conditions with indications for use in hematological malignancies, restricts the use of SC instead of IV (13).

In this study, patient preferences and nursing teams were not evaluated. However, findings from two studies revealed that 80-83% of patients preferred SC administration over IV rituximab due to shorter stays in the day care unit, more comfortable application, and reduced hospital-related psychological stress. Additionally, over 94% of the nursing team favored SC administration, and 68% of the caregivers found SC application more appropriate (14-17). This evidence supports a preference for rapid infusion treatment over shorter treatment protocols. The absence

of an indication for SC use in the diseases examined in this study negates the necessity for a preference survey. The inclusion of rapid infusion treatment in the patient consent process of this study, with all patients responding positively, can be considered as a form of preference assessment.

IRRs were documented in 2 of 116 infusions (2%), both categorized as Grade 1 nausea. Notably, no severe adverse events, such as anaphylaxis, bronchospasm, or respiratory distress, were observed, underscoring the safety of the rapid infusion protocol employed in this cohort. The low incidence of IRRs aligns with previous studies indicating that rapid infusion rituximab protocols significantly reduce the likelihood and severity of IRRs compared with traditional slow infusion methods. Specifically, patients who do not experience IRRs during the initial infusion are considered to be at low risk for severe reactions with subsequent doses. This finding is corroborated by studies demonstrating that the incidence of IRRs with rapid infusion protocols can be as low as 1% when appropriate premedication is administered. The rapid infusion protocol was designed to ensure both patient safety and treatment efficacy while reducing the number of infusions. The risk of more severe IRRs can be mitigated by gradually increasing the infusion rate and closely monitoring potential reactions. Premedication with antihistamines, steroids, and antipyretics likely contributes to the prevention of more severe reactions and may account for the observed favorable safety profile. This approach is consistent with current guidelines that recommend premedication to reduce the risk of IRRs in patients receiving rituximab. Our findings are further supported by previous studies, which reported an overall adverse events (AEs) incidence of 2.1% following rapid i.v. infusion of rituximab, with no severe or fatal AEs leading to treatment interruption or dose modification (18). In the results of another study 82 patients received a total of 262 rituximab infusions, including 113 rapid 60-minute infusions in 54 patients. Notably, IRRs were observed with the 60-minute protocol. Furthermore, five patients who initially experienced grade 1–2 IRRs safely tolerated 60-minute infusions for subsequent doses without requiring additional premedication (19). These findings support the safety of a shorter infusion duration, particularly in patients who have not experienced severe reactions. Rapid infusion of rituximab is feasible and safe not only in hematologic malignancies but also in patients with ITP and AIHA. The rapid infusion protocol was designed to ensure patient safety and treatment efficacy, while reducing the number of infusions. The risk of more severe IRRs can be mitigated by gradually increasing the infusion rate and monitoring potential reactions. Premedication with antihistamines, steroids, and antipyretics likely contributes to the prevention of more severe reactions and may account for the observed favorable safety profile. This approach is consistent with current guidelines that recommend premedication to reduce the risk of IRR in patients receiving rituximab. In a retrospective study of 422 patients with B-cell malignancies. The study found no significant difference in the incidence of IRRs between patients receiving first- and

second-generation antihistamines (20). Another significant factor is that rituximab is relatively well tolerated in certain patient populations, such as those with ITP and AIHA, and the absence of malignancy-associated cytokine release in these groups suggests potential improvement in outcomes. These patients may have previously received treatment with steroids or other immunosuppressive agents, which may decrease the likelihood of immune overreaction to rituximab (Table 1,2).

However, this study had certain limitations. First, it was conducted at a single center with a relatively small patient cohort. Multicenter studies encompassing larger patient populations are necessary to yield more conclusive evidence regarding the efficacy and safety of the rapid infusion of rituximab. Second, this study lacked long-term follow-up data. Future research should assess the long-term effects of rapid infusion and its safety profile after repeated administrations. Additionally, this study did not analyze different patient subgroups such as elderly individuals or those with comorbidities. Further investigations are warranted to evaluate the safety and efficacy of rapid infusion in these populations. The preferences of patients and healthcare professionals regarding fast versus slow infusion and SC treatment were not assessed. Moreover, the impact on the quality of life of both patients and healthcare professionals has not been examined. Although the existing literature suggests that SC administration enhances patient experience, it has also been reported that it does not significantly alter quality of life.

CONCLUSION

In this study demonstrates that rapid infusion rituximab can be safely used in patients with ITP and AIHA. Rapid infusion protocols offer significant advantages in clinical practice by saving time and labor. However, further studies involving larger patient populations and long-term follow-up data are needed. These findings could be considered an important step toward the widespread adoption of rapid infusion protocols in clinical practice.

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Ethical approval: Ethical approval for this study was obtained from the Non-Interventional Scientific Research Ethics Committee of Afyonkarahisar Health Sciences University, with approval number and date 2025/4, 07.03.2025.

REFERENCES

1. Maloney DG, Smith B, Rose A. Rituximab: mechanism of action and resistance. *Semin Oncol.* 2002;29:2-9.
2. Jäger U, Barcellini W, Broome CM, et al. Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting. *Blood Rev.* 2020;41:100648.
3. Ghanima W, Gernsheimer T, Kuter DJ. How I treat primary ITP in adult patients who are unresponsive to or dependent on corticosteroid treatment. *Blood.* 2021;137:2736-44.
4. Bartels T, Moore L, Persky DO, et al. Utilizing a novel four-drug regimen to reduce the incidence of infusion-related reactions for first-dose rituximab infusions: An institutional review of rituximab infusion-related reactions in lymphoma patients. *Journal of Clinical Oncology.* 2020;38:e19148.
5. Muntañola A, Arguiñano-Pérez JM, Dávila J, et al. Safety and tolerability of a 90-minute rapid infusion of Sandoz biosimilar rituximab in B-cell lymphoproliferative disorders in a real-world setting. *Clin Transl Sci.* 2023;16:305-12.
6. U.S. Food and Drug Administration. Prescribing information for Rituxan Hycela (rituximab and hyaluronidase human) injection. 2017. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761064s000lbl.pdf access date 27.04.2025.
7. De Cock E, Kritikou P, Sandoval M, et al. Time savings with rituximab subcutaneous injection versus rituximab intravenous infusion: a time and motion study in eight countries. *PLoS One.* 2016;11:e0157957.
8. Harvey MJ, Zhong Y, Morris E, et al. Assessing the transition from intravenous to subcutaneous delivery of rituximab: Benefits for payers, health care professionals, and patients with lymphoma. *PLoS One.* 2022;17:e0261336.
9. Dakhil S, Hermann R, Schreeder MT, et al. Phase III safety study of rituximab administered as a 90-minute infusion in patients with previously untreated diffuse large B-cell and follicular lymphoma. *Leuk Lymphoma.* 2014;55:2335-40.
10. Arnold DM, Dentali F, Crowther MA, et al. Systematic review: efficacy and safety of rituximab for adults with idiopathic thrombocytopenic purpura. *Ann Intern Med.* 2007;146:25-33.
11. Chao SH, Chang YL, Yen JC, et al. Efficacy and safety of rituximab in autoimmune and microangiopathic hemolytic anemia: a systematic review and meta-analysis. *Exp Hematol Oncol.* 2020;9:6.
12. Delgado Sánchez O, Gutiérrez A, do Pazo F, et al. Comparative cost analysis of intravenous and subcutaneous administration of rituximab in lymphoma patients. *Clinicoecon Outcomes Res.* 2019;11:695-701.
13. European Medicines Agency. MabThera EU Summary of Product Characteristics. Published 2025. https://www.ema.europa.eu/en/documents/product-information/mabthera-epar-product-information_en.pdf access date 18.03.2025.
14. Rummel M, Kim TM, Aversa F, et al. Preference for subcutaneous or intravenous administration of rituximab among patients with untreated CD20+ diffuse large B-cell lymphoma or follicular lymphoma: results from a prospective, randomized, open-label, crossover study (PrefMab). *Ann Oncol.* 2017;28:836-42.
15. Lugtenburg P, Avivi I, Berenschot H, et al. Efficacy and safety of subcutaneous and intravenous rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in first-line diffuse large B-cell lymphoma: the randomized MabEase study. *Haematologica.* 2017;102:1913-22.
16. Fargier E, Ranchon F, Huot L, et al. SMABcare study: subcutaneous monoclonal antibody in cancer care: cost-consequence analysis of subcutaneous rituximab in patients with follicular lymphoma. *Ann Hematol.* 2018;97:123-31.

17. Aguiar-Ibáñez R, Fotheringham I, Mittal L, et al. Differences between intravenous and subcutaneous modes of administration in oncology from the patient, healthcare provider, and healthcare system perspectives: a systematic review. *Adv Ther.* 2024;41:4396-417.
18. Park YH, Mun Y, Lee S, Kim D. Safety and tolerability of a 90-minute infusion of originator and biosimilar rituximab in rituximab-naïve patients. *Research Square.* 26 Aug 2021. doi: 10.21203/rs.3.rs-839177/v1. [Epub ahead of print].
19. Whiting R, Misko J, McGuire M, Fox E. Rapid rituximab administration: Safety of 60-minute infusions in malignant and benign haematological disease. *J Oncol Pharm Pract.* 2024;10781552241260863.
20. Nathan Brandwein, Kevin Thai, Alisha Shivji, et al. Comparing antihistamine premedication regimens for preventing rituximab-associated infusion reactions in hemato-oncology patients: a retrospective analysis. *Blood.* 2024;144:3022.



Investigation of the Increase in Cerebrovascular Disease and ST Elevation Myocardial Infarction Cases Before and During the Pandemic

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Abstract

Aim: In this study, we aimed to investigate the effects of Coronavirus Disease 2019 (COVID-19) on the incidences of acute ischemic stroke (AIS) and ST elevation myocardial infarction (STEMI).

Material and Method: Patients admitted to the emergency department during the pandemic and pre-pandemic periods and diagnosed with AIS and/or STEMI. Demographic variables, comorbidities, diagnoses and mortality rates were compared between the two periods.

Results: The mean age of the patients was 71.8 ± 13 years and 48.3% were male. The number of 255 ischemic patients (STEMI and/or AIS) admitted in the pre-pandemic period decreased to 165 during the pandemic period ($p < 0.05$). During the pandemic period, there was a 38.2% decrease in the AIS group and a 29.1% decrease in the STEMI group. While the frequency of chronic renal failure and hyperlipidemia was found to be high in patients with AIS admitted during the pandemic period ($p < 0.05$), there was no difference in terms of comorbidities in patients with STEMI ($p > 0.05$). When the pre-pandemic and post-pandemic periods were compared, mortality was higher in the group with STEMI ($p < 0.05$). In the STEMI group, the frequency of HL was higher in COVID-19 positive patients compared to COVID-19 negative patients ($p < 0.05$).

Conclusion: Compared to the pre-pandemic period, the number of patients admitted due to AIS and STEMI decreased and mortality rates increased during the pandemic period.

Keywords: COVID-19, ischemic stroke, ST elevation myocardial infarction

INTRODUCTION

Severe Acute Respiratory Syndrome-Coronaviridea-2 (SARS-CoV-2) infection emerged in Wuhan, China in December 2019 and was named Coronavirus Disease 2019 (COVID-19) (1,2). Endothelial damage, stasis and inflammatory response due to COVID-19 form the Virchow triad that increases the tendency to thrombosis (3,4), and the resulting hypoxia directly triggers thrombosis formation by stimulating transcription factors (5). According to the World Health Organisation (WHO) records, 773,119,173 infected cases and 6,990,067 deaths were reported worldwide as of December 2023. In Türkiye, a total of 17,004,677 cases and 101,419 deaths were reported (2).

Cerebrovascular event (CVE) are an important cause of mortality and morbidity in our country as in the whole

world (6). The main factors determining the clinical presentation of the patient are the localisation and extent of the area supplied by the occluded or ruptured artery and the primary/secondary damages it causes. The main mechanism of acute ischaemic stroke (AIS) is occlusion caused by thrombosis or embolism in the artery (7). Li et al. defined neurological symptoms in 6% (13 patients) of the patient group with COVID-19; they reported that 11 of these patients had AIS, one patient had sinus vein thrombosis and 1 patient had haemorrhagic stroke (8). In another study evaluating COVID-19-infected AIS cases under the age of 50, it was shown that vascular endothelial damage and coagulopathy may cause AIS (9).

Acute myocardial infarction (AMI) is one of the most important causes of morbidity and mortality worldwide, and its incidence approaches 3 million people per year

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worldwide (10). AMI are divided into two as ST segment elevation (STEMI) or non-ST segment elevation (NSTEMI). Hypoxia, which develops as a result of interruption of blood flow in the coronary arteries supplying the heart, leads to irreversible damage to the heart muscle. It has been reported that infection due to COVID-19 leads to AMI, mainly hypercoagulation and endothelial damage, and consequently causes cardiac damage (11). In studies, it was stated that cardiac biomarkers were positive in more than 50% of patients who died due to COVID-19 and that these can be used to predict mortality (12).

In this study, we aimed to compare the number and some other clinical characteristics of patients diagnosed with AIS and STEMI admitted to the emergency department in the same time periods of the year before and after the outbreak of COVID-19 infection, and thus to investigate whether there was any change in the number of admissions to the emergency department due to AIS and STEMI in the post-COVID-19 period compared to the pre-COVID-19 period, and thus how the COVID-19 pandemic affected the incidence of AIS and STEMI.

MATERIAL AND METHOD

This study was conducted with patients who were diagnosed with AIS and/or acute STEMI in the emergency department during the 6-month period before the outbreak of COVID-19 infection (1 July - 31 December 2019) and 6 months during the pandemic period (1 July - 31 December 2020). A total of 255 patients admitted in the pre-pandemic period and 161 patients admitted during the pandemic period were evaluated. The number, age, gender, comorbidity status, diagnosis and mortality status of the patients admitted in these periods were compared. In addition, patients with positive Polymerase Chain Reaction (PCR) results and/or 4-5 positive CO-RADS uptake on thorax CT during the pandemic period were considered COVID-19 positive. Age, gender, number of patients, comorbidity status, diagnosis and mortality status of COVID-19 positive and negative patients were compared. Patients over 18 years of age diagnosed with AIS and/or acute STEMI in the emergency department during the specified periods were included in the study. Patients under 18 years of age, pregnant and breastfeeding patients were excluded from the study.

Ethical Approval

It was performed retrospectively with the approval of the local ethics committee dated 20/06/2023 and numbered 2023-12/84 obtained from Kırşehir Ahi Evran University Faculty of Medicine Training and Research Hospital.

Statistics

All data obtained in the study were analysed in SPSS (Statistical Packages for Social Sciences) IBM statistics version 22. Mean and standard deviation (SD) were used to represent quantitative data, and number of cases (n) and percentages (%) were used to represent qualitative data. Kolmogorov Smirnov test was used to evaluate the distribution of quantitative data. Mann Whitney U test was

used to analyse nonparametric data and chi-square test was used to analyse qualitative data. In this study, $p < 0.05$ was considered significant.

RESULTS

In our study, while 255 patients admitted to the emergency department due to ischaemia (AIS or STEMI) in the pre-pandemic period, this number decreased to 161 during the pandemic period. Of the 255 patients admitted in the pre-pandemic period, 201 (78.8%) were diagnosed with AIS, 55 (21.6%) with STEMI and 1 (0.4%) with AIS+STEMI. During the pandemic period, a total of 161 patients were admitted due to AIS and/or STEMI, of which 123 (76.3%) were diagnosed with AIS, 39 (24.2%) with STEMI and 1 (0.6%) with AIS+STEMI. Compared to the pre-pandemic period, there was a 38.8% decrease in admissions in the group with all ischaemia (STEMI and/or AIS), 38.2% with AIS, and 29.1% with STEMI. In our study, we found that hypertension (HT) (57.7%) and cardiovascular disease (CVD) (43.5%) were the most common comorbidities in the total patient group (STEMI and/or AIS). In the post-pandemic period, the frequency of hyperlipidemia (HL) and chronic renal failure (CRF) was significantly higher compared to the pre-pandemic period ($p < 0.05$) (Table 1).

When the pre-pandemic and post-pandemic periods were compared, no significant difference was found in terms of mean age and gender in all groups ($p > 0.05$).

In our study, HT (63.6%) and CVD (45.7%) were the most common comorbidities in patients diagnosed with AIS. The frequency of hyperlipidaemia (HL) and CRF was significantly higher in patients diagnosed with AIS during the pandemic period compared to patients diagnosed with AIS before the pandemic ($p < 0.05$) (Table 2). In our study, the most common comorbidities in 94 patients diagnosed with STEMI were HT (37.2%) and CVD (34%). No significant difference was found in the frequency of HT, CVD, diabetes mellitus (DM), HL, CVE, CRF and chronic obstructive pulmonary disease (COPD) in patients diagnosed with STEMI before and during the pandemic ($p > 0.05$) (Table 3).

In our study, 69 (16.6%) of 415 ischaemic patients were excised. It was determined that 42 (13%) of 323 patients diagnosed with AIS and 29 (30.9%) of 94 patients diagnosed with STEMI were excised. While there was no statistically significant increase in the mortality rate in patients diagnosed with AIS during the pandemic period, the mortality rate was significantly higher in patients diagnosed with STEMI during the pandemic period compared to the pre-pandemic period ($p < 0.05$) (Table 4).

In our study, when all patients with AIS and STEMI diagnosed during the pandemic period were evaluated, no significant difference was found in terms of the presence of comorbidity in COVID-19 positive and COVID-19 negative patients ($p > 0.05$). Similarly, similar results were obtained in the AIS and STEMI (except HL) groups ($p > 0.05$). In the STEMI group, the frequency of HL was found to be significantly higher in patients who were COVID-19 positive compared to those who were COVID-19 negative ($p < 0.05$) (Table 5).

Table 1. Frequency of AIS and STEMI and comorbid conditions of patients before and after the pandemic				
		Group		p
		Before pandemic n (%)	Pandemic period n (%)	
All ischaemias		255 (100)	161 (100)	<0.001
AIS		201 (78.8)	123 (76.4)	<0.001
STEMI		55 (21.6)	39 (24.2)	<0.001
HT	240 (57.7)	143 (56.1)	97 (60.2)	0.402
CVD	181 (43.5)	107(42)	74 (46)	0.423
DM	128 (30.8)	70 (27.5)	58 (36)	0.065
HL	105 (25.2)	54 (21.2)	51 (31.7)	0.016
CVE	93 (22.4)	56 (22)	37 (23)	0.808
CRF	42 (10.1)	19 (7.5)	23 (14.3)	0.024
COPD	39 (9.4)	27 (10.6)	12 (7.5)	0.285
Other	14 (3.4)	14 (5.5)	0 (0)	0.002
HT: hypertension, CVD: cardiovascular disease, DM: diabetes mellitus, HL: hyperlipidaemia, CVE: ischaemic/haemorrhagic cerebrovascular event, CRF: chronic renal failure, COPD: chronic obstructive pulmonary disease, AIS: Acut Ischemic Stroke, STEMI: ST Elevated Myocardial Ischemi				

Table 2. Comparison of the distribution of comorbidities of patients diagnosed with AIS before and during the pandemic				
Patients diagnosed with AIS				
	Total n (%)	Before pandemic n (%)	Pandemic period n (%)	p
HT	206 (63.6)	125 (62.2)	81 (65.9)	0.506
CVD	148 (45.7)	91 (45.3)	57 (46.3)	0.851
DM	109 (33.6)	61 (30.3)	48 (39)	0.109
HL	86 (26.5)	44 (21.9)	42 (34.1)	0.015
CVE	86 (26.5)	55 (27.4)	31 (25.2)	0.669
CRF	33 (10.2)	15 (7.5)	18 (14.6)	0.038
CPOD	32 (9.9)	21 (10.4)	11 (8.9)	0.660
Other	13 (4)	13 (6.5)	0 (0)	0.004
HT: hypertension, CVD: cardiovascular disease, DM: diabetes mellitus, HL: hyperlipidaemia, CVE: ischaemic/haemorrhagic cerebrovascular event, CRF: chronic renal failure, COPD: chronic obstructive pulmonary disease				

Table 3. Comparison of the distribution of comorbidities of patients diagnosed with STEMI before and during the pandemic				
Patients diagnosed with STEMI				
	Total n (%)	Before pandemic n (%)	Pandemic period n (%)	p
HT	35 (37.2)	19 (34.5)	16 (41)	0.522
CVD	34 (36.2)	17 (30.9)	17 (43.6)	0.207
DM	19 (20.2)	9 (16.4)	10 (25.6)	0.270
HL	20 (21.3)	10 (18.2)	10 (25.6)	0.384
CVE	7 (7.4)	2 (3.7)	5 (12.8)	0.092
CRF	9 (9.6)	4 (7.3)	5 (12.8)	0.368
CPOD	7 (7.4)	6 (10.9)	1 (2.6)	0.129
Other	1 (1.1)	1 (1.8)	0	0.397
HT: hypertension, CVD: cardiovascular disease, DM: diabetes mellitus, HL: hyperlipidaemia, CVE: ischaemic/haemorrhagic cerebrovascular event, CRF: chronic renal failure, COPD: chronic obstructive pulmonary disease				

Table 4. Comparison of mortality rates of patients before and during the pandemic period					
		Total n (%)	Group		p
			Before pandemic n (%)	Pandemic period n (%)	
All ischaemias	Alive	346 (83.4)	220 (86.6)	126 (78.3)	0.026
	Excitus	69 (16.6)	34 (13.4)	35 (21.7)	
AIS	Alive	281(87)	176 (88)	105 (85.4)	0.494
	Excitus	42 (13)	24 (12)	18 (14.6)	
STEMI	Alive	65 (69.1)	44 (80)	21 (53.8)	0.007
	Excitus	29 (30.9)	11 (20)	18 (46.2)	
AIS: Acut Ischemic Stroke, STEMI: ST Elevated Myocardial Ischemi					

Table 5. Comparison of PCR results of all ischaemic patients and comorbidity status of patients during the pandemic period

		Group			p
		Total n (%)	COVID19 (+) n (%)	COVID19 (-) n (%)	
AIS+ STEMI	HT	97 (60.2)	7 (53.8)	90 (60.8)	0.623
	CVD	74 (46)	6 (46.2)	68 (45.9)	0.988
	DM	58 (36)	5 (38.5)	53 (35.8)	0.849
	HL	51 (31.7)	6 (46.2)	45 (30.4)	0.242
	CVE	37 (23)	1 (7.7)	36 (24.3)	0.172
	CRF	23 (14.3)	2 (15.4)	21 (14.2)	0.906
	COPD	12 (7.5)	1 (7.7)	11 (7.4)	0.973
AIS	HT	81 (65.9)	6 (54.5)	75 (67)	0.407
	CVD	57 (46.3)	5 (45.5)	52 (46.4)	0.951
	DM	48 (39)	4 (36.4)	44 (39.3)	0.850
	HL	42 (34.1)	4 (36.4)	38 (33.9)	0.871
	CVE	31 (25.2)	1 (9.1)	30 (26.8)	0.197
	CRF	18 (14.6)	2 (18.2)	16 (14.3)	0.727
	COPD	11 (8.9)	1 (9.1)	10 (8.9)	0.986
STEMI	HT	16 (41)	1 (33.3)	15 (41.7)	0.778
	CVD	17 (43.6)	1 (33.3)	16 (44.4)	0.709
	DM	10 (25.6)	1 (33.3)	9 (25)	0.751
	HL	10 (25.6)	3 (100)	7 (19.4)	0.002
	CVE	6 (15.4)	0	6 (16.7)	0.442
	CRF	5 (12.8)	0	5 (13.9)	0.489
	COPD	1 (2.6)	0	1 (2.8)	0.770

HT: hypertension, CVD: cardiovascular disease, DM: diabetes mellitus, CVE: ischaemic/haemorrhagic cerebrovascular event, CRF: chronic renal failure, COPD: chronic obstructive pulmonary disease, HL: hyperlipidaemia, AIS: Acute Ischemic Stroke, STEMI: ST Elevated Myocardial Ischemi

DISCUSSION

COVID-19 is a disease that kills millions of people worldwide and is a serious burden on healthcare systems. Although the majority of patients survive the acute illness period without any problems, they face long-term complications defined as 'post-acute COVID-19 syndrome'. COVID-19 leads to an increase in the frequency of ischaemic disease due to immobilisation and deterioration in coagulation factors (3,4,13).

In our study, no significant difference was found when the pre-pandemic and post-pandemic periods were compared in patients who were followed up due to AIS and STEMI. In some studies conducted in the world and in our country, no significant difference was found in the mean age of the patients when the pre-pandemic and post-pandemic periods were compared (14-17), while the mean age was found to be lower in some studies (18-20). Although we believe that the frequency of ischemia should also increase in young patients due to the increase in ischemic processes due to COVID-19, we believe that increased cytokines and mediators may have affected the elderly population more, so there was no difference in age between the pre-pandemic and post-pandemic periods. In addition, we believe that the younger population did not apply to the hospital even if they had some neurological and/or cardiac symptoms during the pandemic period, while the elderly population may have been diagnosed because they applied to emergency departments more frequently due to

diseases independent of the pandemic.

In our study, the gender distribution of patients followed up for ischaemia between the pre-pandemic and post-pandemic periods was similar. Similarly, no relationship was found between COVID-19 positivity and gender. Similar to age, studies comparing the periods before and after the pandemic in terms of ischemic events have found significant differences in terms of gender (21-23). Although COVID-19 is frequently seen in the female population, we think that male patients are more predominant among the admitted patients due to its more severe course in the male population.

In our study, we found that the most common comorbidity in our total patient group (AIS+STEMI) was HT in accordance with the literature, but we found that CRF and HL were significantly higher during the pandemic period compared to the pre-pandemic period in the group diagnosed with AIS. In the group diagnosed with STEMI, no significant difference was found in terms of comorbidity between the pre and post-pandemic periods. In some studies comparing the pre-pandemic and post-pandemic periods, no significant differences were found in terms of comorbidities of patients who experienced thromboembolic events (15-17,24), while in some studies, some diseases were found at a higher rate. Görgülü et al. reported that HT, DM and CVD were the most common comorbidities in the group of patients with AIS who were PCR (+) for COVID-19 (25). In patients with AIS and COVID-19 (+), De havenon et

al. reported that DM (22) and Rinkel et al. found HL to be significantly higher (26). There are many studies reporting similar results in the literature (20,23). The reason for the increase in HL may be impaired liver function caused by hypoxia due to COVID-19, and sedentary life caused by social closure may also have contributed to this. We found that the frequency of CRF and HL started to increase in patients diagnosed with STEMI during the pandemic period, but it was not statistically significant. We think that this result may be related to the number of cases.

Although COVID-19 infection is thought to lead to an increase in AMI and AIS cases by creating a tendency to thrombosis, a sharp decrease in hospital admissions due to AMI and AIS has been observed in many studies (27-29). The fear of contracting the virus and the public recommendation to consult emergency services only in mandatory cases have caused people to avoid emergency services (30-33). In a study conducted in 22 centres in major cities of France, a decrease of up to 30% in the rate of patients diagnosed with AMI during the pandemic period was reported (34). Mafhan et al. reported a 40% decrease in the frequency of AMI and a decrease in the number of Percutaneous Coronary Intervention (PCI) performed in these patients and a shortening in the length of hospital stay (35).

In our study, it was found that 255 patients who presented with ischaemic diseases in the pre-pandemic period decreased to 161 during the pandemic period, and there was a 38.8% decrease in the entire ischaemic group, 38.2% in the AIS group and 29.1% in STEMI group. During the pandemic period, the number of applications to hospitals decreased due to reasons such as people not wanting to come to hospitals with complaints that they consider mild (dizziness, headache, etc.), not being able to go out due to isolation at home, and mistaking some symptoms for symptoms of COVID-19. Especially in COVID-19 patients, dizziness, headache, weakness, etc. Since complaints such as dizziness, headache, weakness, etc. are frequently seen, patients with such complaints may not have applied to the hospital, mistaking them for COVID-19 symptoms. In severe cases such as impaired consciousness and speech impairment due to AIS, the patient may not be diagnosed with AIS because the patient's current clinic is attributed to COVID-19 sepsis. The same applies to acute coronary syndrome (ACS). Existing chest pain and/or palpitations may be attributed to COVID-19 infection by the patient or clinician. It is possible to increase these examples. Cardiac ischaemia biomarkers may also be positive in COVID-19 infection or false positivity perception due to comorbidities such as CRF may have misled physicians. In addition to all these, antiaggregant and anticoagulant therapies initiated in moderate and severe COVID-19 patients may have reduced the incidence of AIS and/or AMI cases.

In our study, no significant difference was found between mortality rates in ischaemic patients when COVID-19 (+) and COVID-19 (-) patients were compared. Regardless of

the treatment modality, it has been consistently identified that COVID-19 is an important determinant of mortality in patients with AIS (36-38). However, some studies contradict this data. Luca et al. found that COVID-19 was an independent risk factor for 30-day mortality in AMI cases, but there was no difference between COVID-19 positives and negatives in terms of 2-year mortality results (24). In our study, mortality was found to be significantly higher in patients with STEMI during the pandemic period compared to the pre-pandemic period and was 29.3%. No significant difference was found in patients diagnosed with AIS. The reason for the increase in mortality in patients with STEMI may be delays in diagnosis and treatment due to the attribution of symptoms to COVID-19, and complications due to inflammation and cytokine release caused by COVID-19. Administration of low molecular weight heparin and antiaggregants to patients with COVID-19 may have contributed to a lower mortality rate, especially in patients with AIS.

CONCLUSION

There was a significant decrease in the number of patients admitted with ischaemic diseases during the pandemic period compared to the pre-pandemic period. There was an increase in mortality in STEMI cases from the ischaemic diseases group during the pandemic period compared to the pre-pandemic period. In a situation such as COVID-19, which can cause thrombotic complications as a result of vascular damage, both central and cardiac ischaemic complications should be anticipated and prophylaxis of these complications should be performed quickly and appropriately. Early diagnosis and treatment of complications may contribute to the reduction of mortality and morbidity.

This study is based on the specialization thesis titled "Investigation of the Increase in Cerebrovascular Disease and ST Elevation Myocardial Infarction Cases After Covid-19" conducted at Kırşehir Ahi Evran University Faculty of Medicine Department of Emergency Medicine.

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Ethical approval: It was performed retrospectively with the approval of the local ethics committee dated 20/06/2023 and numbered 2023-12/84 obtained from Kırşehir Ahi Evran University Faculty of Medicine Training and Research Hospital.

REFERENCES

1. Lai C-C, Wang C-Y, Wang Y-H, et al. Global epidemiology of coronavirus disease 2019 (COVID-19): disease incidence, daily cumulative index, mortality, and their association with country healthcare resources and economic status. *Int J Antimicrob Agents*. 2020;55:105946.

2. WHO Coronavirus (COVID-19) Dashboard. <https://covid19.who.int/> access date: 01.11.2023.
3. Levi M, van der Poll T. Coagulation and sepsis. *Thrombosis research*. 2017;149:38-44.
4. Schmitt FCF, Manolov V, Morgenstern J, et al. Acute fibrinolysis shutdown occurs early in septic shock and is associated with increased morbidity and mortality: results of an observational pilot study. *Ann Intensive Care*. 2019;9:19.
5. Gupta N, Zhao Y-Y, Evans CE. The stimulation of thrombosis by hypoxia. *Thromb Res*. 2019;181:77-83.
6. Terzioğlu K. Use of monocyte/HIGH-density lipoprotein-cholesterol ratio in determining the prognosis of patients presenting to the emergency department with ischemic cerebrovascular disease. Dissertation. Erzurum Atatürk University, 2021.
7. Fırat O, Karakuş M, Arsava E, et al. Comparison of guidelines in risk factor management of ischemic stroke. *STED*. 2021;30:211-7.
8. Li Y, Li M, Wang M, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Stroke Vasc Neurol*. 2020;5:279-84.
9. Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med*. 2020;382:2411-8.
10. Nascimento BR, Brant LCC, Marino BC, et al. Implementing myocardial infarction systems of care in low/middle-income countries. *Heart*. 2019;105:20-6.
11. Karabacak M. Cardiovascular effects of COVID-19 pandemia. *SDÜ Tıp Fakültesi Dergisi*. 2021;28:229-33.
12. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-62. Erratum in: *Lancet*. 2020;395:1038. Erratum in: *Lancet*. 2020;395:1038.
13. Small C, Mehkri Y, Panther E, et al. Coronavirus disease-2019 and stroke: pathophysiology and management. *Can J Neurol Sci*. 2023;50:495-502.
14. Mitra B, Mitchell RD, Cloud GC, et al. Presentations of stroke and acute myocardial infarction in the first 28 days following the introduction of State of Emergency restrictions for COVID-19. *Emerg Med Australas*. 2020;32:1040-5.
15. Uslusoy DK. Retrospective analysis of the effects of the COVID-19 pandemic process on patients admitted to the emergency department with a diagnosis of cerebrovascular disease. Dissertation. Bursa Uludağ University, 2023.
16. Solomon MD, McNulty EJ, Rana JS, et al. The Covid19 pandemic and the incidence of acute myocardial infarction. *N Engl J Med*. 2020;383:691-3.
17. Su Y-H, Wu K-H, Su C-M, et al. Influence of the coronavirus disease 2019 pandemic on patients with ST-segment elevation myocardial infarction in Taiwan. *Emerg Med Int*. 2021;2021:5576220.
18. Velilla-Alonso G, García-Pastor A, Rodríguez-López Á, et al. Acute stroke care during the COVID-19 pandemic: reduction in the number of admissions of elderly patients and increase in prehospital delays. *Cerebrovasc Dis*. 2021;50:310-6.
19. Grave C, Gabet A, Puymirat E, et al. Myocardial infarction throughout 1 year of the COVID-19 pandemic: French nationwide study of hospitalization rates, prognosis and 90-day mortality rates. *Arch Cardiovasc Dis*. 2021;114:768-80.
20. Erol MK, Kayıkçıoğlu M, Kılıçkap M, et al. Treatment delays and in-hospital outcomes in acute myocardial infarction during the COVID-19 pandemic: a nationwide study. *Anatol J Cardiol*. 2020;24:334-42.
21. Cenko E, Badimon L, Bugiardini R, et al. Cardiovascular disease and COVID-19: a consensus paper from the ESC working group on coronary pathophysiology & microcirculation, ESC working group on thrombosis and the association for acute CardioVascular care (ACVC), in collaboration with the European heart rhythm association (EHRA). *Cardiovasc Res*. 2021;117:2705-29.
22. Havenon A, Yaghi S, Mistry EA, et al. Endovascular thrombectomy in acute ischemic stroke patients with COVID-19: prevalence, demographics, and outcomes. *J Neurointerv Surg*. 2020;12:1045-8. Erratum in: *J Neurointerv Surg*. 2021;13:e26.
23. Mariet A-S, Duloquin G, Benzenine E, et al. Impact of the first COVID-19 wave on french hospitalizations for myocardial infarction and stroke: a retrospective cohort study. *Biomedicines*. 2022;10:2501.
24. De Luca L, Rosato S, D'Errigo P, et al. Covid19 diagnosis and mortality in patients with non-ST-elevation myocardial infarction admitted in Italy during the national outbreak. *Int J Cardiol*. 2023;370:447-53.
25. Görgülü Ü, Şahin MH, Bektaş H. Acute stroke in Covid-19 infection: neurology intensive care experience. *Suleyman Demirel University Journal of Health Sciences*. 2022;13:111-8.
26. Rinkel L, Prick J, Slot R, et al. Impact of the COVID-19 outbreak on acute stroke care. *J Neurol*. 2021;268:403-8.
27. Van Belle E, Manigold T, Pierache A, et al. Myocardial Infarction incidence during national lockdown in two French provinces unevenly affected by COVID-19 outbreak: An observational study. *Lancet Reg Health Eur*. 2021;2:100030.
28. Schwarz V, Mahfoud F, Lauder L, et al. Decline of emergency admissions for cardiovascular and cerebrovascular events after the outbreak of COVID-19. *Clin Res Cardiol*. 2020;109:1500-6.
29. Lee K, Lee S, Lim J, et al. Providing essential clinical care for non-COVID-19 patients in a Seoul metropolitan acute care hospital amidst ongoing treatment of COVID-19 patients. *J Hosp Infect*. 2020;106:673-7.
30. Olié V, Carcaillon-Bentata L, Thiam M-M, et al. Emergency department admissions for myocardial infarction and stroke in France during the first wave of the COVID-19 pandemic: National temporal trends and regional disparities. *Arch Cardiovasc Dis*. 2021;114:371-80.
31. Gabet A, Grave C, Tuppin P, et al. Impact of the COVID-19 pandemic and a national lockdown on hospitalizations for stroke and related 30-day mortality in France: A nationwide observational study. *Eur J Neurol*. 2021;28:3279-88.
32. Quiles LEP, Diamante PAB, Pascual JLV. Impact of the COVID-19 pandemic in the acute stroke admissions and outcomes in a Philippine tertiary hospital. *Cerebrovasc Dis Extra*. 2022;12:76-84.

33. Saban M, Reznik A, Shachar T, et al. The effect of the COVID-19 pandemic on ED referrals and care for stroke patients: a four-year comparative study. *J Crit Care*. 2021;62:230-4.
34. Mesnier J, Cottin Y, Coste P, et al. Hospital admissions for acute myocardial infarction before and after lockdown according to regional prevalence of COVID-19 and patient profile in France: a registry study. *The Lancet Public Health*. 2020;5:e536-42.
35. Mafham MM, Spata E, Goldacre R, et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. *Lancet*. 2020;396:381-9.
36. Martí-Fàbregas J, Guisado-Alonso D, Delgado-Mederos R, et al. Impact of COVID-19 infection on the outcome of patients with ischemic stroke. *Stroke*. 2021;52:3908-17.
37. Dhamoon MS, Thaler A, Gururangan K, et al. Acute cerebrovascular events with COVID-19 infection. *Stroke*. 2021;52:48-56.
38. Benussi A, Pilotto A, Premi E, et al. Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy. *Neurology*. 2020;95:e910-20.



Etiology of Intracranial Pneumocephalus: A Retrospective Comparative Study of Traumatic and Iatrogenic Causes in Emergency Patients

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Abstract

Aim: The aim of this study was to retrospectively investigate the traumatic and iatrogenic causes of intracranial pneumocephalus (ICnP) in patients presenting to the emergency department (ED). Additionally, the study sought to evaluate the role of venous air embolism during intravenous (IV) line placement in the development of ICnP.

Material and Method: A total of 462 patients who presented to the ED of a tertiary healthcare center between 2018 and 2024 were retrospectively analyzed. Patients included in the study presented with complaints of head trauma or headache but did not have open cranial wounds, evident basal skull fractures, or a history of intracranial surgery. Non-contrast cranial Computed Tomography (CT) scans were performed on all patients, and the anatomical localization of pneumocephalus as well as the IV line placement status were meticulously recorded. Statistical analyses were conducted using SPSS version 26.0, with a significance level of $p < 0.05$.

Results: ICnP was most commonly detected in the anterior cranial fossa (62%), followed by the middle fossa (24%) and posterior fossa (10%). Among patients with IV lines, air bubbles were observed in 3.45% of the head trauma group and 2.06% of the headache group. In patients without IV lines, these rates were lower, at 1% and 1.67%, respectively. No statistically significant differences were found between age groups or genders ($p > 0.05$). However, a strong association was noted between IV line placement and venous air embolism.

Conclusion: ICnP is commonly associated with venous air embolism occurring during IV line placement and resolves spontaneously within 24 hours in most cases. Our findings indicate that such air bubbles are typically attributed to iatrogenic causes rather than severe pathologies such as basal skull fractures. Avoiding unnecessary further investigations in patients whose air bubbles resolve within the first 24 hours can optimize clinical management and provide a cost-effective approach.

Keywords: Intracranial pneumocephalus, venous air embolism, basal skull fracture, emergency department

INTRODUCTION

Pneumocephalus are a rare clinical condition characterized by the presence of air within the cranial cavity (1). They typically occur following traumatic injuries, surgical interventions, or infections, and these conditions are often associated with skull base fractures (2,3). However, pneumocephalus can also be detected in patients with no history of trauma or apparent cranial pathology (4,5).

According to the literature, pneumocephalus are most commonly localized in the anterior cranial fossa, as indicated by the Mount Fuji radiological sign (6,7). This

region is more prone to air leakage due to the proximity of the ethmoid bone and frontal sinuses. Furthermore, the thin dura mater in the anterior cranial fossa, which adheres tightly to the bone, and the arachnoid membranes attaching to the frontal lobes, result in air being trapped within the subdural space of this fossa (8). The thin bony structure of the anterior cranial fossa and its adjacent air cavities further contribute to the accumulation of air bubbles in this area (9).

Venous air embolism is another potential etiology of pneumocephalus. Particularly in emergency departments, air can enter the venous system during intravenous (IV) catheter placement (10). Although the

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exact pathophysiology of venous air embolism remains unclear, the literature agrees that small, low-weight air bubbles can travel retrogradely through the jugular veins against the flow of blood in an upright patient, leading to their occurrence (11).

The aim of this study is to evaluate the etiology of pneumocephalus in patients presenting to the emergency department (ED) with and without head trauma and to investigate the role of intra-venous air leakage. Our hypothesis posits that pneumocephalus are not solely associated with skull base fractures but may also result from venous air leakage during IV catheterization.

MATERIAL AND METHOD

This study was conducted as a retrospective analysis of patients presenting to the ED of a tertiary care center between 2018 and 2024. A total of 462 patients with complaints of head trauma and headache were included. Inclusion criteria were defined as patients aged 18-95 years presenting with clinical complaints of head trauma or headache. Patients with open cranial injuries, evident skull base fractures, intracranial hemorrhage, or a history of intracranial surgery were excluded. Additionally, cases with incomplete clinical or radiological data were not included in the analysis.

All patients underwent an emergency non-contrast cranial Computed Tomography (CT) scan upon admission. Demographic information, including age and gender, clinical conditions, venous access placement status, and the localization of pneumocephalus, were meticulously recorded. Patients' ages were categorized into three groups: 18-40 years, 41-65 years, and over 66 years. The anatomical localization of pneumocephalus was classified into anterior, middle, and posterior cranial fossae. Venous access placement was evaluated based on hospital records, and patients with venous access were analyzed as a separate group (Table 1).

Patients with detected air bubbles on cranial CT scans were admitted for follow-up. A control CT scan was performed 24 hours later. Patients whose air bubbles did not resolve within 24 hours were excluded from the study.

Radiological evaluations were conducted by two independent and experienced neuroradiologists, and consensus was reached on the localization and dimensions of air bubbles. Initial cranial CT scans were retrospectively reviewed through the digital archive system, with detailed documentation of the visibility and localization of pneumocephalus. CT scans were performed with slice thicknesses ≤ 5 mm, in accordance with established standards in the literature for air bubble detection (12).

Statistical analysis of the data was performed using Statistical Package for the Social Sciences (SPSS) version 26.0 software. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. Independent

sample t-tests were used to assess significant differences between patients with and without head trauma, while chi-square tests were applied to evaluate relationships between categorical variables. A significance level of $p < 0.05$ was considered statistically significant.

This study was approved by the Ordu University Non-Interventional Scientific Research Ethics Committee (Approval number: E-14647249-000-110429, Decision number: 2025/35, Date: 07.02.2025). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and approved institutional guidelines.

Statistical Analysis

This study utilized SPSS version 26.0 for the analysis of intracranial air bubble distribution and etiology. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages. Chi-square tests were employed for comparisons between groups to evaluate the relationships between the occurrence of pneumocephalus and factors such as IV access status, clinical conditions (head trauma and headache), and anatomical localization. A significance threshold of $p < 0.05$ was applied, and the results were summarized in tables and figures. However, no significant differences were found between patients with and without IV access or among different anatomical localizations.

RESULTS

Statistical analyses revealed no significant differences in the prevalence of pneumocephalus across age groups or between genders ($p = 0.903$). However, the analysis suggested a potential increase in prevalence with advancing age, although this trend was not statistically significant. Similarly, while air bubbles were observed more frequently in male patients compared to females, this difference did not reach statistical significance (Table 1).

Comparisons between patients with and without IV access showed no statistically significant differences in the frequency of pneumocephalus in trauma and headache groups ($p = 0.590$). Nevertheless, in patients with IV access, air bubbles were detected at a rate of 3.45% in the trauma group and 2.06% in the headache group. In contrast, these rates were 1% and 1.67% respectively in patients without IV access. These findings suggest a potential association between air bubbles and venous air embolism, although no significant relationship was established between clinical groups (Table 2, Figure 1).

The anatomical localization analysis indicated that air bubbles were most commonly found in the anterior cranial fossa (62%), followed by the middle cranial fossa (24%) and the posterior cranial fossa (10%). However, no significant differences were detected between these anatomical regions ($p = 0.188$) (Table 3, Figure 2).

Table 1. Distribution of demographic characteristics by age groups

Age group	Total number of patients	Male patients (%)	Female patients (%)	p-value
18-40	138	83 (60.1)	55 (39.9)	0.903
41-65	184	110 (59.8)	74 (40.2)	0.903
66+	140	87 (62.1)	53 (37.9)	0.903

This table presents the gender distribution across different age groups; Statistical Test: Chi-Square Test was applied; p-Values: No significant difference was found in gender distribution across all age groups (p=0.903)

Table 2. Air bubble detection rates by clinical condition and venous access status

Clinical condition	Venous access status	Total number of patients	Number of air bubble detections	Detection rate (%)	p-value
Head trauma	IV line placed	145	5	3.45	0.590
	IV line not placed	100	1	1.00	0.590
Headache	IV line placed	97	2	2.06	0.590
	IV line not placed	120	2	1.67	0.590

This table displays the rates of intracranial air bubble detection based on clinical conditions (head trauma and headache) and the presence or absence of venous access; Statistical Test: Chi-Square Test was applied; p-Values: No significant differences were found between patients with and without venous access (p=0.590)

Table 3. Anatomical localization of air bubbles

Localization	Total number of detections	Male detection (%)	Female detection (%)	p-value
Anterior fossa	162 (62%)	70	60	0.188
Middle fossa	62 (24%)	30	20	0.188
Posterior fossa	26 (10%)	15	5	0.188

This table illustrates the distribution of air bubbles based on anatomical localization Statistical Test: Chi-Square Test was applied; p-Values: No significant differences were found among the anatomical localizations (p=0.188)

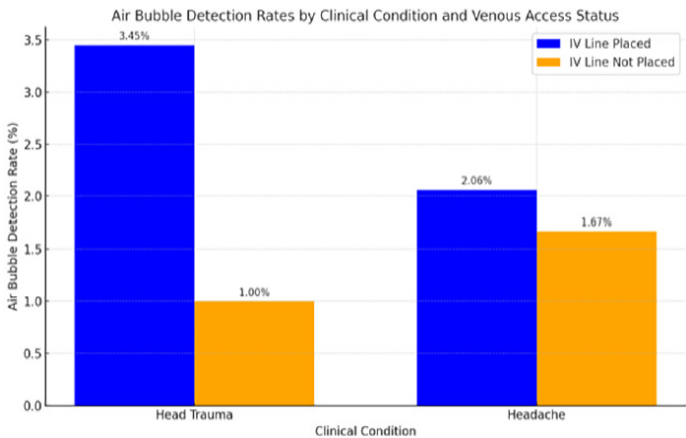


Figure 1. Air bubble detection rates by clinical condition and venous access status; This bar chart illustrates the detection rates of pneumocephalus across two clinical conditions: trauma and headache, stratified by IV access status; Detection rates were higher in cases with IV access (3.45% for trauma, 2.06% for headache) compared to cases without IV access (1.0% and 1.67%, respectively); No significant differences between the groups (p=0.590)

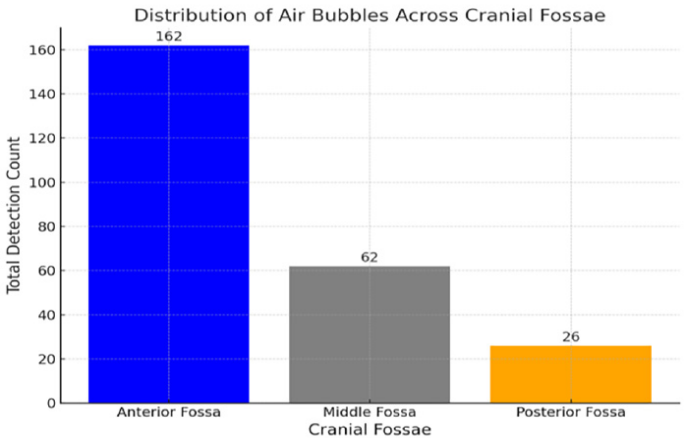


Figure 2. Distribution of pneumocephalus across cranial fossae; This bar chart shows the distribution of pneumocephalus across the cranial fossae; The anterior fossa exhibited the highest prevalence (162 cases, 62%), followed by the middle fossa (62 cases, 24%) and posterior fossa (26 cases, 10%); While the anterior fossa demonstrated a higher frequency, the differences between the fossae were not statistically significant (p=0.188)

DISCUSSION

This study retrospectively investigated the etiology of pneumocephalus in patients presenting to the ED with complaints of closed head trauma and headache, demonstrating that this phenomenon predominantly arises from iatrogenic causes. Our findings indicate that while the occurrence of pneumocephalus shows some variation in patients with IV lines, these differences are not statistically significant. The disappearance of most of these air bubbles within 24 hours in short-term follow-up is considered an important indicator to rule out the possibility of a basal skull fracture (Figure 3).

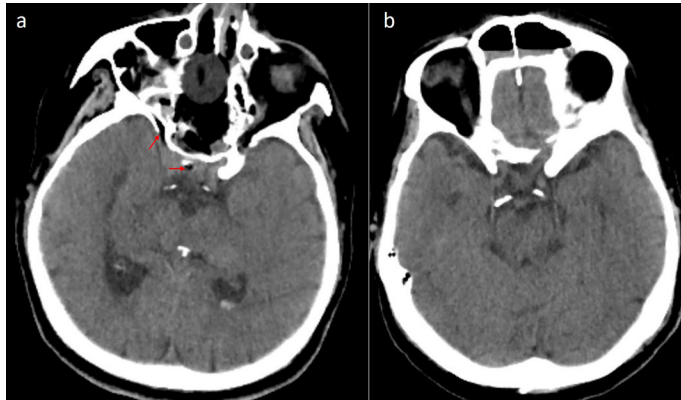


Figure 3. A. A brain computed tomography (CT) scan of a patient with blunt head trauma who was admitted to the emergency department; The scan shows pneumocephalus within the cranial cavity, indicated by red arrows; B. A follow-up brain CT scan taken 24 hours later demonstrates the spontaneous disappearance of the previously observed air bubbles

Detecting basal skull fractures using cranial CT imaging is often challenging (13). The structural characteristics of the anterior cranial fossa, including its predisposition to air leakage, may contribute to the accumulation of air bubbles in this region. In patients with traumatic basal skull fractures, two prominent symptoms are commonly observed: rhinorrhea and periorbital ecchymosis (14,15). Among patients presenting these symptoms, 80% and 76%, respectively, were found to have basal skull fractures (16,17). However, basal skull fractures were detected in only 19%-48% of patients with periorbital ecchymosis and 10%-30% of those with rhinorrhea (18-20). Thus, the presence of symptoms or cranial CT imaging alone may not suffice for diagnosing basal skull fractures. The literature emphasizes the importance of considering air bubbles detected on cranial CT scans (21).

Although air bubbles may serve as an indicator, their presence does not necessitate immediate and unnecessary further investigations, as air bubbles do not always indicate basal skull fractures (22,23). In our study, air bubbles were detected in 3.45% of patients with trauma and IV lines and 2.06% in headache patients with IV lines. Conversely, these rates were 1% and 1.67%, respectively, in patients without IV lines. These data suggest that head trauma alone is insufficient to cause pneumocephalus, which are more likely associated with venous air embolism occurring during IV placement. The literature notes that venous air

embolisms are typically harmless and resolve completely within 1-3 days, sometimes within hours or up to a week (24-26). This can be attributed to the reabsorption of air through the venous circulation or its transfer into pulmonary circulation (27). Small venous air embolisms are generally eliminated via the pulmonary circulation and follow a clinically benign course (28).

In our study, air bubbles were found to disappear on follow-up CT scans conducted 24 hours after the initial cranial CT in patients with IV lines. Although further investigations were performed in some patients despite the disappearance of air bubbles, no significant findings were observed. Therefore, deferring further tests in patients whose air bubbles disappear within 24 hours and who do not develop new symptoms is recommended. However, additional evaluations should be performed in cases where air bubbles persist. The disappearance of air bubbles within 24 hours and the absence of additional findings related to basal skull fractures in further investigations have allowed for the safe discharge of such patients.

One of the strengths of this study is the retrospective analysis of a large patient group (n=462) with detailed evaluations of these groups. However, the study has certain limitations. For instance, the lack of cases developing new symptoms within 24 hours has limited our ability to distinguish between harmless and harmful air embolisms. Furthermore, advanced imaging techniques were not used to directly demonstrate venous air embolism, and the small sample size of patients without IV lines restricts the generalizability of the findings. These limitations highlight the need for larger-scale prospective studies.

Additionally, our study provided short-term follow-up of cerebral venous air embolism up to 24 hours but did not evaluate the long-term effects of air bubbles. While the literature generally agrees that small venous air embolisms do not pose significant short-term problems, long-term follow-up could have provided a more precise understanding of the extent to which the rapid resolution of air bubbles reduces the likelihood of basal skull fractures (29). Although methods such as hyperbaric oxygen therapy and Trendelenburg positioning have been suggested to accelerate air bubble absorption, there is no consensus in the literature regarding their clinical benefits (30,31). Furthermore, adequate training of ED personnel on IV line placement and air evacuation can reduce the risk of venous air embolism, improve patient care, and enhance efficiency in healthcare systems (32).

CONCLUSION

Intracranial pneumocephalus (ICnP) is associated with iatrogenic venous air embolism, particularly during IV line placement. This phenomenon typically resolves spontaneously within 24 hours, does not require additional treatment, and follows a benign clinical course. Avoiding unnecessary further investigations in cases where air bubbles resolve within the first 24 hours offers a cost-

effective approach, optimizing patient management and improving resource utilization within the healthcare system.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: This study was approved by the Ordu University Non-Interventional Scientific Research Ethics Committee (Approval number: E-14647249-000-110429, Decision number: 2025/35, Date: 07.02.2025).

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REFERENCES

- Gorissen Z, Hakvoort K, van den Boogaart M, et al. Pneumocephalus: a rare and life-threatening, but reversible, complication after penetrating lumbar injury. *Acta Neurochir (Wien)*. 2019;161:361-5.
- Ramsden RT, Block J. Traumatic pneumocephalus. *J Laryngol Otol*. 1976;90:345-55.
- Wankhade BS, Beniamine MMK, Alrais ZF, et al. What should an intensivist know about pneumocephalus and tension pneumocephalus?. *Acute Crit Care*. 2023;38:244-8.
- Lee JS, Park YS, Kwon JT, Suk JS. Spontaneous pneumocephalus associated with pneumosinus dilatans. *J Korean Neurosurg Soc*. 2010;47:395-8.
- Wakefield BT, Brophy BP. Spontaneous pneumocephalus. *J Clin Neurosci*. 1999;6:174-5.
- Jakhere SG, Yadav DA, Jain DG, Balasubramaniam S. Does the Mount Fuji Sign always signify "tension" pneumocephalus? An exception and a reappraisal. *European Journal of Radiology Extra*. 2011;78:e5-7.
- Piccirilli M, Anichini G, Cassoni A, et al. Anterior cranial fossa traumas: clinical value, surgical indications, and results-a retrospective study on a series of 223 patients. *J Neurol Surg B Skull Base*. 2012;73:265-72.
- Kaplanoglu H, Kaplanoglu V, Dilli A, et al. An analysis of the anatomic variations of the paranasal sinuses and ethmoid roof using computed tomography. *Eurasian J Med*. 2013;45:115-25.
- Dabdoub CB, Salas G, Silveira Edo N, Dabdoub CF. Review of the management of pneumocephalus. *Surg Neurol Int*. 2015;6:155.
- Allioui S, Zaimi S, Sninate S, Abdellaoui M. Air bubbles in the brain: retrograde venous gas embolism in the cavernous sinus. *Radiology Case Rep*. 2020;15:1011-3.
- Carneiro AC, Diaz P, Vieira M, et al. Cerebral venous air embolism: a rare phenomenon. *Eur J Case Rep Intern Med*. 2019;6:001011.
- Hosaka A, Yamaguchi T, Yamamoto F, Shibagaki Y. Cerebral venous air embolism due to a hidden skull fracture secondary to head trauma. *Case Rep Neurol Med*. 2015;2015:730808.
- Imaging in skull fractures: practice essentials, radiography, computed tomography. <https://emedicine.medscape.com/article/343764-overview?form=fpf> access date 15.02.2025.
- Tarolli C, Scully MA, Smith AD 3rd. Teaching NeuroImages: unmasking raccoon eyes: a classic clinical sign. *Neurology*. 2014;83:e58-9.
- Saad M, Mowafy AA, Naser AM, et al. Analysis of moderate and severe traumatic brain injury associated with skull base fracture: a local tertiary center experience. *Egypt J Neurosurg*. 2024;39:62.
- Le C, Strong EB, Luu Q. Management of anterior skull base cerebrospinal fluid leaks. *J Neurol Surg B Skull Base*. 2016;77:404-11.
- Herbella FA, Mudo M, Delmonti C, et al. 'Raccoon eyes' (periorbital haematoma) as a sign of skull base fracture. *Injury*. 2001;32:745-7.
- Baugnon KL, Hudgins PA. Skull base fractures and their complications. *Neuroimaging Clin N Am*. 2014;24:439-65.
- Shafiei M, Aminmansour B, Mahmoodkhani M, et al. Basilar skull fractures and their complications in patients with traumatic brain injury. *Korean J Neurotrauma*. 2022;19:63-9.
- Naidu B, Vivek V, Visvanathan K, et al. A study of clinical presentation and management of base of skull fractures in our tertiary care centre. *Interdisciplinary Neurosurgery*. 2021;23:100906.
- Togo M, Hoshi T, Matsuoka R, et al. Multiple small hemorrhagic infarcts in cerebral air embolism: a case report. *BMC Res Notes*. 2017;10:599.
- Field PJ, Hulka F. Multiple systemic venous air emboli after fatal basilar skull fracture. *Trauma Case Rep*. 2022;38:100608.
- Choi YY, Hyun DK, Park HC, Park CO. Pneumocephalus in the absence of craniofacial skull base fracture. *J Trauma*. 2009;66:E24-7.
- Červeňák V, Všianský V, Cviková M, et al. Cerebral air embolism: neurologic manifestations, prognosis, and outcome. *Front Neurol*. 2024;15:1417006.
- Wong SS, Kwaan HC, Ing TS. Venous air embolism related to the use of central catheters revisited: with emphasis on dialysis catheters. *Clin Kidney J*. 2017;10:797-803.
- Kwon KE, Park NH, Kim SJ, Park JY. Stroke caused by cerebral air embolism after central venous catheter removal: a case report. *J Korean Soc Radiol*. 2019;80:975-80.
- Giraldo M, Lopera LM, Arango M. Venous air embolism in neurosurgery. *Rev Colomb Anestesiol*. 2015;43:40-4.
- Rubinstein D, Symonds D. Gas in the cavernous sinus. *AJNR Am J Neuroradiol*. 1994;15:561-6.
- Alif M, Jalal MJA, Vijayakumar N, et al. Gas in the venous sinus: An incidental finding. *Neurol India*. 2017;65:878-80.
- Ortega MA, Fraile-Martinez O, García-Montero C, et al. A general overview on the hyperbaric oxygen therapy: applications, mechanisms and translational opportunities. *Medicina (Kaunas)*. 2021;57:864.

31. Calverley RK, Dodds WA, Trapp WG, Jenkins LC. Hyperbaric treatment of cerebral air embolism: a report of a case following cardiac catheterization. *Can Anaesth Soc J.* 1971;18:665-74.
32. McCarthy CJ, Behraves S, Naidu SG, Oklu R. Air embolism: practical tips for prevention and treatment. *J Clin Med.* 2016;5:93.



Effects of Menstrual Symptoms on Social Appearance Anxiety in University Students

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Abstract

Aim: This study aims to determine the effect of menstrual symptoms on social appearance anxiety in university students.

Material and Method: This study was planned as a descriptive and cross-sectional study, and the sample consisted of 264 female students studying at a foundation university in Istanbul that provides education in the field of health sciences. Data were collected using an online survey method with a personal information form prepared by the literature, the Social Appearance Anxiety Scale (SAAS), and the Menstruation Symptom Scale (MSS). Participants evaluated the SAAS in two forms specific to the menstrual and non-menstrual periods.

Results: The mean age of the participants was 18.93 ± 1.12 , and the mean total MSS score was 71.47 ± 18.28 . It was determined that a significant portion of the participants (76.5%) reported that their social lives were affected during the menstrual period. The social appearance anxiety scores during the menstrual period (SAAS 34.56 ± 17.14) were found to be higher than those during the non-menstrual period (SAAS 32.54 ± 16.43) ($p < 0.05$). A significant and positive correlation was found between MSS and SAAS scores during the menstrual period ($r = 0.321$, $p < 0.05$).

Conclusion: This study determined that menstrual symptoms negatively affect social appearance anxiety in university students. Menstrual symptoms may increase social appearance anxiety, leading to adverse effects on social life and mental well-being, which healthcare professionals should consider. In this regard, it is recommended that healthcare professionals adopt a supportive approach toward women and provide guidance on this issue.

Keywords: Menstruation, menstrual cycle, body image

INTRODUCTION

Women experience various physical and psychological symptoms during the premenstrual and postmenstrual periods (1,2). These symptoms vary from person to person and can manifest at physical, emotional, cognitive, and behavioral levels (2-4). However, these symptoms physiological, psychological, and social effects on women are not yet fully understood. Additionally, existing knowledge regarding what menstruation represents for women and its impact on body image remains insufficient.

Although the menstrual cycle is a natural process, it has been observed that women tend to develop more negative thoughts about their bodies during menstruation (5-7). Body image is defined as a concept shaped by the positive or negative emotions and thoughts an individual

holds about their body (8). It has been suggested that fluctuations in estrogen and progesterone hormone levels during the menstrual period, along with the physical and psychological changes women experience, may negatively impact body image (9).

This process can lead women to feel intense anxiety about their bodies. In particular, negative thoughts concerning their bodies and how others perceive them are referred to as social appearance anxiety (7,10).

Nurses who frequently interact with women should consider the physical and psychological effects of menstrual symptoms and plan appropriate care interventions accordingly. Healthcare professionals who engage directly with women can assess general health and menstrual history to identify individuals at risk at an

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early stage. Therefore, routine gynecological follow-ups should consider physiological conditions and the impact of menstrual symptoms on body image and psychosocial well-being. Menstrual symptoms can affect quality of life and contribute to social appearance anxiety.

While existing studies have focused on body image and psychological issues during premenstrual and menstrual periods, research examining the impact of menstrual symptoms on social appearance anxiety remains limited. Given the established relationship between social appearance anxiety and negative body image, further research in this field is needed. This study aims to determine the impact of menstrual symptoms on social appearance anxiety among university students, thereby raising awareness in nursing practice and contributing to the field. Nurses must approach menstrual symptoms as a biological process affecting individuals' psychological and social well-being. Nurses should adopt a supportive approach to empower women by providing guidance, counseling, and education.

Research Questions

- Does social appearance anxiety among university students vary between the menstrual period and non-menstrual periods?
- Do sociodemographic characteristics, menstrual history, general health status, and psychosocial factors specific to this period influence social appearance anxiety during menstruation among university students?

MATERIAL AND METHOD

Research Design

This study was conducted using a descriptive and cross-sectional design to evaluate the relationship between menstrual symptoms and social appearance anxiety among university students.

Population and Sample

In February 2021, the study population consisted of female students enrolled at a foundation university in Istanbul that provides education in the field of health sciences (N=412). Since the total number of individuals in the population was known, the sample size was calculated using the sample size determination formula. A study conducted in Türkiye reported a PMS prevalence rate of 70.2%, which was used to determine the event probability (p-value) (11). It was determined that a minimum of 181 students needed to be included in the study. The sample of this study consisted of 264 students.

Inclusion Criteria

Participants were required to meet the following inclusion criteria:

- Being a female student,
- Having the ability to speak and understand Turkish,
- Having access to online participation,
- Voluntarily agreeing to participate in the study.

Data Collection

The data were collected online using Google Forms between January and February 2021. The survey link was shared with students via institutional email and online student platforms, without any face-to-face interaction. Prior to participation, students were informed about the study's purpose and requirements. Online informed consent was obtained before accessing the questionnaire. Students used their unique institutional email addresses to prevent duplicate responses; multiple submissions from the same email were not allowed.

The data collection tools included the "Personal Information Form," the "Menstrual Symptom Scale (MSS)," and the "Social Appearance Anxiety Scale (SAAS)."

- **Personal Information Form:** This section consisted of 27 questions to assess participants' sociodemographic characteristics, gynecological history, and general health status.
- **MSS:** Chesney and Tasto (12) developed the MSS to assess menstrual pain and symptoms. Negriff et al. (13) re-evaluated the factor structure and usability of the scale in adolescents, while Güvenç et al. (14) conducted its Turkish validity and reliability study. The MSS is a 22-item, 5-point Likert-type scale in which participants rate the menstrual symptoms they experience on a scale ranging from 1 (never) to 5 (always). The scale comprises three subdimensions: Negative Effects/Somatic Complaints, Menstrual Pain Symptoms, and Coping Strategies. The minimum score that can be obtained from the scale is 22, while the maximum score is 110. The total score represents the severity of menstrual symptoms, and subdimension scores are calculated based on the average of the items within each category. Higher scores indicate increased severity of menstrual symptoms. The Cronbach's Alpha coefficient of the original scale was 0.86 (14). This study calculated the Cronbach's Alpha coefficient for the MSS as 0.912, indicating high internal consistency and reliability.
- **SAAS:** The SAAS is a five-point Likert-type scale comprising 16 items, assessing individuals' anxiety regarding their physical appearance. The total score ranges from 16 to 80, with higher scores indicating more significant social appearance anxiety. Permission to use the scale was obtained from the original authors. The Cronbach's Alpha coefficient of the original scale was 0.93 (10). In this study, the SAAS was administered twice separately: once for the menstrual period and once for the non-menstrual period. The Cronbach's Alpha coefficient for the menstrual period was calculated as 0.961 and for the non-menstrual period as 0.963, indicating high internal consistency and reliability.

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 25.0.

Descriptive statistics, including frequency and percentage values, were used to summarize the data. The normality of data distribution was assessed using the Shapiro-Wilk test. Non-parametric tests were used for data that did not follow a normal distribution. Spearman's correlation analysis was applied to examine relationships between numerical variables, while the Wilcoxon test was used to compare data obtained at different time points from the same sample. A significance level of $p < 0.05$ was considered statistically significant.

Ethical Approval

Ethical approval for the study was obtained from the İstanbul University-Cerrahpaşa Social and Human Sciences Research Ethics Committee on December 22, 2020, with decision number 88264. Institutional permission was also secured from the private university where the study was conducted.

Participants were provided with detailed information about the study, and it was emphasized that their personal data would be protected. Before proceeding with the questionnaire, they were required to read the informed consent statement and indicate their consent by selecting the "I agree to participate" option in the

online form. This study complied with the principles of the Declaration of Helsinki.

RESULTS

A total of 264 individuals participated in the study. Most participants were 19 years old (47%) or 18 years old (35.6%). All participants studied in health-related programs such as medicine, nursing, pharmacy, and dentistry. Nearly all participants were single (99.2%), and most reported a moderate income level (85.6%). Regarding health-related factors, 72.3% of participants had a normal BMI, while nearly all reported not consuming alcohol (93.6%) and not smoking (88.6%). Additionally, 92.4% had no chronic health conditions (Table 1). Menarche occurred between ages 11–14 in 89.4% of participants. The most common menstrual symptoms were tension/irritability (82.6%), menstrual cramps (78.4%), and acne (69.7%). Additionally, 76.5% of participants reported that menstruation affected their social life (Table 2). The mean MSS score was 71.47 ± 18.28 (Table 3). A statistically significant difference was found in SAAS scores between the menstrual and non-menstrual periods ($p < 0.05$) (Table 4). A strong positive correlation was observed between SAAS scores in both periods ($r = 0.893$, $p < 0.05$) (Table 5).

Table 1. Participant characteristics (N=264)			
Demographics		N=264	%
Age ($\bar{X} \pm SD$, 18.93 $\pm$ 1.12)	21 and above	12	4.5
	20	34	12.9
	19	124	47.0
	18 and below	94	35.6
Marital status	Married	2	0.8
	Single	262	99.2
Income level	Good	31	11.7
	Average	226	85.6
	Poor	7	2.7
General health			
Body mass index (BMI)	Obese	4	1.5
	Overweight	25	9.5
	Normal	191	72.3
	Underweight	44	16.7
Smoking habits	No	234	88.6
	Yes	30	11.4
Alcohol consumption	No	247	93.6
	Yes	17	6.4
Regular exercise habit	No	164	62.1
	Yes	100	37.9
Presence of chronic illness	No	244	92.4
	Yes	20	7.6
Total		264	100.0

Table 2. Menstrual history			
		N=264	%
Age at menarche ($\bar{X} \pm SD$, 12.99 $\pm$ 1.13)	15 and older	25	9.5
	11-14	236	89.4
	10 and younger	3	1.1
Pain during menstruation	Sometimes	88	33.3
	No	7	2.7
	Yes	169	64.0
Menstrual regularity (between 21-35 days)	Irregular	67	25.4
	Regular	197	74.6
Menstrual symptoms	Bloating	150	56.8
	Acne	184	69.7
	Edema	90	34.1
	Weight gain	76	28.8
	Cramps	207	78.4
	Increased emotional sensitivity (e.g., crying)	157	59.5
	Tension, irritability	218	82.6
	Sensitivity to unpleasant odors	78	29.5
Does menstrual symptoms affect social life?	No	62	23.5
	Yes	202	76.5
Frequency of menstrual symptoms' impact on social life	Always	18	6.8
	Often	53	20.1
	Sometimes	161	61.0
	Never	32	12.1
Effect of menstrual symptoms on body image	No effect	79	29.9
	Sensitivity to unpleasant odors	43	16.3
	Feeling less attractive	53	20.1
	Feeling heavier	89	33.7
Impact of menstrual symptoms on mental health	Always	51	19.3
	Often	66	25.0
	Sometimes	147	55.7
Impact of menstrual symptoms on self-esteem	Always	108	40.9
	Often	32	12.1
	Sometimes	124	47.0
Total		264	100.0

Table 3. MSS and subscale scores			
	Mean $\pm$ SD	Min-Max	Median
MSS	71.47 $\pm$ 18.28	22.00-107.00	71.00
Negative effects/somatic complaints	40.57 $\pm$ 11.37	13.00-65.00	41.00
Menstrual pain symptoms	22.39 $\pm$ 5.83	6.00-30.00	24.00
Coping strategies	8.50 $\pm$ 3.77	3.00-15.00	8.00

Table 4. Comparison of SAAS scores according to menstrual period					
	Mean±SD	Min-Max	Median	Test value	p
SAAS non-menstrual period	32.54±16.43	16.00-80.00	25.50	-5.921**	0.000*
SAAS menstrual period	34.56±17.14	16.00-80.00	28.00		
*p<0.05 ** Wilcoxon test					

Table 5. Correlation between MSS and SAAS scores			
		SAAS menstrual period	SAAS non-menstrual period
MSS score	r	0.321	0.220
	p	0.000*	0.000*
*r : Spearman Correlation, *p<0.05			

When comparing SAAS scores during menstruation with participants' demographic characteristics, general health status, and menstrual history, only BMI and menstrual regularity had a statistically significant effect (p<0.05). No significant differences were found for other variables (p>0.05). A statistically significant

difference was observed in SAAS scores between participants classified as obese and those with normal BMI during menstruation (p<0.05) (Table 6). Similarly, SAAS scores were significantly different between participants with irregular and regular menstrual cycles (p<0.05) (Table 7).

Table 6. Comparison of SAAS menstruation period scores based on participant characteristics (N=264)						
Demographics		Mean±SD	Min-Max	Median	Test value	p
Age	21 and above	25.91±10.04	16.00-55.00	22.50	5.128**	0.163
	20	30.79±13.44	16.00-70.00	26.00		
	19	33.59±15.77	16.00-78.00	28.00		
	18 and below	38.31±19.89	16.00-80.00	31.50		
Income level	Good	30.61±15.03	16.00-76.00	26.00	3.285**	0.194
	Average	34.80±17.20	16.00-80.00	28.00		
	Poor	44.42±21.34	16.00-70.00	43.00		
General health						
Body mass index (BMI)	Obese	52.25±17.74	26.00-64.00	59.50	8.822***	0.032*
	Overweight	40.84±21.20	18.00-80.00	37.00		
	Normal	32.68±16.02	16.00-80.00	26.00		
	Underweight	37.59±17.68	16.00-74.00	32.00		
Smoking habits	No	34.60±17.06	16.00-80.00	28.00	3334.000**	0.655
	Yes	34.26±18.10	16.00-78.00	24.00		
Alcohol consumption	No	34.81±17.27	16.00-80.00	28.00	1748.000**	0.248
	Yes	30.94±15.14	16.00-62.00	22.00		
Regular exercise habit	No	34.14±16.12	16.00-80.00	28.00	8036.500**	0.786
	Yes	35.27±18.76	16.00-80.00	26.00		
Presence of chronic illness	No	34.54±17.32	16.00-80.00	27.00	2248.000**	0.558
	Yes	34.90±15.15	18.00-70.00	30.00		
*p<0.05, **Mann Whitney U test, ***Kruskal Wallis test						

Table 7. Comparison of SAAS menstruation period scores based on menstrual history						
		Mean±SD	Min-Max	Median	Test Value	p
Age at menarche	15 and older	37.52±18.36	17.00-73.00	29.00	0.829***	0.661
	11-14	34.28±17.01	16.00-80.00	28.00		
	10 and younger	32.00±21.70	18.00-57.00	21.00		
Pain during menstruation	Sometimes	30.82±14.27	16.00-73.00	24.00	5.711***	0.058
	No	30.42±7.63	22.00-44.00	27.00		
	Yes	36.68±18.44	16.00-80.00	28.00		
Menstrual regularity (between 21-35 days)	Irregular	37.50±17.87	16.00-80.00	29.00	5500.000**	0.042*
	Regular	33.56±16.82	16.00-80.00	27.00		
Does menstrual symptoms affect social life?	No	27.59±13.72	16.00-70.00	22.00	3873.500**	0.000*
	Yes	36.70±17.54	16.00-80.00	30.00		
Frequency of menstrual symptoms' impact on social life	Always	42.16±19.45	18.00-71.00	41.00	18.445***	0.000*
	Often	41.77±19.21	16.00-80.00	38.00		
	Sometimes	32.28±15.65	16.00-80.00	26.00		
	Never	29.84±15.15	17.00-70.00	22.00		
Effect of menstrual symptoms on body image	No effect	24.29±9.54	16.00-57.00	21.00	65.345***	0.000*
	Sensitivity to unpleasant odors	35.00±13.25	17.00-70.00	33.00		
	Feeling less attractive	47.49±19.95	17.00-80.00	50.00		
	Feeling heavier	35.78±16.78	16.00-78.00	29.00		
Impact of menstrual symptoms on mental health	Always	35.72±17.52	16.00-71.00	28.00	21.902***	0.000*
	Often	44.36±21.38	16.00-80.00	39.00		
	Sometimes	29.76±12.40	16.00-70.00	25.00		
Impact of menstrual symptoms on self-esteem	Always	26.41±12.92	16.00-71.00	22.00	78.035***	0.000*
	Often	55.65±17.83	23.00-80.00	59.00		
	Sometimes	36.22±15.04	16.00-78.00	30.00		
*p<0,05, **Mann Whitney U test, ***Kruskal Wallis test						

DISCUSSION

A literature review reveals that most studies on menstrual symptoms have been conducted predominantly with adolescents. In this study, late adolescents were specifically chosen as the sample group, considering that menstrual symptoms commonly appear in this age range and the likelihood of experiencing higher social appearance anxiety. A study conducted in Türkiye with nursing students, which examined factors associated with premenstrual syndrome and sleep quality, reported the participants' mean age as 21.03±1.35 (15). Another study investigating the relationship between premenstrual syndrome and cultural sensitivity reported the mean age as 20.8±1.6 (16). In this study, the mean age of participants was 18.93±1.12 (Table 1). This mean age is lower than in previous studies because the research was conducted at a

newly established university with only first-year students. The body mass index (BMI) values of the participants in this study were found to be consistent with the findings of other studies conducted with similar age groups in Türkiye and other countries (17-20). Likewise, participants' smoking rates showed parallels with other studies conducted on individuals of similar age groups (17,21-23). The fact that most studies on menstrual symptoms have been conducted on individuals from similar age groups may explain the consistency in these rates. However, the regular exercise rates among participants differed from studies conducted with similar age groups in Türkiye and other countries (24-27). For example, in a study conducted in Spain examining coping strategies for dysmenorrhea, 72.8% of the 224 university students were found to exercise regularly (25). In another study conducted

in Athens, 53.9% of 637 nursing students reported exercising regularly (27). Conversely, a study conducted in Egypt to determine the epidemiology of dysmenorrhea reported that only 20.9% of 1,908 university students engaged in regular exercise (26). Different rates were also observed in studies conducted in Türkiye. For instance, in a study involving 207 secondary school students, 46.4% reported exercising regularly (24). In this study, the rate was found to be 37.9% (Table 1).

In Türkiye, women's regular exercise habits are influenced by various factors such as social norms, academic workload, and socioeconomic conditions. Among university students, low rates of physical activity may be attributed to intense academic schedules, limited access to sports facilities, and societal perceptions that discourage women from participating in sports.

In this study, 76.5% of participants reported that their social lives were affected during menstruation (Table 2). Similarly, a study conducted in Nigeria found that 55.7% of women reported disruption in daily tasks and difficulties continuing their education during menstruation (28). Another study in Türkiye reported that 92% of university students' social lives were negatively affected during their menstrual period (29). The difference in these rates could be associated with various factors, such as the severity of menstrual symptoms, perceived stress levels, and sociocultural differences. Moreover, the fact that this study's sample consisted solely of first-year students and had a lower mean age than other studies may also contribute to the discrepancy. As first-year students may still be adapting to their academic and social environments, their perceptions of how menstruation affects their social lives might differ. Additionally, the cultural taboo surrounding menstruation in Türkiye and women's difficulty in expressing their experiences may result in underrecognition of the social impact of menstruation. This situation could lead to the normalization of restrictions experienced during menstruation and reduced awareness of its social consequences.

Participants reported experiencing symptoms such as tension, irritability, acne, pain, tearfulness, sensitivity, and bloating most frequently before or during menstruation (Table 2). These findings are consistent with those of other studies in the literature (18,24). Furthermore, the MSS scores obtained in this study align with those reported in previous studies conducted with individuals of similar age groups (Table 3) (30-32). This case may be explained by the fact that the sample group, composed of young individuals, is more sensitive to menstrual symptoms.

A significant and positive correlation was found between SAAS scores during menstruation and MSS scores (Table 5). It was observed that as the frequency of menstrual symptoms increased, social appearance anxiety also increased. There are no existing studies in the current literature directly examining the relationship between menstrual symptoms and social appearance anxiety. Social appearance anxiety is defined as a socially based

form of anxiety shaped by negative thoughts regarding one's body and how it is perceived by others (10). The literature primarily focuses on the relationship between menstruation and body image within this context.

One study reported that women felt more attractive during ovulation, while perceptions of attractiveness significantly declined during the late luteal phase. In the premenstrual period, women described feeling "fat and unclean" and expressed increased body dissatisfaction (33). A positive correlation was also found between the menstrual cycle phase and body image concerns, with body dissatisfaction being more pronounced in the premenstrual phase (34). Such negative body image may lead to concerns about physical appearance in social settings, suggesting that the physical and emotional changes experienced during menstruation may increase social appearance anxiety.

However, some studies report different findings. For instance, one study found that women with a positive attitude toward premenstrual syndrome were more satisfied with their body image and felt healthier and more physically comfortable (35). Each woman's experience of menstruation and its psychosocial effects may vary individually. Numerous factors may influence body image during menstruation, such as general anxiety levels, body satisfaction, cultural background, attitudes towards menstruation, and severity of PMS symptoms. Therefore, it may not be sufficient to explain social appearance anxiety based on a single variable.

This study found a statistically significant relationship between body mass index (BMI), menstrual regularity, and social appearance anxiety. Participants within the obesity range had significantly higher SAAS scores during menstruation compared to those in the normal BMI range (Table 6). Similarly, participants with irregular menstrual cycles had higher SAAS scores during menstruation than those with regular cycles (Table 7). Previous literature has reported that increased BMI is associated with more severe premenstrual syndrome (PMS) symptoms and that there is a significant relationship between body composition and PMS severity (36). Additionally, it has been emphasized that academic stress and BMI are associated with the prevalence of PMS (37). Irregular menstruation has also been linked to hormonal imbalances and increased PMS severity (38).

The findings of this study show that increased severity of menstrual symptoms is associated with higher levels of social appearance anxiety (Table 5). Previous studies have indicated that menstrual symptoms may affect body image (33,34). Accordingly, it can be suggested that high BMI and irregular menstruation may increase the severity of menstrual symptoms, which in turn may contribute to heightened social appearance anxiety.

CONCLUSION

Menstrual symptoms are believed to contribute to social appearance anxiety in women. This study supports previous research and aligns with existing literature.

Although menstruation is a natural function of the female body, studies on its relationship with body image remain limited. These findings may help develop interventions to reduce social appearance anxiety in women.

This study was conducted with first-year university students in health-related programs. As the university had recently admitted its first cohort of students, all participants were in their first year. Therefore, the results cannot be generalized to a broader population. Future studies should include participants from different age groups and academic backgrounds to improve validity and applicability. Women's health nurses and midwives are key in addressing the physical and psychological effects of menstrual symptoms. Considering their potential link to social appearance anxiety, nursing care should include individualized psychosocial counseling and support. Training programs should be developed to enhance the skills of healthcare professionals in menstrual health literacy, psychosocial counseling, and body image concerns. Interactive workshops, simulation-based training, and case discussions can help professionals provide better support. Future research should explore sociocultural factors influencing menstrual experiences and their psychological effects, using more extensive and diverse samples.

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REFERENCES

- Meng Y, Chang L, Hou L, et al. Menstrual attitude and social cognitive stress influence autonomic nervous system in women with premenstrual syndrome. *Stress*. 2022;25:87-96.
- Ozgocer T, Ucar C, Yildiz S. Daily cortisol awakening response and menstrual symptoms in young females. *Stress Health*. 2022;38:57-68.
- Weon HW, Son HK. An analysis of menstrual symptoms, menstrual attitudes, physical stress and psychological stress according to the menstrual cycle phase. *Iran J Public Health*. 2023;52:1161-9.
- Wei SM, Schiller CE, Schmidt PJ, et al. The role of ovarian steroids in affective disorders. *Curr Opin Behav Sci*. 2018;23:103-12.
- Allyn K, Seidman L, Evans S, et al. Impact of primary dysmenorrhea on self-image in adolescents and young adults. *J Pain*. 2019;20:S57-8.
- Kvalem IL, Dahr Nygaard IM, Træen B, et al. Menstrual attitudes in adult women: a cross-sectional study on the association with menstruation factors, contraceptive use, genital self-image, and sexual openness. *Womens Health (Lond)*. 2024;20:17455057241249553.
- Ashar G, Kamat V. Relationship between attitude towards menstruation, self-esteem and social appearance anxiety among Indian cis-gendered women who menstruate. *Indian J Ment Health*. 2022;9:135-41.
- Cash TF, Szymanski ML. The development and validation of the Body-Image Ideals Questionnaire. *J Pers Assess*. 1995;64:466-77.
- Ryan S, Ussher JM, Perz J. Women's experiences of the premenstrual body: negotiating body shame, self-objectification, and menstrual shame. *Womens Reprod Health*. 2020;7:107-26.
- Doğan T. Sosyal Görünüş Kaygısı Ölçeği'nin (SGKÖ) Türkçe uyarlaması: geçerlik ve güvenirlik çalışması. *Hacettepe Univ Egit Fak Derg*. 2010;39:151-9.
- Yaşar Ö, Karaca PP, Aksu SÇ. Premenstrual syndrome and affecting variables in university students. *Balıkesir Sağlık Bilim Derg*. 2019;8:147-52.
- Chesney MA, Tasto DL. The development of the menstrual symptom questionnaire. *Behav Res Ther*. 1975;13:237-44.
- Negriff S, Dorn LD, Hillman JB, Huang B. The measurement of menstrual symptoms: factor structure of the menstrual symptom questionnaire in adolescent girls. *J Health Psychol*. 2009;14:899-908.
- Güvenç G, Seven M, Akyüz A. Adaptation of the Menstrual Symptom Questionnaire into Turkish. *TAF Prev Med Bull*. 2014;13:367-74.
- Özer E, Güvenç G. Determination of premenstrual syndrome-related factors in nursing students and investigation of their relationship with sleep quality. *TOĞU Sağlık Bilim Derg*. 2023;3:184-97.
- Tokat MA, Özberk H, Derin E, et al. The effect of cultural sensitivity and differences on premenstrual syndrome in nursing students. *Sürekli Tıp Eğitimi Derg*. 2024;33:253-62.
- Bakır N, Beji NK. Premenstrual syndrome prevalence and affecting factors among university students. *Inonu Univ J Health Sci Vocational Sch*. 2021;9:264-77.
- Chen L, Tang L, Guo S, et al. Primary dysmenorrhea and self-care strategies among Chinese college girls: a cross-sectional study. *BMJ Open*. 2019;9:e026813.
- Hu Z, Tang L, Chen L, et al. Prevalence and risk factors associated with primary dysmenorrhea among Chinese female university students: a cross-sectional study. *J Pediatr Adolesc Gynecol*. 2020;33:15-22.
- Şener N, Taşhan ST. Evaluating the relationship between dysmenorrhea and personality traits in university students. *Koç Univ J Nurs Educ Res*. 2020;17:148-54.
- Kartal YA, Kaykısız EY. Investigation of the relationship between eating behaviors and premenstrual syndrome symptoms of midwifery students in the COVID-19 outbreak. *Medical Sciences (NWSAMS)*. 2020;15:133-43.

22. Koyucu RG, Ölmez R. Determination of premenstrual syndrome levels of faculty of health sciences students in COVID19 process. *Acibadem Univ J Health Sci*. 2021;12:496-501.
23. Nasser AM, Zhang X. Knowledge and factors related to smoking among university students at Hodeidah University, Yemen. *Tob Induc Dis*. 2019;17:42.
24. Erbaş N, Altunbaş N. According to some variables in girls a high school determining the premenstrual syndrome violence and perceived stress level. *Acibadem Univ J Health Sci*. 2021;12:479-86.
25. Parra-Fernández ML, Onieva-Zafra MD, Abreu-Sánchez A, et al. Management of primary dysmenorrhea among university students in the South of Spain and family influence. *Int J Environ Res Public Health*. 2020;17:5570.
26. Shehata NA, Arafa AE, El Wahed HAA, et al. Epidemiology of dysmenorrhea among university students in Egypt. *Int J Womens Health Wellness*. 2018;4:073.
27. Vlachou E, Owens DA, Lavdaniti M, et al. Prevalence, wellbeing, and symptoms of dysmenorrhea among university nursing students in Greece. *Diseases*. 2019;7:5.
28. Ezebialu IU, Ezenyeaku CC, Umeobika JC. Prevalence of dysmenorrhea and its contribution to school absenteeism among Nigerian undergraduate students. *Ann Health Res*. 2021;7:59-66.
29. Bilir E, Yıldız Ş, Yakın K, Ata B. The impact of dysmenorrhea and premenstrual syndrome on academic performance of college students, and their willingness to seek help. *Turk J Obstet Gynecol*. 2020;17:196-201.
30. Baltaş Z, Şevgin Ö, Hoşbaş BD. Telerehabilitation in primary dysmenorrhoea: a randomised controlled trial. *İstanbul Gelişim Univ Sağlık Bilim Derg*. 2023;21:806-18.
31. Bilgen FG, İpekçi NN. Determination of nursing students' menstrual health and genital hygiene behaviors according to their taking the obstetrics and general diseases nursing course: the case of Kilis province. *Bandırma Onyedi Eylül Univ Sağlık Bilim ve Araşt Derg*. 2023;6:131-9.
32. Siyahtaş GF, Altay BN, Erdem M. The relationship between women's menstrual attitudes levels and menstruation symptoms. *Turk J Fam Med Prim Care*. 2024;18:426-32.
33. Ryan S, Ussher JM, Hawkey A. Mapping the abject: women's embodied experiences of premenstrual body dissatisfaction through body-mapping. *Fem Psychol*. 2022;32:199-223.
34. Cantoni C, Salaris A, Monti A, et al. Probing corporeal awareness in women through virtual reality induction of embreathment illusion. *Sci Rep*. 2024;14:9302.
35. McPherson ME, Korfine L. Menstruation across time: Menarche, menstrual attitudes, experiences, and behaviors. *Womens Health Issues*. 2004;14:193-200.
36. Thakur H, Pareek P, Sayyad MG, Otiv S. Association of premenstrual syndrome with adiposity and nutrient intake among young Indian women. *Int J Womens Health*. 2022;665-75.
37. Yunisari SZ, Panggayuh A, Kusmiwiyati A. The relationship of academic stress and body mass index (BMI) with premenstrual syndrome in class 9 students of SMPN 1 Sumberpucung. *J Pendidikan Kesehatan*. 2023;12:149-61.
38. Elvan A. Does premenstrual syndrome affect physical activity and quality of life? A cross-sectional study. *J Exerc Ther Rehabil*. 2023;10:115-21.



Continuous Glucose Monitoring Systems in Diabetes Management: A Qualitative Analysis Based on User Experiences

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Abstract

Aim: Continuous glucose monitoring systems are widely employed in diabetes management to improve blood glucose control and reduce the risk of hypoglycemia. These technologies enable real-time monitoring of glucose levels, thereby optimizing treatment processes. However, user-based data regarding the effectiveness and usability challenges of continuous glucose monitoring systems remain limited. This study aims to analyze the experiences of individuals using continuous glucose monitoring systems by examining the role of these devices in diabetes management, their advantages, and the issues encountered.

Material and Method: A total of 193 user comments collected from Reddit, YouTube, and Şikayetvar platforms were evaluated through content analysis.

Results: The results indicate that continuous glucose monitoring systems enhance users' quality of life, facilitate glucose tracking, and contribute positively to hypoglycemia management. Nevertheless, technical and design-related issues—such as fluctuations in sensor accuracy, connectivity problems, high costs, and skin irritations—were frequently reported. In particular, false hypoglycemia alarm notifications were found to be especially bothersome.

Conclusion: Users call for improvements in calibration procedures, the development of customizable alarm systems, and the provision of longer-lasting, cost-effective sensors. The findings offer valuable feedback for enhancing continuous glucose monitoring systems and provide recommendations for manufacturers and healthcare professionals to optimize the use of this technology in diabetes management. Future research should focus on more comprehensive studies to evaluate the long-term effectiveness of continuous glucose monitoring systems.

Keywords: Continuous glucose monitoring system, diabetes, diabetes management, health technology hypoglycemia

INTRODUCTION

Diabetes is a widespread public health issue globally and is one of the chronic diseases that adversely affect individuals' quality of life. Diabetes mellitus is a high-cost disease associated with increased mortality due to both its acute and vascular complications (1). Consequently, ensuring and sustaining effective care for the growing diabetic population remains an important concern for health systems worldwide (2). Effective management of diabetes—including the control of diabetes-related complications—is therefore essential. The primary goal in treating this disease is to maintain blood glucose within normal limits through optimal glycemic control. Achieving this objective requires patient education, appropriate dietary support, sufficient physical activity, regular self-

monitoring of blood glucose, and consistent adherence to prescribed medications (3).

Self-monitoring of blood glucose (SMBG) is pivotal in attaining target blood glucose levels for diabetic individuals using insulin, oral antidiabetics, or medical nutrition therapy. The frequency of home SMBG is determined on an individual basis. For patients administering insulin several times a day, SMBG is required 3–4 times daily; for type 1 diabetic patients under basal-bolus insulin therapy, pregnant women, insulin pump users, and uncontrolled type 2 diabetic patients, 3–4 measurements per day are recommended; whereas for other type 2 diabetic patients, 3–4 measurements per week are generally advised. Furthermore, in diabetic individuals whose fasting and preprandial glucose levels are controlled yet who do not

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reach target levels of glycated hemoglobin (HbA1c), SMBG is recommended during dietary and pharmacological treatment aimed at balancing postprandial glycemia (4). Self-monitoring enables the early detection of hypoglycemia and hyperglycemia, facilitates timely intervention, and is also critical for the early diagnosis and prevention or delay of complications. Increased frequency of home blood glucose monitoring is associated with improved glycemic control in the course of type 1 diabetes. In situations with high glycemic fluctuations, unrecognized hypoglycemia may occur. Some patients deliberately reduce or skip their insulin dose due to fear of hypoglycemia. In cases suspected of Munchausen syndrome (where patients intentionally manipulate treatment to their detriment), patients may intentionally manipulate their treatment. In such cases, even temporary CGM systems are the most effective option for blood sugar tracking (5).

Self-monitoring of blood glucose is a key element of effective diabetes management. Diabetic individuals typically use glucometers at home to monitor their blood glucose levels; however, measurement errors can occur. Many of these errors are related to device performance and user operation. Inaccurate measurements affecting glycemic control may lead to inappropriate treatment, emphasizing the importance of proper usage techniques.

Conventional glucometers measure glucose in capillary blood obtained from the fingertip. The discomfort associated with repeated measurements throughout the day, along with the risk of skin injuries resulting from erroneous or multiple punctures (6) and the inability to provide continuous monitoring, has led to the replacement of this method with less invasive, more comfortable, and uninterrupted glucose monitoring sensors (7). This technological advancement enables diabetic patients to monitor their glucose levels in real time and to respond more swiftly to fluctuations.

Glucose sensors are distinguished by the convenience they offer compared to fingertip measurements and the enhanced sense of security they provide in managing blood glucose. In addition to tracking instantaneous glucose levels, these devices offer data on glucose trends, rates of change, and directional shifts, thereby delivering a more comprehensive approach to diabetes management (8). These features allow users to optimize their diet, exercise, and medication regimens, demonstrating that these sensors are effective tools for long-term diabetes management (9).

Continuous glucose monitoring systems provide significant benefits, particularly for patients with type 1 diabetes and other groups. Individuals who perform frequent and regular SMBG, those with diminished hypoglycemia awareness or recurrent hypoglycemic episodes, patients experiencing marked glycemic variability, and those whose HbA1c levels remain above target can benefit substantially from CGM usage (10). Moreover, CGM offers valuable support for individuals experiencing discrepancies between CGM readings and HbA1c levels, for athletes, and for those

employed in high-risk professions prone to hypoglycemia (11).

Continuous glucose monitoring systems represent a rapidly advancing technological trend. Wearable, minimally invasive CGM sensors are capable of monitoring blood glucose levels almost in real time over several consecutive days, thereby providing a significant innovation in diabetes management. This technology is increasingly becoming prevalent among diabetic individuals requiring insulin therapy, as continuous monitoring enhances the effectiveness of the treatment process.

Devices used in continuous glucose monitoring consist of three main components. First, a small sensor—with an adhesive patch—that is placed under the skin (typically on the abdomen or arm) to secure its position; these are known as disposable sensors. Alternatively, implantable sensors, which are inserted into the body, are also used. CGM sensors estimate interstitial glucose levels and need to be replaced at specific intervals depending on their type (often every few weeks). The second component is a transmitter, which wirelessly sends data to the third component—a receiver device (or a software program on a smartphone or insulin pump) where the data are stored and displayed.

Glucose sensors are widely utilized by diabetic individuals, and user feedback based on personal experience varies. The benefits of CGM have been demonstrated in numerous studies involving both type 1 and type 2 diabetic patients, showing improvements in HbA1c, reductions in hypoglycemic events, decreased glycemic variability, and alleviation of diabetes-related distress (12-14). In the literature, studies have predominantly focused on controlling blood glucose levels with CGM systems (15,16). However, there is a limited amount of research addressing the issues or complications arising from their use. User reviews provide valuable insights into the effectiveness, ease of use, challenges encountered, reliability, and impact on quality of life associated with these devices.

The Importance of Continuous Glucose Monitoring Systems in Nursing

Continuous glucose monitoring sensors have become a critical component in diabetes management within nursing practice. With the use of these sensors, nurses can more effectively assess patients' glycemic control and detect hypoglycemic or hyperglycemic episodes at an early stage, enabling timely intervention (17). This is particularly advantageous for nurses working in intensive care, endocrinology, and home care settings, as monitoring patients' real-time glucose values aids in optimizing medication and insulin dosages (18,19).

Moreover, issues such as false alarms and measurement errors are among the challenges that nurses must address during patient education. Strengthening educational programs is essential to enhance patient safety and treatment adherence. By providing training on CGM systems, nurses can increase patients' awareness regarding proper sensor usage, alarm settings, and strategies to improve

blood glucose measurement accuracy. The effective use of glucose sensors not only reinforces the role of nurses in diabetes management but also contributes to higher quality patient care and the prevention of complications.

This study aims to conduct a qualitative analysis of user comments related to glucose sensors. The research seeks to evaluate the effectiveness of the devices, the technical issues encountered during their use, and the adaptation of individuals to this technology based on user experiences. The findings are expected to offer recommendations for the improvement of glucose sensors as well as to contribute to understanding how diabetic patients approach this technology. In this context, the study intends to present a new perspective on diabetes management and technology integration by examining patient experiences with glucose sensor use within a scientific framework.

The following research questions were addressed in this study:

- What is the effectiveness of the devices?
- What difficulties are encountered during use?
- What is the level of technical reliability of the devices?
- How do glucose sensors affect users' quality of life?

Ethical Considerations of the Study

This study did not require ethics committee approval, as it was compiled from anonymous and publicly accessible data sources. Nonetheless, all data were handled anonymously, and only general evaluations that did not contain any personal information were performed. The research was conducted in accordance with the ethical principles governing qualitative research.

MATERIAL AND METHOD

Research Design

This study was designed as a qualitative, cross-sectional investigation to examine user experiences with CGM systems. The research aimed to uncover the advantages, disadvantages, and challenges encountered during the use of these devices by analyzing user comments. Within the framework of qualitative research, the study employed an interpretative phenomenological approach, which was chosen for its focus on understanding individuals' lived experiences. The analysis was conducted using content analysis, with data systematically evaluated through an inductive approach to develop meaningful themes. The inductive method was preferred because the analysis was based entirely on user comments without reference to any pre-established theory. Content analysis is an approach for drawing objective and systematic inferences from verbal or written sources, and it aims to reveal general trends related to the subject under investigation (20).

Research Universe and Sample

The research universe comprised users who employ continuous glucose monitoring systems and post comments about these devices online. The sample was drawn from data obtained on platforms where CGM

users are highly active, specifically Reddit, YouTube, and Şikayetvar.com.

Data Sources

Reddit: One hundred comments meeting the inclusion criteria were collected from discussions where diabetic patients and CGM users share their experiences and recommendations. Notably, the r/diabetes subreddit is an active platform for such exchanges. [<https://www.diabetesdaily.com/forum/forums/continuous-glucose-monitors-SGIs.84/page-2>]

YouTube: Sixty comments were retrieved from video descriptions and comment sections related to user experiences with continuous glucose monitors, using keywords such as "Continuous Glucose Monitor User Experiences" and "Glukoz izleme sensörü kullanımı."

Şikayetvar (Türkiye): Thirty-three comments that met the inclusion criteria were collected from the Şikayetvar.com platform, where Turkish users express their complaints regarding CGM devices.

These platforms were selected due to their ability to capture experiences from participants across various geographical regions and socio-economic backgrounds.

Participant Profile

No direct participants were involved in the study; instead, anonymous user comments from online platforms served as the data source. These comments represent the diverse experiences of individuals from various age groups, genders, and diabetes types. The written expressions predominantly reflect experiences from groups such as patients with type 1 and type 2 diabetes, individuals diagnosed with prediabetes, and parents of children with diabetes.

Data Collection Process

Between January 2024 and December 2024, a total of 193 comments relevant to the study's objectives were included. Data collection was terminated once repetitive comments began to appear and data saturation was reached. The comments and complaints were thematically selected from publicly accessible platforms and compiled anonymously. The selection criteria for the comments were as follows:

Inclusion Criteria

Comments must contain detailed experiences related to CGM systems.

They should provide information about advantages, disadvantages, or user recommendations.

They must address technical issues, user satisfaction, design and comfort aspects, cost and accessibility challenges, or potential improvements suggested by users.

The comment must have been posted within the last year (2024).

Exclusion Criteria

Comments that are not directly related to CGM systems or contain superficial information have been excluded.

Single-word comments or those with disconnected statements have been excluded.

Comments with commercial intent, brand promotions, or sponsored content have not been included.

Comments containing personal health information, private patient details, or violating patient privacy have been excluded.

Comments with meaningless, incoherent, or machine-translated inconsistencies have been excluded.

Comments containing profanity, insults, or offensive language have been excluded.

Data Analysis

The data obtained from glucose sensor users were analyzed using Microsoft Word, following these steps:

1. Data Compilation

Comments from platforms such as Reddit, YouTube, and Şikayetvar were collected and grouped under separate

headings for each platform (Table 1). These comments were consolidated into text files, which served as the primary dataset for the study.

2. Coding and Thematic Classification

First-Level Coding: The comments were carefully read, and primary themes were identified. These themes were defined as main headings in a Word document.

Second-Level Coding: Under each identified theme, more specific sub-themes were classified. Each comment was categorized accordingly (Table 2).

3. Grouping of Comments

The comments were organized into tables as evidence supporting the relevant themes, using the "Insert > Table" function in Word.

4. Summarization of Themes

For each theme, a summary of the corresponding findings was prepared. This section was structured using headings (e.g., "User Satisfaction and Positive Experiences"), and the supporting findings for each sub-theme were listed as bullet points.

Table 1. Summary of CGMS data by source and codes					
Main theme	User satisfaction and positive experiences (n)	Technical issues and perceived deficiencies (n)	Ease of use and design issues (n)	Solution suggestions and needs of users (n)	Practical applications of results (n)
Reddit (n=100)	34	59	10	4	20
Şikayet var (n=33)	3	18	6	3	7
Youtube (n=60)	13	15	3	10	44
n: Number of user comments; Data is taken from Reddit, YouTube, and Şikayet var; Some comments were included in all relevant categories because they addressed more than one theme					

Table 2. Thematic classification of glucose sensor user comments	
Main theme	Sub themes
User satisfaction and positive experiences	Impact on quality of life; tracking trends; alert mechanisms
Technical issues and perceived deficiencies	Accuracy problems; alarm systems; connection and calibration deficiencies
Ease of use and design issues	Sensor placement; adhesives; cost barriers
User solution suggestions and needs	Calibration demands; customizable alarms; improved designs
Practical applications of results	Role in diabetes management; improvements by manufacturers

RESULTS

Although continuous glucose monitoring systems offer significant advantages in diabetes management, they also involve various technical and design challenges based on user experiences. The findings of this study provided a comprehensive evaluation of user satisfaction, the problems encountered, and the suggested solutions. All the outputs obtained are presented in Table 3. The study reached the following findings:

1. User Satisfaction and Positive Experiences

• Sub-themes and Key Findings:

Impact on Quality of Life: Glucose sensors have increased quality of life by reducing the need for finger pricking.

Blood Glucose Tracking: They have provided the opportunity to track blood glucose trends. By ensuring continuous monitoring of blood glucose, they have facilitated adherence to diets.

Alarm Systems: Users have indicated that they are satisfied with the alerts for hypoglycemia and hyperglycemia.

2. Technical Problems and Perceived Shortcomings

• Sub-themes and Key Findings:

Accuracy Problems: It has been reported that the sensors work less accurately during the first 24 hours and on the last day.

Alarm Systems: The alarm systems (especially at night) giving false alarms have caused discomfort.

Connectivity and Calibration Shortcomings: Bluetooth connectivity issues and calibration deficiencies have been frequently mentioned.

3. Ease of Use and Design Problems

• Sub-themes and Key Findings:

Sensor Placement: Difficulties in sensor placement and, in some cases, pain have been reported.

Sensor Adhesiveness: Allergic reactions and skin irritation have occurred due to the adhesive materials.

Cost Barriers: The high cost of sensors has created accessibility issues for individuals with low income.

Data Saturation

Data saturation was achieved as the data began to exhibit recurring themes without adding any new information. Comments from different platforms have enhanced the generalizability of the findings.

Table 3. Content Analysis Table Based on Sensor User Experiences		
Main themes	Sub-themes	Main findings/inferences
User satisfaction and positive experiences	Impact on quality of life; tracking trends; alert mechanisms	Sensors improve quality of life by reducing the need for finger pricks and providing real-time glucose monitoring; alerts create a sense of security.
Technical issues and perceived deficiencies	Accuracy problems; alarm systems; connection and calibration deficiencies	Accuracy issues in measurements, especially on the first and last days; frequent false alarms; Bluetooth connection drops.
Ease of use and design issues	Sensor placement; adhesives; cost barriers	Difficulty in installation; allergic reactions to adhesive; high cost limits access.
Users' solution suggestions and needs	Calibration demands; customizable alarms; improved designs	Users demand calibration features, customizable alarms, and durable adhesives; the need for longer life and lower cost is paramount.
Practical applications of results	Role in diabetes management; improvements by manufacturers	Design and calibration improvements can increase user satisfaction; findings provide a roadmap for technology development.
User comments were analyzed thematically from Reddit, YouTube and Şikayetvar platforms		

DISCUSSION

This study aimed to examine the user experiences of individuals using continuous glucose monitoring systems, thereby elucidating the role, advantages, encountered challenges, and technical issues of these devices in diabetes management. Although the positive effects of CGM systems on glycemic control have been widely investigated in the literature, qualitative studies based on user experiences remain limited. This research offers a comprehensive perspective on the practical use of these devices by analyzing user comments from various platforms.

User Satisfaction and Positive Experiences

The findings indicate that CGM systems provide significant benefits in terms of enhancing quality of life, facilitating blood glucose monitoring, and contributing to the management of hypoglycemia/hyperglycemia. Users reported that these systems reduce the need for finger pricking, thereby making the diabetes management process less invasive and more comfortable. Additionally, by offering the opportunity to monitor blood glucose trends, they have helped individuals improve adherence to dietary and physical activity regimens. The alarm systems for hypoglycemia and hyperglycemia have generally been positively evaluated by users and have been highlighted as an important feature that increases the sense of security.

These findings are consistent with studies in the literature showing that CGM improves HbA1c levels, reduces

hypoglycemic events, and stabilizes glycemic variability (7,12,15). For example, the study titled Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes highlights the important role of sensors in lowering HbA1c levels and improving blood glucose control (13). It has been observed that these systems provide more detailed information about glycemic variability by detecting fluctuations in glucose levels, their duration, and frequency (21). The study's findings support these results in terms of diabetic individuals' adaptation to technology and the long-term effects of continuous glucose monitoring.

Technical Problems and Perceived Shortcomings

The findings of the study have revealed that, despite the many advantages of CGM systems, they also encompass certain technical issues and design deficiencies. One of the most frequently mentioned problems by users is fluctuations in sensor accuracy. In particular, users reported that measurements are less reliable during the first 24 hours and in the final days of the sensor's lifespan. This situation is consistent with the existing concerns in the literature regarding the accuracy and calibration requirements of CGM systems. For instance, a study conducted on critically ill patients after abdominal surgery and solid organ transplantation determined that real-time continuous glucose monitoring required additional calibration during the first 24–48 hours (22). It was considered that the participants in that study might have experienced accuracy errors due to their inexperience with calibration (22). However, in the present study,

individuals who have been diabetic for many years and have been using CGM systems attributed the inaccurate measurements to deficiencies in the devices' calibration processes. These findings indicate that there remain areas needing improvement in the accuracy and reliability of CGM systems, and that calibration processes, in particular, have a decisive impact on the user experience.

In the comments included in the study, it was reported that the sensors' measurement errors are particularly higher during the first days and decrease over time. Additionally, some users stated that the devices give false alarms and continuously report low glucose levels, especially during the night. This situation indicates that, despite the ease of use of CGM systems, users are still prompted to verify with fingertip glucose measurements.

There are studies in the literature that investigate the accuracy of CGM devices (23-25). A systematic review revealed that the accuracy of various CGM sensors available on the market—both in terms of numerical accuracy and clinical accuracy measured by error grids—is sufficient in the overall glycemic and hyperglycemic range. However, the accuracy rates in hypoglycemia were found to be limited (25). Another limitation of CGM is that glucose levels are measured from the interstitial fluid rather than from the blood. Since it takes time for glucose to pass from the bloodstream to the interstitial fluid, there is a natural delay between the actual blood glucose level and the level measured by the CGM. This delay varies by user and device, but is generally between 5 and 15 minutes (24). A measurement taken during this period may be erroneously evaluated. However, it has been argued that deviations of more than ± 40 mg/dl in these measurements might be unacceptable (26). Therefore, when providing CGM training to diabetic patients, education should cover both calibration techniques (for models requiring calibration) and the need to consult healthcare professionals for deviations exceeding ± 40 mg/dl.

Almost all CGM systems perform less accurately during hypoglycemic episodes and provide the most accurate measurements during hyperglycemia (23). However, the comparative performance among systems may vary significantly among patients. In situations where glucose levels change rapidly or where symptoms do not match the readings in the hypoglycemic range, it is very important to verify glucose values with blood glucose measurements (27).

In the study, false alarm notifications emerged as a significant issue. Users reported that the false alerts from hypoglycemia or hyperglycemia alarm systems, especially during nighttime, adversely affected their sleep quality. Such false alarms may be caused by factors such as the individual lying on the arm where the sensor is located, leading to compression-induced low readings or pressure-induced sensitivity reductions resulting in false hypoglycemia readings (28,29). In some devices, alarm functions are available to warn users of a hypoglycemic condition, and people tend to rely on these alarms. The National Institute for Health and Care Excellence

recommends verifying hypoglycemic values with a finger-prick test (30). CGM systems are not sufficiently accurate to detect hypoglycemia, a common side effect of diabetes treatment (31). Therefore, individuals using these sensors should be educated on hypoglycemia alarm settings and proper sensor usage. In the study, users indicated that they adjusted these false alarms by configuring the alarm thresholds; some users even reported that they turned off the alarms while sleeping.

The higher the hypoglycemia threshold is set, the higher the likelihood of detecting hypoglycemia. However, this increased threshold also raises the risk of false alarms (32). There are costs associated with this suboptimal alarm performance. The irritation caused by false alarms and additional finger-pricking tests may lead some patients to opt for the comfort of a lower alarm setting rather than the safety of a higher one. Recently, the concept of "alarm fatigue" has emerged to describe this situation (33). Alarm fatigue occurs when a CGM user is exposed to a high frequency of alarms that are no longer perceived as important—especially false or ineffective alarms—resulting in a risk of neglecting real alerts. Education should start with wise alarm settings. In most cases, the selected hypoglycemia alarm threshold is approximately 70 mg/dl, and this setting allows for a reduction of more than 50% in the time spent in hypoglycemia (34). However, this alarm threshold is not universal and should be adjusted in collaboration with the healthcare team according to age, medical history, and the individual's hypoglycemia awareness threshold. It is also possible to enable alarms only during periods when hypoglycemia occurs more frequently (e.g., at night, during intense physical activities, while fasting, etc.). When the hypoglycemia alarm is deactivated, an emergency low blood sugar alarm (<54 mg/dl), which is non-adjustable or cannot be disabled (factory setting), is triggered depending on the device (34). Therefore, optimizing the hypoglycemia alarm thresholds of CGM systems according to individual needs and ensuring that users receive proper education to manage these alarms effectively emerges as a necessity for system reliability and patient safety.

Ease of Use and Design Issues

CGM users have reported that the sensor placement process is challenging and, in some cases, can cause pain. It has been reported that some individuals experience allergic reactions and skin irritation due to the adhesive materials used to secure the sensor to the skin. In the literature, skin reactions associated with CGM use have been identified as a significant concern, particularly among individuals with sensitive skin (35). In a study conducted by F. Lambardo et al. (2022) involving 64 children and adolescents with type 1 diabetes who used insulin pumps and continuous glucose monitoring devices, 27.8% of participants exhibited symptoms such as a history of allergic diseases, itching, discharge, and edema, with this skin irritation being attributed to the sensor adhesives (36). In fact, there is still no developed precaution to prevent skin problems. It has been observed that individuals with

sensitive skin are satisfied with sensors applied with a hydrocolloid patch or topical corticosteroid skin barrier spray (37). Raising awareness among CGM users about alternative adhesive materials, protective barrier products, and measures appropriate for their individual skin types could be effective in minimizing skin reactions and enhancing both user comfort and treatment adherence.

Another significant issue is the high cost of sensors and accessibility limitations. Users have reported that the high prices of CGM devices make them difficult to access, particularly for low-income individuals. This situation indicates that cost-reducing measures are necessary to promote the widespread use of CGM. In a recent study by Messer et al. (2020), cost was identified as the greatest barrier to diabetes device usage among adolescents (38). Similarly, a survey among pediatric and adult clinicians emphasized that cost is the most significant factor hindering the widespread use of these devices, with approximately 50% of healthcare professionals considering it a major problem for patients (39). In fact, for adult type 1 diabetic patients using multiple daily injections and experiencing poor glycemic control, although the initial cost of CGM is high, it has been shown to be a cost-effective option in the long term by improving glucose control and reducing the risk of non-severe hypoglycemia (40). However, as is the case with any new technology in healthcare, cost and insurance coverage remain potential barriers to accessing these devices. In order for CGM technology to reach a broader audience, policies aimed at reducing costs, expanding insurance coverage, and minimizing access barriers need to be developed.

User Solutions and Expectations

The user comments included in the study demonstrate that they offer some suggestions for making CGM systems more user-friendly. Users, in particular, have emphasized needs such as:

- Improving calibration systems,
- Developing customizable alarm systems,
- Producing sensors that can be used for a longer period and at a lower cost,
- Resolving technical issues related to connectivity and data transfer.

These suggestions are regarded as important considerations for future product development processes by CGM manufacturers and healthcare providers.

Strengths and Limitations of the Study

This study offers an important contribution as one of the first qualitative analyses based on user experiences with CGM technologies. By collecting user comments from various platforms (Reddit, YouTube, and Şikayetvar), it has enabled a comprehensive analysis of the experiences of individuals from different geographical regions and socio-economic backgrounds.

The sample is based solely on data obtained from online platforms, and therefore may not represent the entire population of CGM users. Because the participants are anonymous, detailed demographic information (such as age, gender, and duration of diabetes) could not be determined. Since the user comments are based on personal experiences, they may be subjective and require support from clinical validations. Only data collected from specific platforms were examined, and other social media or patient forums were not included. Considering these limitations, it is recommended that future studies include surveys or semi-structured interviews with a broader user base.

CONCLUSION

In conclusion, glucose sensors provide a valuable alternative in situations where finger-pricking is challenging (e.g., in cases of neuropathy or manual dexterity issues) and make diabetes management more accessible. These innovations, which enhance user satisfaction, are considered an important step towards better glycemic control and improved quality of life. However, issues such as technical shortcomings, high cost, and fluctuations in sensor accuracy need to be addressed.

In this regard, the following recommendations are proposed:

- CGM manufacturers should implement technological improvements to enhance sensor accuracy.
- Customizable alarm systems should be developed to prevent false alarms.
- Sensor adhesives should be developed using more skin-friendly materials.
- The cost of CGM systems should be reduced to ensure broader accessibility for users.
- More comprehensive clinical studies should be conducted to examine the long-term effectiveness of CGM technologies in detail.

For diabetic individuals to effectively monitor their glucose levels, it is crucial for healthcare professionals to provide guidance that takes into account factors such as cost and accessibility, which will significantly contribute to improved patient compliance and treatment efficacy.

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Ethical approval: Ethics Committee approval is not required. This study is based solely on publicly available user-generated content obtained from open-access online platforms (Reddit, YouTube, and Şikayetvar). No personal, identifiable, or sensitive information was collected, and no direct interaction with human subjects occurred. Therefore, the study does not meet the criteria requiring ethical approval, in line with standard research ethics guidelines for secondary qualitative data analysis.

REFERENCES

- World Health Organization. Diabetes. Published 2024. <https://www.who.int/news-room/fact-sheets/detail/diabetes> access date 21.02.2025.
- Seuring T, Archangelidi O, Suhrcke M. The economic costs of type 2 diabetes: a global systematic review. *Pharmacoeconomics*. 2015;33:811-31.
- Eroğlu N. Diagnosis, treatment, and monitoring for the prevention of diabetes complications. *İzmir Katip Çelebi University Journal of Health Sciences*. 2019;4:31-3.
- Turkish Society of Endocrinology and Metabolism (TEMĐ). Guideline for the diagnosis, treatment, and monitoring of diabetes mellitus and its complications – 2022. In: Turkish Society of Endocrinology and Metabolism, eds. *Diabetes Diagnosis and Treatment Guidelines*. Ankara: Turkish Society of Endocrinology and Metabolism Publications; 2022;1-356.
- Deiss D, Bolinder J, Riveline JP, et al. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. *Diabetes Care*. 2006;29:2730-2.
- Heinemann L. Finger pricking and pain: a never-ending story. *J Diabetes Sci Technol*. 2008;2:919-21.
- Klonoff DC, Ahn D, Drincic A. Continuous glucose monitoring: a review of the technology and clinical use. *Diabetes Res Clin Pract*. 2017;133:178-92.
- Beck RW, Hirsch IB, Laffel L, et al.: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. The effect of continuous glucose monitoring in well-controlled type 1 diabetes. *Diabetes Care*. 2009;32:1378-83.
- Reddy N, Verma N, Dungan K. Monitoring technologies—Continuous glucose monitoring, mobile technology, biomarkers of glycemic control. In: Feingold KR, Anawalt B, Blackman MR, et al, eds. *Endotext* [Internet]. MDText.com, Inc.; 2000-. Updated July 8, 2023. <https://www.ncbi.nlm.nih.gov/books/NBK279046/> access date 21.02.2025.
- Peters AL, Ahmann AJ, Battelino T, et al. Diabetes technology—Continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2016;101:3922-37.
- Danne T, Nimri R, Battelino T, et al. International consensus on use of continuous glucose monitoring. *Diabetes Care*. 2017;40:1631-40.
- Vigersky R, Shrivastav M. Role of continuous glucose monitoring for type 2 in diabetes management and research. *J Diabetes Complications*. 2017;31:280-7.
- Beck RW, Riddlesworth T, Ruedy K, et al. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. *JAMA*. 2017;317:371-8.
- Ida S, Kaneko R, Murata K. Utility of real-time and retrospective continuous glucose monitoring in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. *J Diabetes Res*. 2019;2019:4684815.
- Seidu S, Kunutsor SK, Ajjan RA, Choudhary P. Efficacy and safety of continuous glucose monitoring and intermittently scanned continuous glucose monitoring in patients with type 2 diabetes: a systematic review and meta-analysis of interventional evidence. *Diabetes Care*. 2024;47:169-79.
- Jancev M, Vissers TACM, Visseren FLJ, et al. Continuous glucose monitoring in adults with type 2 diabetes: a systematic review and meta-analysis. *Diabetologia*. 2024;67:798-810.
- Perez-Guzman MC, Shang T, Zhang JY, et al. Continuous glucose monitoring in the hospital. *Endocrinol Metab (Seoul)*. 2021;36:240-55.
- Perez-Guzman MC, Duggan E, Gibanica S, et al. Continuous glucose monitoring in the operating room and cardiac intensive care unit. *Diabetes Care*. 2021;44:e50-2.
- Chow KW, Kelly DJ, Rieff MC, et al. Outcomes and healthcare provider perceptions of real-time continuous glucose monitoring (rtCGM) in patients with diabetes and COVID-19 admitted to the ICU. *J Diabetes Sci Technol*. 2021;15:607-14.
- Metin O, Ünal Ş. Content analysis technique: Its use in doctoral theses in communication sciences and sociology. *Anadolu University Social Sciences Journal*. 2022;22:273-94.
- Richardson R. Do metrics of temporal glycemic variability reveal abnormal glucose rates of change in type 1 diabetes? *J Diabetes Sci Technol*. 2024 Nov 11. doi: 10.1177/19322968241298248 [Epub ahead of print].
- Voglová Hagerf B, Protus M, Nemetova L, et al. Accuracy and feasibility of real-time continuous glucose monitoring in critically ill patients after abdominal surgery and solid organ transplantation. *Diabetes Care*. 2024;47:956-63.
- Nagl K, Berger G, Aberer F, et al. Performance of three different continuous glucose monitoring systems in children with type 1 diabetes during a diabetes summer camp. *Pediatr Diabetes*. 2021;22:271-8.
- Sato J, Hirose T, Watada H. Continuous glucose monitoring system: Is it really accurate, safe and clinically useful? *J Diabetes Investig*. 2012;3:225-30.
- Dávila-Ruales V, Gilón LF, Gómez AM, et al. Evaluating the precision and reliability of real-time continuous glucose monitoring systems in ambulatory settings: a systematic review. *Ther Adv Endocrinol Metab*. 2024;15:20420188241304459.
- Kovatchev BP, Patek SD, Ortiz EA, Breton MD. Assessing sensor accuracy for non-adjunct use of continuous glucose monitoring. *Diabetes Technol Ther*. 2015;17:177-86.
- Aberer F, Hajnsek M, Rumpler M, et al. Evaluation of subcutaneous glucose monitoring systems under routine environmental conditions in patients with type 1 diabetes. *Diabetes Obes Metab*. 2017;19:1051-5.
- Helton KL, Ratner BD, Wisniewski NA. Biomechanics of the sensor-tissue interface—effects of motion, pressure, and design on sensor performance and foreign body response—Part I: Theoretical framework. *J Diabetes Sci Technol*. 2011;5:632-46.
- Idi E, Prendin F, Facchinetti A, et al. Detection of compression artifacts in time series data from continuous glucose monitoring sensors using matched filters. 19th International Conference on Body Sensor Networks (BSN), 4–7 October 2023. Cambridge, UK., 1-4.

30. National Institute for Health and Care Excellence (NICE). FreeStyle Libre for glucose monitoring (Medtech innovation briefing MIB110). Published September 29, 2017. <https://www.nice.org.uk/advice/mib110/resources/freestyle-libre-for-glucose-monitoring-pdf-2285963268047557> access date 21.02.2025.
31. Lindner N, Kuwabara A, Holt T. Non-invasive and minimally invasive glucose monitoring devices: a systematic review and meta-analysis on diagnostic accuracy of hypoglycemia detection. *Syst Rev*. 2021;10:145.
32. McGarraugh G, Bergenstal R. Detection of hypoglycemia with continuous interstitial and traditional blood glucose monitoring using the FreeStyle Navigator Continuous Glucose Monitoring System. *Diabetes Technol Ther*. 2009;11:145-50.
33. Shivers JP, Mackowiak L, Anhalt H, Zisser H. "Turn it off!": Diabetes device alarm fatigue considerations for the present and the future. *J Diabetes Sci Technol*. 2013;7:1789-94.
34. Oriot P, Ponchon M, Weber E, et al. Benefits and limitations of hypo/hyperglycemic alarms associated with continuous glucose monitoring in individuals with diabetes. *Diabetes Epidemiol Manag*. 2023;9:100125.
35. Berg AK, Olsen BS, Thyssen JP, et al. High frequencies of dermatological complications in children using insulin pumps or sensors. *Pediatr Diabetes*. 2018;19:733-40.
36. Lombardo F, Bombaci B, Alibrandi A, et al. The impact of insulin-induced lipodystrophy on glycemic variability in pediatric patients with type 1 diabetes. *Children (Basel)*. 2022;9:1087.
37. Rigo RS, Levin LE, Belsito DV, et al. Cutaneous reactions to continuous glucose monitoring and continuous subcutaneous insulin infusion devices in type 1 diabetes mellitus. *J Diabetes Sci Technol*. 2021;15:786-91.
38. Messer LH, Tanenbaum ML, Cook PF, et al. Cost, hassle, and on-body experience: Barriers to diabetes device use in adolescents and potential intervention targets. *Diabetes Technol Ther*. 2020;22:760-7.
39. Tanenbaum ML, Adams RN, Hanes SJ, et al. Optimal use of diabetes devices: clinician perspectives on barriers and adherence to device use. *J Diabetes Sci Technol*. 2017;11:484-92.
40. Wan W, Skandari MR, Minc A, et al. Cost-effectiveness of continuous glucose monitoring for adults with type 1 diabetes compared with self-monitoring of blood glucose: the DIAMOND randomized trial. *Diabetes Care*. 2018;41:1227-34.



Can the PAN-Immune Inflammation Value Be Used as a Biomarker for Differentiating Epididymo-orchitis and Testicular Torsion in Children?

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Abstract

Aim: No study in the literature has investigated the role of the pan-immune inflammation value (PIV) in the differential diagnosis of epididymo-orchitis (EO) and testicular torsion (TT) in children. This study aims to evaluate the utility of PIV and other inflammatory indices in the differential diagnosis of EO and TT in children.

Material and Method: A retrospective analysis was conducted on 258 children who presented with scrotal pain between January 2019 and December 2023. Patients were divided into EO (n=187) and TT (n=71) groups, with the TT group further classified into orchiectomy (n=24) and detorsion (n=47) subgroups. The diagnostic power of hematological parameters, including derived indices such as PIV, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), in distinguishing TT from EO was investigated. Diagnostic performance was assessed using ROC analysis, and logistic regression models evaluated the predictive value of significant variables.

Results: TT patients exhibited significantly higher levels of white blood cells (WBC), neutrophil count, NLR, SIRI, and PIV compared to the EO group. PIV values were found to be significantly higher in the testicular detorsion group compared to the orchiectomy group. ROC analysis demonstrated weak diagnostic performance for NLR (AUC=0.580), SII (AUC=0.568), SIRI (AUC=0.599), and PIV (AUC=0.585), while WBC (AUC=0.673) and neutrophil count (AUC=0.634) showed poor performance. Multivariate logistic regression identified WBC (OR=2.52) and NLR (OR=2.6) as significant predictors of TT, with NLR values >3.39 associated with a 2.6-fold increased likelihood of TT.

Conclusion: Our study demonstrates that NLR and WBC, with high specificity, can predict TT, while SIRI and SII have limited diagnostic performance. Although PIV shows potential as a biomarker with varying sensitivity and specificity across different thresholds, its contribution in multivariate models appears less significant. However, it may be effective in predicting testicular viability in TT. Larger sample sizes and multicenter studies are required to further validate the clinical utility of these biomarkers.

Keywords: PAN-immune inflammation value, PIV, epididymo-orchitis, testicular torsion, diagnosis

INTRODUCTION

Acute scrotum is one of the most critical pediatric emergencies, presenting with sudden-onset redness, swelling, and pain in the inguinoscrotal region, particularly in the neonatal and adolescent periods but occurring at any age (1). Testicular torsion (TT) and epididymo-orchitis (EO) are among the leading causes of acute scrotal pain (2). While TT is a surgical emergency characterized by sudden testicular blood flow impairment due to the torsion of the spermatic cord around its axis, infection and inflammation

play a primary role in the pathogenesis of EO (3). TT is most frequently confused with EO, as the similarity of symptoms between these two clinical conditions, especially in the early stages, complicates the differential diagnosis (4). Rapid confirmation or exclusion of TT is critical to preventing potential testicular loss. Accurate differentiation is vital for avoiding unnecessary surgical interventions and ensuring that TT is not overlooked (1). Delay or misdiagnosis can result in permanent ischemic damage and necrosis of the testis (1).

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Doppler ultrasonography is a commonly used imaging modality in TT with high sensitivity (88.9%) and specificity (98.8%) (5). However, its limitations include operator dependency, preserved arterial flow in early stages, and challenges in examining prepubertal children (6). The primary reason for the limitations of Doppler ultrasonography in differentiating testicular torsion from epididymo-orchitis in prepubertal children is the thinner testicular vascular structures and lower blood flow in this age group (7). Additionally, nonspecific clinical findings in prepubertal patients and difficulty in patient cooperation contribute to diagnostic uncertainty (8). Additionally, delays in diagnosis using ultrasonography may lead to testicular loss, and international guidelines do not recommend relying solely on ultrasound for diagnosis (9). Therefore, more reliable diagnostic methods are being investigated.

Routine blood tests play a significant role in assessing inflammatory processes and early disease diagnosis. A complete blood count (CBC) is a routinely accessible laboratory test characterized by its simplicity of execution, affordability, and capacity to deliver critical hematological data, including quantitative measurements of leukocytes, lymphocytes, neutrophils, monocytes, platelets, and morphological indicators such as mean platelet volume. Ratios derived from these parameters are used as inflammation indices, aiding in the diagnosis, progression, and risk assessment of many diseases (10). Recently, indices such as the PIV have been investigated for their potential as prognostic biomarkers (11). However, there is no research in the literature investigating the role of PIV in differentiating EO from TT in children. This study evaluates the utility of PIV and other inflammatory markers in distinguishing EO from TT in pediatric patients.

MATERIAL AND METHOD

Approval from the Hitit University Non-Interventional Research Ethics Committee was granted under decision number 2024-08 on 03.04.2024. In this study, children who presented with scrotal pain to Hitit University Erol Olçok Training and Research Hospital between January 1, 2019, and December 31, 2023, were retrospectively analysed. Patients were divided into two main groups: those diagnosed with EO and those with TT. Among the TT patients who underwent surgery, a further subdivision was made into two subgroups: patients who underwent testis detorsion and those who underwent orchiectomy. Demographic data such as age and gender, along with calculated values for PIV, systemic immune-inflammation index (SII), systemic immune-inflammation response index (SIRI), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), were compared between the groups. Given the retrospective nature of this study, to ensure the reliability of statistical evaluations, a negligible number of patients with missing laboratory records for key parameters were excluded as part of the exclusion criteria and were not included in the analyses. Since complete datasets for the variables of interest were available for all patients ultimately included in the study, no imputation techniques were used.

PIV, SII, and SIRI are composite biomarkers derived from routine blood parameters to assess systemic inflammation and immune response. PIV is calculated using the formula $(\text{neutrophil} \times \text{monocyte} \times \text{platelet}) / \text{lymphocyte}$, SII is determined as $(\text{platelet} \times \text{neutrophil}) / \text{lymphocyte}$, and SIRI is obtained by $(\text{neutrophil} \times \text{monocyte}) / \text{lymphocyte}$. These indices have been increasingly utilized in various inflammatory and oncological conditions due to their potential prognostic value. In this study, these inflammatory markers were calculated from complete blood count parameters and analysed to evaluate their diagnostic utility in differentiating EO from TT.

Statistical Analysis

All data analyses were performed using SPSS statistics software (Version 22, SPSS Inc., Chicago, IL, USA) under Hitit University's licensed access. Categorical variables were expressed as counts (n) with corresponding percentages (%), and group comparisons for these variables were conducted using the chi-square test. For continuous variables, normality assumptions were verified through the Kolmogorov-Smirnov test, Shapiro-Wilk test, and visual inspections of histograms and Q-Q plots. Normally distributed data were reported as mean $\pm$ standard deviation (SD), while non-normal data were presented as median (minimum–maximum) values. Variance homogeneity was assessed using Levene's test. Parametric comparisons between two independent groups were performed with the Student's t test, whereas the Mann-Whitney U test was applied for non-parametric data. For comparisons involving three or more independent groups, the Kruskal-Wallis test was utilized, followed by Dunn-Bonferroni post hoc analyses to identify pairwise differences when statistical significance was detected.

The diagnostic utility of laboratory biomarkers and composite indices (NLR, PLR, SII, SIRI, and PIV) in differentiating TT from EO was evaluated using receiver operating characteristic (ROC) curve analysis. Area under the curve (AUC) values with 95% confidence intervals (CIs) were calculated to quantify discriminatory performance. AUC interpretation followed established criteria: 0.9–1.0 (excellent), 0.8–0.9 (good), 0.7–0.8 (moderate), 0.6–0.7 (poor), and 0.5–0.6 (non-informative). Optimal cutoff thresholds were determined using the Youden index, with corresponding sensitivity and specificity values reported for the most robust predictors. To evaluate the relationships between newly categorized variables (determined using optimal cutoffs) and TT likelihood, univariate and multivariate logistic regression models were developed. Results were expressed as adjusted odds ratios (ORs) with 95% CIs. A two-tailed p-value <0.05 defined statistical significance for all tests.

RESULTS

Data from a total of 258 pediatric patients were analysed. The EO group consisted of 187 patients (72.5%), while the torsion group, comprising orchiectomy and testis detorsion cases, included 71 patients (27.5%). The distribution was

further subdivided into EO (n=187, 72.5%), orchiectomy (n=24, 9.3%), and testis detorsion (n=47, 18.2%). The mean age was 10.23 ± 4.58 years (range: 0–17), and the mean hospital stay was 1.03 ± 1.98 days (range: 0–19).

Comparisons of sociodemographic features and laboratory parameters across study groups are presented in Table 1. The torsion group had a significantly higher mean age and length of hospital stay than the EO group ($P=0.001$, $P<0.001$, respectively). No significant differences were observed for side distribution, CRP, lymphocyte, monocyte, platelet, PLR, MLR, or SII values ($P>0.05$). However, WBC, neutrophil count, NLR, SIRI, and PIV values were significantly higher in the torsion group ($P<0.001$, $P=0.001$, $P=0.046$, $P=0.014$, $P=0.035$, respectively; Table 1).

Table 2 presents the statistical findings for PIV comparisons among EO, orchiectomy, and testis detorsion groups, revealing significant differences ($P<0.001$). Post-hoc tests indicated that PIV values were significantly higher in the testis detorsion group compared to other groups ($P<0.001$ for all comparisons). No significant differences were noted between other groups ($P>0.05$). Figure 1 illustrates the distribution of PIV values among the groups.

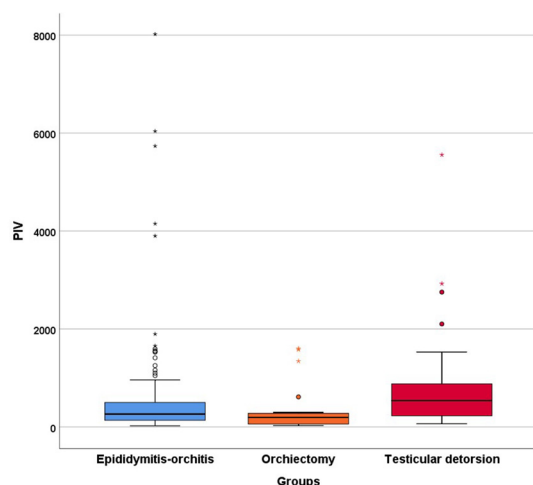


Figure 1. Boxplot with jitter illustrating the distribution of pan-immune-inflammation values (PIV) between epididymo-orchitis, orchiectomy and testicular detorsion groups

The findings of the ROC analysis performed to determine the success of laboratory blood values and indices in differentiating EO from TT, as well as the sensitivity and specificity values calculated using the cut-off points determined by the ROC analysis, are presented with 95% confidence intervals in Table 3. According to the ROC analysis AUC values, NLR, SII, SIRI, and PIV showed weak performance in predicting torsion ($AUC=0.580$, $AUC=0.568$, $AUC=0.599$, $AUC=0.585$, respectively), while WBC and neutrophil values exhibited poor performance ($AUC=0.673$, $AUC=0.634$; Table 2). Optimal cut-off values calculated using the Youden index were WBC 8.75, neutrophil 6.62, NLR 3.39, SII 911, SIRI 0.888, and PIV 531 and 179.6. There were two different cut-off points calculated for the PIV based on the maximum sensitivity and specificity values determined using the Youden index. Therefore, sensitivity and specificity values were calculated for both cut-off

points. According to these cut-off points, the calculated sensitivity and specificity values were 70.4% and 59.4% for WBC, 46.5% and 79.1% for neutrophil count, 35.2% and 88.2% for NLR, 36.6% and 82.4% for SII, 66.2% and 54% for SIRI, 42.3% and 77.5% for the first PIV cut-off (PIV-1), and 80.3% and 36.9% for the second PIV cut-off (PIV-2), respectively. The ROC curves plotted to evaluate the success of significant laboratory blood values and indices in distinguishing between EO and TT are presented in Figure 2. Additionally, boxplots showing the distribution of PIV values for the proposed two different cut-off points among the study groups are shown in Figure 3.

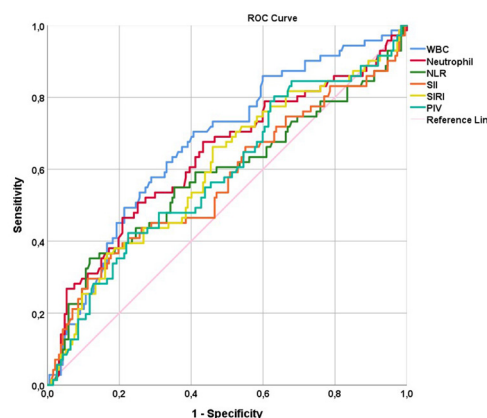


Figure 2. ROC curves illustrating the predictive performance of significant biomarkers in diagnosing epididymo-orchitis and testicular torsion

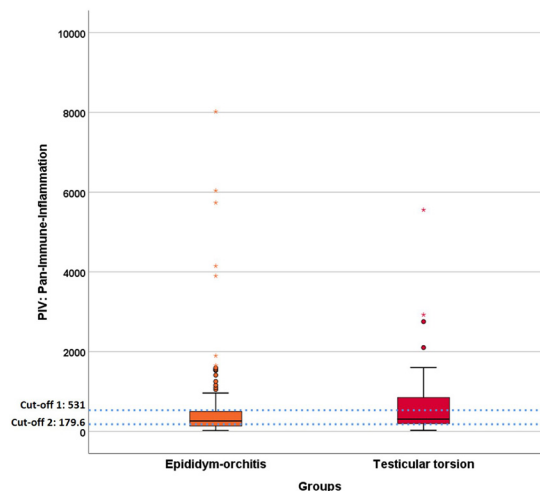


Figure 3. Boxplot with jitter illustrating the distribution of pan-immune-inflammation values (PIV) between epididymo-orchitis, and testicular torsion groups

Univariate and multivariate binary logistic regression analysis results, performed to determine the effects of laboratory blood values and indices on TT using the new categorical variables created based on the cut-off points determined by the ROC analysis, are presented in Table 4. In the univariate model, the effect of age was significant at the $P<0.10$ level ($P=0.066$). In the univariate model, WBC, neutrophil, NLR, SII, SIRI, PIV-1, and PIV-2 values were significant at the $P<0.01$ level ($P<0.001$, $P<0.001$, $P<0.001$, $P=0.001$, $P=0.004$, $P=0.002$, $P=0.009$, respectively). Since neutrophils were used in calculating the PIV index and NLR, SII, and SIRI were highly correlated with PIV ($r=0.852$, $r=0.927$, $r=0.959$, $P<0.001$, respectively), they were not

included simultaneously in the multivariate model despite being significant in the univariate model. In the model established with age, WBC, and PIV-1 index, PIV-1 was not significant ($P=0.463$). Similarly, PIV-2 was not significant ($P=0.469$) in the model with age, WBC, and PIV-2. In the multivariate model established with age, WBC, and SIRI index, SIRI was not significant ($P=0.509$). In the model with age, WBC, and SII index, SII was not significant ($P=0.373$).

In the model with age, WBC, and NLR index, age was not significant ($P=0.188$). Therefore, the final multivariate model was established with the WBC and NLR index, as presented in Table 4. In the multivariate model, the odds ratio (OR) for WBC was 2.52 (95% CI: 1.33–4.8), and for NLR, it was 2.6 (95% CI: 1.26–5.34). Patients with an NLR value greater than 3.39 were 2.6 times more likely to have TT compared to those with an NLR value less than 3.39 (Table 4).

Table 1. Statistical findings for the comparison of sociodemographic characteristics and laboratory blood values between epididymo-orchitis, and testicular torsion groups

	Groups		P values
	Epididym-orchitis (n=187)	Testicular torsion (n=71)	
Side (right/left)	100 (53.5%) / 87 (46.5%)	34 (47.9%) / 37 (52.1%)	0.422 ^a
Age	10 (0-17) (9.90±4.008)	13 (0-17) (11.08±5.766)	0.001^c
Length of stay	0 (0-19) (0.95±2.273)	1 (0-3) (1.24±0.746)	<0.001^c
CRP	3.22 (0.20-153.60) (9.07±21.24)	3.22 (3.05-39.90) (6.62±9.059)	0.926 ^c
WBC	8.25 (2.36-25.71) (8.76±3.318)	10.78 (1.88-20.52) (10.66±3.498)	<0.001^c
Lymphocyte count	2.77 (0.66-11.62) (3.16±1.701)	2.78 (0.66-10.13) (3.36±2.109)	0.947 ^c
Neutrophil count	4.14 (0.48-22.70) (4.84±3.197)	5.92 (0.38-17.39) (6.40±3.668)	0.001^c
Monocyte count	0.62 (0.17-3.30) (0.69±0.364)	0.65 (0.31-1.94) (0.73±0.319)	0.243 ^c
Platelet count (10 ³)	310.1±85.34 (302 (107-517))	294.7±85.40 (292 (102-648))	0.200 ^b
NLR	1.420 (0.064-19.824) (2.13±2.575)	1.829 (0.193-12.56) (3.05±2.982)	0.046^c
PLR	108.8 (25.47-483.7) (119.7±62.72)	102.5 (24.06-419.6) (116.9±69.08)	0.367 ^c
MLR	0.21 (0.06-1.52) (0.27±0.212)	0.22 (0.06-1.46) (0.28±0.213)	0.253 ^c
SII	414 (27.47-7097) (636.4±792.1)	439.8 (43.06-3268) (854.1±815.7)	0.090 ^c
SIRI	0.86 (0.05-23.40) (1.69±2.99)	1.13 (0.10-16.63) (2.21±2.65)	0.014^c
PIV	261.9 (22.9-8019) (515.5±943.3)	309.9 (25.8-5555) (639.4±835.1)	0.035^c

^aChi-square test, ^bStudent's t test, ^cMann-Whitney U test, CRP: C-reactive protein, WBC: white blood cell count, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, PIV: pan-immune-inflammation value, M: male, F: female

Table 2. Statistical findings for the comparison of PIV values between epididymo-orchitis, orchiectomy and testicular detorsion groups

	Epididymo-orchitis (1) (n=187)	Orchiectomy (2) (n=24)	Testicular detorsion (3) (n=47)	P value	Post-hoc P value
PIV					
Median	261.8	195.6	537.3		1-2: 0.224
(min-max)	(22.88-8019)	(25.84-1601)	(63.94-5555)	<0.001	1-3: <0.001
(mean±SD)	(515.5±943.2)	(340.7±470.6)	(791.8±938.1)		2-3 <0.001

Kruskal-Wallis test following Dunn-Bonferroni post-hoc tests, PIV: pan-immune-inflammation value

Table 3. Results of ROC analysis for laboratory blood values and inflammatory indices in distinguishing testicular torsion from Epididymo-orchitis, with sensitivity and specificity values based on cut-off points

Variables	AUC	95% CI		Cut-off	Sensitivity	Specificity
		Lower bound	Upper bound			
WBC	0.673	0.600	0.746	8.75	70.4% (58.2-80.4)	59.4% (51.9-66.4)
Neutrophil count	0.634	0.553	0.715	6.62	46.5% (34.7-58.6)	79.1% (72.5-84.6)
NLR	0.580	0.495	0.666	3.39	35.2% (24.5-47.5)	88.2% (82.5-92.3)
SII	0.568	0.484	0.653	911	36.6% (25.7 - 49)	82.4% (76 - 87.4)
SIRI	0.599	0.519	0.679	0.888	66.2% (53.9-76.7)	54% (46.6-61.3)
PIV-1	0.585	0.505	0.665	531	42.3% (30.8-54.5)	77.5% (70.8-83.2)
PIV-2				179.6	80.3% (68.8-88.4)	36.9% (30-44.3)

CRP: C-reactive protein, WBC: white blood cell count, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, PIV: pan-immune-inflammation value, AUC: area under curve, CI: confidence interval

Table 4. Results of univariate and multivariate binary logistic regression analyses to evaluate the effect of risk factors in distinguishing testicular torsion from epididymo-orchitis

	Univariate		Multivariate (Final model)	
	P values	OR (CI 95%)	P values	OR (CI 95%)
Age	0.066	1.061 (0.996-1.131)	ns	
WBC ≥8.75	<0.001	3.477 (1.933-6.256)	0.005	2.521 (1.325-4.798)
Neutrophil ≥6.62	<0.001	3.296 (1.836-5.914)	ni	
NLR ≥3.39	<0.001	4.076 (2.108-7.883)	0.010	2.596 (1.262-5.340)
SII ≥911	0.001	2.696 (1.462-4.972)	ni	
SIRI ≥0.888	0.004	2.300 (1.301-4.065)	ni	
PIV-1 ≥531	0.002	2.526 (1.410-4.525)	ni	
PIV-2 ≥179.6	0.009	2.381 (1.236-4.587)	ni	
Multivariate model: Nagelkerke R Square=0.136, Classification accuracy: 74%				
Values below P<0.05 were shown bold, ni: not included, ns: not significant (P>0.05); WBC: white blood cell count, NLR: neutrophil-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, PIV: pan-immune-inflammation value, OR: odds ratio, CI: confidence interval				

DISCUSSION

TT accounts for 10–15% of acute scrotal diseases in children and results in an orchiectomy rate of 42% among patients undergoing surgery for TT (12). Rapid and accurate diagnosis of TT is critical (13). However, TT must be distinguished from other conditions that can cause acute scrotal pain, particularly EO (14). The diagnosis of TT primarily relies on clinical symptoms, physical examination, and color Doppler ultrasonography (15). Scrotal color Doppler ultrasonography is an effective method for diagnosing TT, with sensitivity (88.9%) and specificity (98.8%) (5). However, in cases of early or partial torsion, as well as atypical presentations that may be influenced by the operator’s subjective assessment, there is a risk of misdiagnosis or missed diagnosis (16). In addition to operator dependency, it has disadvantages such as limited accessibility and delays in emergencies. Preparation for surgery and the duration of the operation may also narrow the critical therapeutic window for testicular salvage.

The European Association of Urology (EAU) pediatric urology guidelines recommend manual detorsion without anesthesia in patients with testicular torsion (TT). Despite successful manual detorsion, the guidelines emphasize the necessity of emergency surgical intervention and contralateral testicular fixation within the first 24 hours (17). A recent study evaluating the approaches of pediatric surgeons and urologists in Türkiye reported that only 14.7% of participants performed manual detorsion, while 70.5% never attempted it, and 14.7% considered it only when immediate surgery was unavailable. Additionally, among those who performed manual detorsion, 71.4% still proceeded with surgical intervention within 24 hours. The low utilization of manual detorsion may be attributed to concerns about incomplete detorsion, the risk of recurrent torsion, and delayed definitive management (18).

In recent years, it has been reported that hematological parameters (MPV, PLR, NLR, PLT, and leukocytes) at admission may differ between patients with TT and EO (19-24). These parameters hold potential as diagnostic

markers for TT. In our study, we investigated the usability of hematological parameters and systemic inflammatory indices in distinguishing between TT and EO in children. Notably, our study is original in that it is the only study in the literature to examine the diagnostic value of PIV in this context.

Our findings show similarities with those of Yılmaz et al. (2022) but also exhibit some differences. In the study by Yılmaz et al. (2022), which included pediatric and adult patients over the age of 12, the AUC values were reported as good for NLR and SIRI and poor for PLR in differentiating TT (22). In our study, PLR was found to be insignificant, and the performance of NLR, SII, and SIRI indices in distinguishing TT was determined to be poor. When comparing the sensitivity and specificity values of NLR with the study by Yılmaz et al. (2022), our study achieved higher specificity but lower sensitivity. While the OR for NLR was reported as 3.27 in the study by Yılmaz et al., the OR for NLR in our study was calculated as 4.076 (95% CI: 2.1–7.9) in the univariate model and 2.6 (95% CI: 1.26–5.34) in the multivariate model. This finding supports that, despite the low sensitivity (35.2%) and high specificity (88.2%) of NLR in our study, it remains a significant predictor in the multivariate model and may be an important marker for TT.

In the study by Yiğman et al. (2024) examining hematological parameters in the differential diagnosis of TT and EO in adult patients, WBC, neutrophil, and platelet levels were reported as insignificant, whereas lymphocyte, monocyte, eosinophil, MPV, NLR, and PLR levels were significant, with AUC values ranging from poor to weak (23). In our study, lymphocyte, monocyte, and platelet levels were found to be insignificant in distinguishing TT from EO, while NLR, SII, SIRI, and PIV indices were significant at a poor level, and WBC and neutrophil levels showed weak significance. Unlike Yiğman et al.’s findings, our study identified WBC as a significant marker for distinguishing TT, and consistent with their findings, the NLR results showed similar AUC values and cut-off points. In logistic regression analyses, Yiğman et al. reported only MPV as significant in their

multivariate model (OR 1.85, 95% CI: 1.33–2.57), whereas in our study, WBC (OR 2.52, 95% CI: 1.33–4.8) and NLR (OR 2.6, 95% CI: 1.26–5.34) were significant predictors. These results suggest that WBC and NLR could also be considered important predictors of TT in children.

In the meta-analysis conducted by Zhu et al. (2019), it was reported that parameters such as NLR and PLT showed significant differences in distinguishing TT from EO, whereas no significant differences were found for WBC, MPV, and PLR between TT and EO patients (24). The pooled results from the meta-analysis indicated that TT patients had lower NLR compared to EO patients (WMD=-1.66, 95% CI=-3.25 to -0.06, $p=.042$; SMD=-0.26, 95% CI=-0.51 to -0.02, $p=.036$) and lower PLT (WMD=-27.39, 95% CI=-48.03 to -6.75, $p=.009$; SMD=-0.31, 95% CI=-0.55 to -0.07, $p=.011$). Similarly, in our study, we found that NLR values were significant in distinguishing TT in children; however, in contrast, TT patients in our study had higher NLR values. The finding that PLR did not show a significant difference in diagnosing TT aligns with Zhu et al. (2019).

In the study by Yucel et al. (2019), which included children over 12 years old and adults, NLR and PLR were found to be significant at good and moderate levels, respectively, in distinguishing TT from EO (4). Similar to the findings of Yucel et al. (2019), our study also calculated the NLR cut-off as 3.39. However, in our study, the AUC and sensitivity values were lower in children. The specificity values, on the other hand, were calculated to be very high, consistent with the study by Yucel et al. (2019).

In our study, we also observed that the PIV index showed high specificity (77.5%) at the PIV-1 cut-off point in distinguishing TT, but with low sensitivity. This finding suggests that when high, it is useful in confirming testicular torsion (TT), as false positives are rare. However, its low sensitivity suggests that PIV alone cannot reliably exclude TT, and additional diagnostic tools (e.g. Doppler ultrasonography, clinical assessment) are necessary in cases with low PIV values. At the PIV-2 cut-off point, however, it showed high sensitivity (80.3%) but with low specificity. These findings suggest that PIV may be a potential biomarker when distinguishing either EO or TT alone. However, the fact that PIV was not significant in our multivariate model indicates that it provides limited contribution when used alongside other biomarkers. Additionally, in our study, PIV values were significantly higher in the testis detorsion group compared to the orchiectomy group, suggesting that it may be an effective marker for predicting testicular viability in TT.

The decision between orchiectomy and testicular preservation in testicular torsion (TT) remains a matter of debate, primarily due to the lack of objective criteria to determine testicular viability. Factors such as symptom duration, degree of torsion, ischemic appearance, and intraoperative findings are commonly used in clinical decision making. However, a recent multicenter study re-evaluating orchiectomy specimens using histopathologic

classification revealed that some cases with severe perioperative findings, late hospital admission or high degree of torsion still exhibited reversible histopathologic changes. These findings suggest that testicular viability assessment based solely on clinical and perioperative parameters may not always be reliable (25). In this context, the significant difference in PIV values between the detorsion and orchiectomy groups in our study suggests that PIV may serve as a complementary marker in assessing testicular viability and guiding surgical decision-making in TT cases.

In conclusion, this study highlights the diagnostic value of biomarkers such as NLR, WBC, and PIV in distinguishing TT and EO. However, it also reveals the limited effectiveness of the SIRI and SII indices and underscores the need for further validation in studies with larger sample sizes.

One limitation of this study is its single-center design. However, the use of a 5-year sample from a single center, covering the period from 2019 to 2023, can be seen as a strength. It provides depth and consistency to the study by ensuring more homogeneous data from the same hospital conditions. This approach can serve as a foundation for future multi-center studies.

CONCLUSION

This study emphasizes the diagnostic value of biomarkers such as NLR, WBC, and PIV in distinguishing TT and EO in children. Our findings suggest that NLR and WBC, especially with high specificity, can serve as important predictors for TT, while indices such as SIRI and SII demonstrate limited diagnostic performance. Although PIV shows potential as a biomarker with varying sensitivity and specificity across different thresholds, its contribution appears less significant in multivariate models. However, it can be considered an effective biomarker for predicting testicular viability in TT. To enhance the clinical utility of these biomarkers, further validation through larger sample sizes and multicenter studies is required.

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REFERENCES

1. Chanchlani R, Acharya H. Acute scrotum in children: a retrospective study of cases with review of literature. *Cureus*. 2023;15:e36259.
2. Diaz EC, Kimball D, Gong EM. Acute scrotal pain in pediatric emergency medicine: evaluation, diagnosis, management, and treatment. *Clin Pediatr Emerg Med*. 2014;15:248-60.
3. Zadig AM, Ásbjörnsson G, Salö M. Acute scrotum in children. *Lakartidningen*. 2024;121:23186.

4. Yucel C, Ozlem Ilbey Y. Predictive value of hematological parameters in testicular torsion: retrospective investigation of data from a high-volume tertiary care center. *J Int Med Res.* 2019;47:730-7.
5. Baker LA, Sigman D, Mathews RI, et al. An analysis of clinical outcomes using color doppler testicular ultrasound for testicular torsion. *Pediatrics.* 2000;105:604-7.
6. McBride CA, Patel B. Acutely painful scrotum: tips, traps, tricks and truths. *J Paediatr Child Health.* 2017;53:1054-9.
7. Kalfa N, Veyrac C, Baud C, et al. Ultrasonography of the spermatic cord in children with testicular torsion: impact on the surgical strategy. *J Urol.* 2004;172:1692-5.
8. Laimer G, Müller R, Radmayr C, et al. Multiparametric ultrasound in torsion of the testicular appendages: a reliable diagnostic tool?. *Med Ultrason.* 2022;24:33-7.
9. Radmayr C, Bogaert G, Bujons A, et al. EAU Guidelines on Pediatric Urology. 1nd edition. European Association of Urology Guidelines Office, Arnhem, The Netherlands, 2024;26-9.
10. Güven DC, Şahin TK, Erul E, et al. The association between the pan-immune-inflammation value and cancer prognosis: a systematic review and meta-analysis. *Cancers.* 2022;14:2675.
11. Fucà G, Guarini V, Antoniotti C, et al. The pan-immune-inflammation value is a new prognostic biomarker in metastatic colorectal cancer: results from a pooled-analysis of the Valentino and TRIBE first-line trials. *Br J Cancer.* 2020;123:403-9.
12. Sharp VJ, Kieran K, Arlen AM. Testicular torsion: diagnosis, evaluation, and management. *Am Fam Physician.* 2013;88:835-40.
13. Bandarkar AN, Blask AR. Testicular torsion with preserved flow: key sonographic features and value-added approach to diagnosis. *Pediatr Radiol.* 2018;48:735-44.
14. Yan Y, Chen S, Chen Z, et al. The applied value of medical history, physical examination, colour-Doppler ultrasonography and testis scintigraphy in the differential diagnosis of acute scrotum. *Andrologia.* Feb 20. 2018. doi: 10.1111/and.12973. [Epub ahead of print].
15. Deng QF, Yang C, Mao C, Chu H. Clinical and hematological analysis of testicular torsion in children. *Front Pediatr.* 2024;12:1399349.
16. Osumah TS, Jimbo M, Granberg CF, Gargollo PC. Frontiers in pediatric testicular torsion: an integrated review of prevailing trends and management outcomes. *J Pediatr Urol.* 2018;14:394-401.
17. Radmayr C, Bogaert G, Burgu B, et al. EAU Guidelines on Pediatric Urology. 1nd edition. European Association of Urology Guidelines Office, Arnhem, The Netherlands, 2023;25-7.
18. Canbaz FA, Gerçel G, Sag S. The management of testicular torsion: a survey of Turkish pediatric surgeons and pediatric urologists. *Ulus Travma Acil Cerrahi Derg.* 2024;30:685-93.
19. Bitkin A, Aydın M, Özgür BC, et al. Can haematologic parameters be used for differential diagnosis of testicular torsion and epididymitis?. *Andrologia.* 2018;50:1-6.
20. Güneş M, Umul M, Altok M, et al. Predictive role of hematologic parameters in testicular torsion. *Korean J Urol.* 2015;56:324-9.
21. Peretti M, Zampieri N, Bertozzi M, et al. Mean platelet volume and testicular torsion: new findings. *Urol J.* 2019;16:83-5.
22. Yilmaz M, Sahin Y, Hacibey I, et al. Should haematological inflammatory markers be included as an adjuvant in the differential diagnosis of acute scrotal pathologies?. *Andrologia.* 2022;54:e14374.
23. Yiğman M, Ekenci BY, Durak HM, Sancı A. Predictive value of hematologic parameters in the differential diagnosis of testicular torsion and epididymo-orchitis. *Androl Bul.* 2024;26:167-72.
24. Zhu J, Song Y, Chen G, et al. Predictive value of haematologic parameters in diagnosis of testicular torsion: Evidence from a systematic review and meta-analysis. *Andrologia.* 2020;52:e13490.
25. Cigsar Kuzu EB, Tiryaki S, Guney N, et al. Low-grade injury following testicular torsion: a multicenter study confirming a disturbing possibility. *Urol Int.* 2023;107:971-6.



Dental Students' Perspectives on Anatomy Education in Dental Faculty

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Abstract

Aim: In dental faculties, Anatomy is taught as a basic science course in the first year of the education program. The effective delivery of this course plays a critical role in equipping students with fundamental anatomical knowledge and preparing them for professional practice. The purpose of this study is to gather feedback from dental students regarding the anatomy curriculum and teaching methods.

Material and Method: This study was conducted with the participation of students enrolled in Dental Faculties during the 2021-2022 academic year. A total of 499 students from 29 different universities who had completed at least one term of anatomy education participated. The survey consisted of 20 questions covering topics such as the role of anatomy education in dental practice, anatomy learning models, the anatomy curriculum, and its relevance to professional requirements."

Results: 63.8% of students reported feeling like doctors when they began their anatomy education, while 75.4% stated that becoming a doctor is impossible without anatomy education. 94% of students found that working on models during practical classes made it easier to understand theoretical anatomy lessons, and 92.5% found that working with 3D programs facilitated understanding of the theoretical lessons. 65.8% of students believed that the anatomy curriculum in dental education should focus solely on head and neck anatomy. Upon transitioning to professional practice, 61.8% of students stated knowing the anatomy of the entire body was unnecessary, yet 53.1% believed they would apply their anatomy knowledge in their careers.

Conclusion: Evaluating dental students' attitudes toward anatomy courses and their learning experiences is important in understanding how they approach a fundamental area of knowledge critical for their profession. We believe that this study may be useful in curriculum planning and the development of teaching methods.

Keywords: Anatomy, dentistry, education, survey

INTRODUCTION

The Faculty of Dentistry was first established in our country in 1908 (1) and gradually developed into an institutionalized structure by drawing on the traditions of general medical disciplines (2). Before beginning their professional training, dental students complete at least two semesters of basic science courses. Anatomy is a fundamental component of basic medical sciences, including physiology, biochemistry, pharmacology, pathology, and microbiology (3), and serves as an indispensable foundation for advanced applications in dental education (4). Anatomy is the oldest branch of medicine that studies the normal form and structure of the body, the organs that make up the body, and the structural and functional relationships between these organs (5). Evolving educational modalities and curricular strategies in the dental faculties have prompted anatomists to develop

new teaching methods, emphasizing the integration of basic science skills into clinical practice. Assessing the effectiveness of knowledge delivery to students and fostering positive feedback are key responsibilities of basic science educators (6). The effectiveness of knowledge delivery to students and fostering positive feedback are key responsibilities of basic science educators (6). Head and neck anatomy serves as the cornerstone of anatomy education in dental faculties (7). Whether the anatomy education given to dental faculty students should cover only head and neck anatomy or whether the entire body's anatomy should be taught has been a subject of debate for many years. In 1981 and 1993, the American Dental Education Association (ADEA) recommended that dental curricula include anatomical structures of the head, neck, thorax, abdomen (including pelvic organs), and upper

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extremities. They decided that having knowledge of the anatomy and functioning mechanisms of the human body would lead to better guidance of patients by dentists (2). One of the goals in the macroscopic anatomy education in dentistry is to emphasize how anatomical areas below the neck are related to future clinical training and long-term dental practice for students (4). With the impact of evolving technology and computer systems, anatomy teaching methods have been updated, and laboratory training, which was once conducted only with cadavers, has been renewed with models and 3D programs. This has made it easier for students to visually see the organs and structures studied theoretically in the body as a whole and relate their anatomical neighbors, thus facilitating understanding in anatomy education.

While evaluations have been made by asking students about anatomy education for medical faculty students in our country (8-17), there have not been sufficient records regarding dental faculty students. Our fundamental goal is to provide anatomy education tailored to the professional needs of dentists and ensure it aligns with the requirements of their profession. In this regard, the aim of our survey study is to contribute to the literature on the restructuring of anatomy education in dental faculties or to provide input into curriculum planning and teaching method evaluations.

MATERIAL AND METHOD

This study was conducted with the ethical approval of the Scientific Research and Publication Ethics Committee of Nuh Naci Yazgan University (NNYU) under approval number 2021/4319, date 05.10.2021. It was sent electronically to the Deans of other Dental Faculties in Türkiye via the NNYU Faculty of Dentistry Dean's Office to reach students. The study was conducted in accordance with the principles of the Helsinki Declaration. The research was carried out electronically between 26 October 2021 and 27 November 2022, for dental students who had taken the General Anatomy course and were still enrolled in the faculty.

According to data published in the August 2021 issue of the Turkish Dental Association Journal, there are a total of 24,000 students in the 1st, 2nd, 3rd, 4th, or 5th year of study at dental faculties across Türkiye (18). These data represent the total number of dental students in Türkiye (n=24,000). Based on this information, the estimated number of students who should respond to the survey was calculated using a 97% confidence interval and a $\pm 5\%$ precision level. The sample size was determined to be n=462 (openepi.com/SampleSize). Based on this, the minimum number of students to be included in the study was identified as at least 462. This comparative and descriptive study was conducted with 499 students from 29 different universities. The students' opinions about their anatomy education were collected through a Likert scale form. To ensure the reliability of the responses, the students' names, surnames, and identification numbers were not included in the survey form. Students were asked to provide their gender, age, and the year of study they were in. The 20 questions in the survey were answered

by students using the following scale: strongly disagree, somewhat disagree, undecided, somewhat agree, and strongly agree. In the analysis, for clearer interpretation of the results, responses "strongly disagree" and "somewhat disagree" were combined as "disagree," "undecided" responses remained as "undecided," and "somewhat agree" and "strongly agree" responses were combined as "agree." The final question was open-ended, asking students to provide any additional thoughts they wished to add.

The survey questions were prepared within four main areas:

1. Students' opinions on the place of anatomy education in dental education.
2. Students' opinions on learning models in anatomy education.
3. Students' opinions on the anatomy curriculum.
4. Students' opinions on the suitability of anatomy education for professional requirements.

The responses to the questions were categorized and evaluated as answers to these four questions.

Statistical analysis was performed using descriptive statistics with the SPSS software package (Version 25.0, SPSS Inc., Chicago, IL, USA). Categorical variables between groups were analyzed using the Chi-square test.

RESULTS

A total of 499 students participated in the study from 29 different universities. Among the participants, 309 were female (61.9%), and 190 were male (38.1%). Of the respondents, 232 were in the last term of their 1st year, 158 were in the last term of their 2nd year, 62 were in the last term of their 3rd year, 26 were in their 4th year, and 21 were in their 5th year.

Regarding the students' opinions on the place of anatomy education in dental schools, 350 students (70.1%) indicated that they chose dental school willingly, 56 (11.2%) chose it unwillingly, and 93 (18.6%) were undecided about whether they wanted to attend. Of these students, 462 (92.5%) stated that they knew they would receive anatomy education when they chose dental school. When asked whether they felt like a doctor when they began anatomy education, 53.8% agreed, 21.2% disagreed, and 15% were uncertain. Additionally, 75.4% of students believed that it was impossible to become a doctor without anatomy education, 16.2% thought it was possible, and 8.4% were undecided (Table 1).

Regarding cadaver-based training, 75.3% of students expressed a desire to have training on cadavers when choosing dental school, and 83.7% wanted to have practical anatomy lessons on cadavers. Furthermore, 78.3% stated that they were not afraid to study anatomy on cadavers. In response to whether working with models in practical lessons helped them understand theoretical anatomy lessons, 88% agreed, and 92.5% found 3D programs helpful in understanding theoretical lessons (Table 2).

Regarding the dental anatomy curriculum, 60.5% of students thought that the dental anatomy curriculum should not be the same as that of medical schools, while 54.1% believed that the entire body anatomy should not be taught systematically, 29.4% thought it should be, and 16.4% were undecided. Additionally, 65.8% of students thought that the anatomy curriculum in dental school should focus only on the head and neck anatomy (Table 3).

When evaluating the adequacy of anatomy education in relation to their professional needs, 59.8% of students felt that they received sufficient education, 7.8% thought it was insufficient, and 48.3% felt it was more than what they needed for their profession. Regarding the use of anatomy knowledge in their professional lives, 61.8% did not believe they needed to know the entire body anatomy, but 53.1% thought they would use anatomy knowledge in their careers (Table 4).

Table 1. Student's views on the place of anatomy education in the faculty of dentistry

	* (n)	** (n)	*** (n)	**** (n)	***** (n)
When I chose dental school, I knew I was going to study anatomy	2.2% (11)	3.2% (16)	2% (10)	18.8% (94)	73.7% (368)
When I started studying anatomy in dental school, I felt like a physician	10.8% (54)	10.4% (52)	15% (75)	35.1% (175)	28.7% (143)
I think that it is not possible to be a physician without anatomy education	8.8% (44)	7.4% (37)	8.4% (42)	26.7% (133)	48.7% (243)

*strongly disagree, **partially disagree, ***undecided, ****partially agree, *****strongly agree

Table 2. Students' views on Learning models in anatomy education

	* (n)	** (n)	*** (n)	**** (n)	***** (n)
When I was choosing the faculty of dentistry, I was terrified to study on cadavers in anatomy education	56.1% (280)	19.2% (96)	16.6% (83)	5.4% (27)	2.6% (13)
I would like to receive training in cadavers in the anatomy laboratory (practical) course	4.6% (23)	2.8% (14)	8.8% (44)	22.6% (113)	61.1% (305)
It scares me to be trained in cadavers in anatomy laboratory (practical) class	60.3% (301)	18% (90)	12.2% (61)	6.4% (32)	3% (15)
Working with models in the anatomy laboratory (practical) course makes it easier for me to understand the theoretical lessons	1.8% (9)	0.8% (4)	3.4% (17)	18% (90)	76% (379)
Working with 3D programs in the anatomy laboratory (practical) course makes it easier for me to understand the theoretical lessons	1.6% (8)	1% (5)	4.8% (24)	21.8% (109)	70.7% (353)

*strongly disagree, **partially disagree, ***undecided, ****partially agree, *****strongly agree

Table 3. Student's views on the anatomy curriculum in the Faculty of Dentistry

	* (n)	** (n)	*** (n)	**** (n)	***** (n)
Anatomy education in the Faculty of Dentistry should be equivalent to the Faculty of Medicine	40.3% (201)	20.2% (101)	12.2% (61)	15.6% (78)	11.6% (58)
The content of the Anatomy course taught in the Faculty of Dentistry should be systematically explained to the whole body anatomy	33.3% (166)	20.8% (104)	16.4% (82)	17.2% (86)	12.2% (61)
The Anatomy course taught in the Faculty of Dentistry should be explained topographically only the anatomy of the head and neck	12% (60)	13.8% (69)	8.4% (42)	27.1% (135)	38.7% (193)

*strongly disagree, **partially disagree, ***undecided, ****partially agree, *****strongly agree

Table 4. Student's thoughts on the suitability of the given Anatomy education for their professional requirements

	* (n)	** (n)	*** (n)	**** (n)	***** (n)
The content of the General Anatomy course I took in the 1st or 2nd year was sufficient for the Faculty of Dentistry	3.8% (19)	4% (20)	32.5% (162)	29.1% (145)	30.7% (153)
The content of the General Anatomy course I took in the 1st or 2nd year was too much for the Faculty of Dentistry	12.8% (64)	12% (60)	26.9% (134)	22.4% (112)	25.9% (129)
I would like to take a topographic anatomy course in 5th grade	23.2% (116)	4.6% (23)	30.9% (154)	18.8% (94)	22.4% (112)
When I graduate as a dentist, I don't need to know all the body anatomy	10.2% (51)	14.8% (74)	13.2% (66)	29.1% (145)	32.7% (163)
When I graduate as a dentist, I will not use the anatomy knowledge I learned in the courses in my professional life	28.7% (143)	24.4% (122)	17.6% (88)	18% (90)	11.2% (56)

*strongly disagree, **partially disagree, ***undecided, ****partially agree, *****strongly agree

When asked whether integrating general anatomy lessons with clinical and radiological anatomy would make them more lasting, 63% (314 students) agreed, 30.9% (154 students) were undecided, and 6.2% (31 students) disagreed.

Lastly, students were asked to provide additional comments regarding general anatomy lessons, and some of the notable responses include:

- "I think we should take a review of head and neck anatomy in the final year."
- "I believe supporting theoretical knowledge with models and cadavers will significantly improve the teaching process."
- "We went into excessive detail on body parts other than the head and neck, which both added unnecessary workload and caused me to neglect areas I should focus on. I find it illogical for dental students to memorize things like the joints, bones, and muscles of the legs. This should definitely have been lighter at my school."
- "I know that anatomy lessons are essential and will be helpful in my career, but I don't think a dental student should memorize the bones of the toes. Receiving the same level of anatomical education as medical students is overwhelming for dental students because we also have dental-specific courses, practical lessons, assignments, and exams."
- "While I think the dental anatomy curriculum is heavy, I believe focusing only on head and neck anatomy would be sufficient. However, this knowledge should be reinforced for two years with cadavers and models in a detailed and repetitive way. If a student wants additional body anatomy knowledge, an elective course can be offered."
- "I would like to apply anatomy lessons to daily life, so I want to learn them well."
- "Although we are not doctors, we should keep in mind that we will be doctors and not be afraid to go into detail."
- "I think a doctor should know a thousand things and use one, but the other 999 should guide their work. Therefore, I believe all branches of medicine should be taught in detail. This will help broaden the perspective of a healthcare professional and allow them to look at the full picture."
- "Head and neck anatomy is often overlooked. Some of the time spent on other systems could be better allocated to reviewing the head and neck anatomy. No one should graduate without knowing it well; it is essential in the clinic. We should spend more time on it rather than diving deep into systems that are less useful."
- "In dental school, we have topics similar to those in medical school, but the lessons we receive in 2 hours are equivalent to the 22 hours spent in medical school. Naturally, we can't cover everything, and I feel I am

receiving inadequate anatomy education."

- "Instead of squeezing everything into the first two years, anatomy education could be more spread out, maybe over three years. This could ease the burden on students. Graduating with a more detailed knowledge of anatomy would allow students to have more accurate and well-rounded opinions in research. However, knowing only the head and neck anatomy in great detail would be more beneficial for our field."
- "I don't remember anything, I struggle with it, regards."
- "I think Latin should be taught in first."

DISCUSSION

In dental schools, effective teaching of anatomy as a first year basic science course is crucial for students to acquire fundamental anatomical knowledge and prepare for professional practice. The aim of this study is to gather feedback from dental students regarding the anatomy curriculum and teaching methods. In an era of easy access to information, it is important for traditionally taught anatomy courses to be more efficient, effective, and linked to clinical situations, to improve student comprehension. Therefore, this study aims to evaluate student thoughts by evaluates students' perspectives on learning methodologies, their views on the anatomy curriculum, and the role of anatomical knowledge in professional practice.

In a survey conducted by Doğan et al., it was emphasized that surveys are crucial for evaluating feedback and reflecting the results in future education and teaching processes. Regular evaluation of the education students receive has been shown to significantly contribute to improving the quality of education, addressing identified deficiencies, and developing new educational strategies that benefit students (7). In a study by Çan, the views of dental and medical students on the anatomy course were assessed. It was stated that in both medical and dental faculties, increasing student interest in anatomy courses, avoiding unnecessary details, providing profession-related knowledge, and relating course topics to clinical situations to boost student engagement were important (19). According to our study's results, most students acknowledged that they came to the faculty knowing anatomy is a fundamental course and that they believed a doctor cannot become one without anatomy education. They also stated that the information learned in the course becomes more permanent and intriguing when linked to clinical practice. In their evaluation of the future of anatomy education in dental schools, Balcioğlu et al. emphasized ongoing debates about integrating basic sciences with clinical content. They also pointed out that questions about how and what should be taught in this regard have emerged as significant issues in educational philosophy debates, citing conflicting articles on the matter (6). In our study, students expressed that they did not want to receive anatomy education equivalent to that of medical faculty, did not want the entire body anatomy to be taught, and preferred to learn only head and neck anatomy. We

believe this view that learning only head and neck anatomy is sufficient needs to be changed. The results we obtained suggest that students should view the human body as a whole, and topics should be taught in an integrative manner.

The impact of new educational tools used in anatomy education on preserving anatomical knowledge and developing future surgical skills remains unclear. More research is needed to evaluate the suitability of different teaching methods and student perceptions in the transition from traditional regional approaches to integrated, system-based, and multi-method teaching paradigms. Additionally, it is important to examine the ability of these methods to meet learning objectives (20). Research has shown that in recent years, dissection-based anatomy education tends to be replaced by projection and computer-based modeling (21). Despite the shift away from cadaver education, the result of our study shows that students still desire cadaver-based training and are not hesitant to work with cadavers. Although 3D programs and models play a significant role in determining the relationships, placement, and formation of anatomical structures, they cannot replace cadaver-based education, which ensures more permanent learning for students. Ostrin's study examined the role of mobile devices and application software in education and concluded that anatomy applications facilitate the observation of structures in 3D, make it easier to understand the placement and orientation of structures, and allow interaction with structures by enabling them to be rotated and layers to be removed (22). In literature reviews conducted by Hwang and Wu, they found that smartphones and tablet PCs have been strongly adopted as mobile learning devices by learners in recent years (23). In a study by Mayfield et al., it was noted that mobile devices, by enabling students to carry learning materials around the lab or cadaver space, offer advantages in anatomy learning through mobile anatomy applications developed using smartphones, providing students with learning formats best suited to their learning styles (24). It is recommended to explore such applications, suggest them to students, and integrate them into anatomy course programs (25). So far, no single teaching tool has been identified that can meet all curriculum requirements (26). The most effective way to teach modern anatomy is to combine various pedagogical resources (plastination, case-based learning (CBL), live anatomy, medical imaging, etc.) to complement each other. Students benefit the most when various and system-based teaching methods are integrated (27). The data obtained from our study supports these findings. Students have stated that working with models and 3D programs makes it easier to understand theoretical knowledge. In line with this result, we believe that while teaching theoretical lessons, it would be beneficial to make use of 3D programs, and in practical lessons, to support the learning process with models and, if possible, cadaver-based education to better understand the relationships between anatomical formations.

CONCLUSION

This study was conducted to support dental students in better understanding the fundamental concepts of anatomy and to provide a solid foundation for their professional practice. It was found that students invest a significant amount of time and effort into the anatomy course, which is filled with intense Latin terminology. Their increased interest in head and neck anatomy, in particular, suggests that this area holds more importance for students. While some opinions suggest that teaching the detailed anatomy of the entire body is unnecessary, it is concluded that students should not be content with only learning head and neck anatomy. The curriculum should be designed in a way that encourages students to learn human anatomy from a holistic perspective. Additionally, it was determined that student feedback is crucial for making educational programs more effective and adopting methods that are understandable to students. Future studies will focus on exploring the relationship between students' attitudes toward anatomy courses and their academic success, and will provide suggestions for improving educational programs based on these findings.

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REFERENCES

1. Ocakoğlu Ö. Türkiye Üniversite Tarihi (5 cilt) Emre Dölen, İstanbul: Bilgi Üniversitesi Yayınları, 2009 (1.Cilt), ISBN: 9786053990994. Değerler Eğitimi Dergisi. 2010;8:259-63.
2. Pamay A, Büyükertan M, Balcıoğlu HA. An investigation on the anatomy education at dental faculties in European and North American universities. Yeditepe Dental Journal. 2017;13:29-33.
3. Bati AH, Ozer MA, Govsa F, Pinar Y. Anxiety of first cadaver demonstration in medical, dentistry and pharmacy faculty students. Surg Radiol Anat. 2013;135:419-26.
4. Guttmann GD, Ma TP, MacPherson BR. Making gross anatomy relevant to dental students. Journal of Dental Education. 2003;67:355-8.
5. Arifoğlu Y. Her Yönüyle Anatomi. 1st edition. İstanbul Tıp Kitabevleri, İstanbul, 2021;2.
6. Balcıoğlu HA, Kökten G, Güven Y. Future perspectives of anatomy in dental education: quo vadis?. Int. J. Morphol. 2010;28:71-3.
7. Doğan Z, Uludağ Ö, Ateşoğlu S, et al. Opinions of students in dentistry faculty on interactive anatomy education. Sdı Sağlık Bilimleri Enstitüsü Dergisi. 2018;9:48-53.

8. Ögetürk M, Kavaklı A, Kuş İ, et al. Tıp öğrencileri nasıl bir anatomi eğitimi istiyor?. TED. 2003;10:7-14.
9. Tuygar Ş, Kuş İ, Saygılı Ö, et al. Evaluation of satisfaction levels and its associated variables for anatomy education in medical students. TED. 2015;14:5-14.
10. Turhan B, Çetkin M, Bahşi İ, Kervancioğlu P. The opinions of medicine faculty students about anatomy education. European Journal of Therapeutics. 2016;22:82-8.
11. Güler H, Ömerli A, Yılmaz F, et al. Erciyes University term 3 medical students' socio-demographic characteristic and opinions on anatomy education. Sağlık Bilimleri Dergisi. 2019;28:9-13.
12. Uygur R, Çağlar V, Topçu B, et al. The assessment of the students' opinions about anatomy education. Int J Basic Clin Med. 2013;1:94-106.
13. Arı İ, Şendemir E. Students' views on anatomy education. Uludağ Üniversitesi Tıp Fakültesi Dergisi. 2003;29:11-4.
14. Kamisli H, Özönur M. Evaluation a Course by interviews of academic staff and student: anatomy. Turkish Journal of Educational Studies. 2015;2:23-47.
15. Gülekon İ. The role of radiological and clinical anatomy in anatomy education: interview with students. Gazi Medical Journal. 2017;28:179-83.
16. Canbolat M. Evaluation of the knowledge of medical faculty students about the anatomical structures on radiological images. Med Records. 2020;2:87-92.
17. Davis CR, Bates AS, Ellis H, Roberts AM. Human anatomy: let the students tell us how to teach. Anat Sci Educ. 2014;7:262-72.
18. Çılgın koşu sürüyor. Türk Dişhekimleri Birliği Dergisi 2021;185:30-4. https://www.tdb.org.tr/tdb/v2/yayinlar/TDB_e-dergi/185/TDBD185.html access date 08.01.2024
19. Çan MA. Metaphors for anatomy lesson of students who received anatomy education in faculty of medicine and faculty of dentistry. Tip Eğitimi Dunyasi. 2022;21:118-27.
20. Estai M, Stuart B. Best teaching practices in anatomy education: a critical review. Ann Anat. 2016;208:151-7.
21. Redwood CJ, Townsend GC. The dead center of the dental curriculum: changing attitudes of dental students during dissection. Journal of Dental Education. 2011;75:1333-44.
22. Ostrin Z, Dushenkov V. The pedagogical value of mobile devices and content-specific application software in the A&P laboratory. Journal of the Human Anatomy and Physiology Society. 2016;20:97-103.
23. Hwang GJ, Wu PH. Applications, impacts and trends of mobile technology-enhanced learning: a review of 2008-2012 publications in selected SSCI journals. International Journal of Mobile Learning and Organisation. 2014;8:83-95.
24. Mayfield CH, Ohara PT., O'Sullivan PS. Perceptions of a mobile technology on learning strategies in the anatomy laboratory. Anat Sci Educ. 2013;6:81-9.
25. Demirtaş İ, Onay T, Günerigök F. Developed mobile applications for anatomy education. TED. 2019;18:41-9.
26. Kerby J, Shukur ZN, Shalhoub J. The relationships between learning outcomes and methods of teaching anatomy as perceived by medical students. Clin Anat. 2011;24:489-97.
27. Biasutto SN, Causa LI, Criado del Río LE. Teaching anatomy: cadavers vs. computers?. Ann Anat. 2006;188:187-90.



Evaluation of Marginal Bone Loss and Peri-Implant Tissue Conditions in Relation to Dental Implant Surface Design: A 12-Month Retrospective Study

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Abstract

Aim: This retrospective study aims to evaluate marginal bone loss and peri-implant tissue conditions in relation to implant surface design.

Material and Method: In our study, data from 50 dental implants placed in patients who underwent routine treatment at the Harran University Faculty of Dentistry Application and Research Center were evaluated. Data obtained for bone loss, gingival and plaque indices were evaluated. Two types of implants were compared based on these data. Type 1 implants feature an HSA (Hybrid Sand Blast and Acid Etched) surface designed to promote osseointegration, whereas Type 2 implants are composed of high-quality titanium alloy and incorporate AB/AE (Acid Etch with Aluminum Oxide Blasting) surface modifications to support osseointegration. The normality of data distribution was evaluated using the Shapiro-Wilk test. Comparisons between groups were made using the Mann-Whitney U test, as it is appropriate for data that does not show normal distribution.

Results: Type 2 implants showed significantly higher gingival index values ($p < 0.05$), while no significant differences were observed in plaque index or bone loss between groups.

Conclusion: Implant neck and surface design may influence soft tissue response, particularly gingival inflammation, highlighting the importance of implant morphology in peri-implant tissue health and long-term outcomes.

Keywords: Dental implant, bone loss, gingival index, plaque index

INTRODUCTION

Dental implants are widely used to replace missing teeth. Since their introduction in 1981, there has been a significant increase in the use of titanium implants (1,2). Tooth loss occurs in individuals for different reasons. Among the various causes of tooth loss, periodontal disease is the most prevalent. This is followed by trauma and developmental defects. The success rate of modern titanium implants used today has improved considerably and also complication and failure rate are quite low (1).

Implants are primarily made of commercially pure titanium (cpTi), a material that is in direct contact with the bone. Titanium is preferred due to its favorable mechanical properties, low failure rates, and good biocompatibility (3). Titanium grades range from 1 to 4, categorized based on

purity and oxygen content. Grade 4 titanium, commonly used in dentistry, contains 0.4% oxygen, which provides optimal mechanical strength (4,5). The success of implant treatment depends on proper surgical and prosthetic protocols. However, peri-implantitis, a pathological condition affecting the tissues around implants, has become increasingly prevalent in recent years (6).

It has also been reported that individuals with periodontitis history are at a increased risk of occurring periimplantitis than those whitouth periodontal disease history (7,8). Peri-implant diseases are classified as peri-implant mucositis and peri-implantitis. Although both conditions involve inflammation, peri-implantitis is distinguished by the presence of bone loss (9). Several treatment approaches are available for peri-implantitis, including non-surgical and surgical methods. However, once the disease develops, the

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healing process is long and the possibility of recurrence remains even after successful treatment (10).

It has been said that the risk of peri-implantitis can be reduced with regular care and proper oral hygiene following implant placement (11). Although it is problematic for patients to comply with postoperative follow-up appointments, early detection of peri-implant diseases is very important to prevent the progression of the disease and manage it at the peri-implant mucositis stage (12). It has been reported that typical symptoms of peri-implant diseases include bleeding gums and implant mobility (13).

Current implant systems have different surfaces, most of which have shown high success in long-term clinical studies. However, these surfaces have generally been developed based on nonstandard in vivo and in vitro tests, and the role of surface chemistry and structure in the early stages of osseointegration is not fully understood. In the future, it has been said that the development of implant surface designs with controlled and standard studies, and approaches such as drug delivery that support osseointegration, can increase early loading and long-term success (14).

This study aims to evaluate post-treatment bone loss and peri-implant tissue conditions by comparing two implant types with different surface and neck characteristics. By assessing plaque and gingival indices along with bone loss, it seeks to determine the impact of implant design on tissue health and the importance of early intervention for long-term success.

MATERIAL AND METHOD

This retrospective study was conducted using routine clinical data collected from patients treated at the Harran University Oral and Dental Health Application and Research Center. Ethical approval was obtained from the Harran University Clinical Research Ethics Committee, and permission was granted by this committee (Reference: HRÜ/24.08.25, Date: 10.06.2024). The study included 50 dental implants that were evaluated periodontally and radiographically to assess post-treatment bone loss and peri-implant tissue conditions. All implant surgeries were performed by a single experienced clinician under local anesthesia. The procedures were carried out following the manufacturer's protocol and surgical recommendations for each implant system. Standard surgical techniques were applied, including sequential drilling according to the specified implant diameter and length. Post-operative care instructions were standardized for all patients to minimize variability in healing outcomes. Two different implant types were analyzed, categorized as Type 1 and Type 2, based on their surface treatment and material composition. Type 1 implants feature HSA (Hybrid Sand Blast & Acid Etched) surface treatment, designed to enhance osseointegration by creating a roughened surface that promotes better bone-implant contact. Type 2 implants are manufactured from high-quality titanium alloy and utilize AB/AE (Acid Etch +

Aluminum Oxide Blasting) surface roughening techniques, which facilitate bone condensation and osseointegration through controlled surface modifications. The implants were evaluated after a 12-month follow-up period using computerized patient records, and all data were systematically documented.

Clinical Measurements

Bone loss and peri-implant tissue conditions were assessed using probing. Measurements were taken from four regions of each implant: buccal, lingual, mesial, distal. The values were recorded, and comparisons were made between the two implant types. In addition, plaque index and gingival index values were recorded to evaluate soft tissue health around the implants.

Plaque Index Assessment

The plaque index was recorded to assess the presence and extent of plaque accumulation on the implant surfaces. The following scale was used:

- 0 = No plaque present; the probe remains completely clean.
- 1 = No visible plaque, but a thin film of plaque becomes apparent after probing.
- 2 = Visible plaque accumulation on the implant surface or detectable plaque mass using a probe.
- 3 = Heavy plaque or calculus deposits that are clearly visible on the implant surface.

Gingival Index Assessment

The gingival index was evaluated to determine the degree of inflammation in the peri-implant tissues. The classification was as follows:

- 0 = Normal gingiva with no signs of inflammation.
- 1 = Mild inflammation, slight discoloration, and minor edema, with no bleeding after probing.
- 2 = Moderate inflammation with redness, edema, and bleeding upon probing.
- 3 = Severe inflammation characterized by significant redness, edema, ulceration, and spontaneous bleeding (15,16).

Statistical Analysis

The normality of the data distribution was evaluated using the Shapiro-Wilk test. The results indicated that none of the three variables satisfied the assumptions of normality ($p < 0.05$). Consequently, non-parametric methods were employed for further analyses. Comparisons between groups were conducted using the Mann-Whitney U test, as it is appropriate for non-normally distributed data. Statistical significance was set at $p < 0.05$. Descriptive statistics, including the mean $\pm$ standard deviation, were calculated and recorded for all variables. All statistical analyses were performed using IBM SPSS Statistics version 20. This approach ensured a robust and reliable evaluation of the dataset while adhering to rigorous statistical standards.

RESULTS

In this study, Type 1 and Type 2 dental implants were evaluated in terms of plaque index, gingival index, and bone loss to compare their effects on peri-implant tissue health.

The plaque index was measured as 0.43±0.05 for Type 1 implants and 0.55±0.07 for Type 2 implants. While the mean value for Type 2 implants was slightly higher, the difference was not statistically significant. This suggests that both implant types exhibit comparable peri-implant conditions within the study period.

The gingival index was recorded as 0.26±0.03 for Type 1 implants and 0.50±0.06 for Type 2 implants. The difference between the two groups was statistically significant (p<0.005), indicating that peri-implant soft tissues around Type 2 implants exhibited a higher degree of inflammation compared to Type 1 implants.

For bone loss, the mean values were 1.23±0.04 mm for Type 1 implants and 1.43±0.09 mm for Type 2 implants. Although Type 2 implants showed slightly greater bone resorption, the difference was not statistically significant, indicating that both implant types provided similar levels of bone stability over the 12-month follow-up period (Table 1).

Table 1. Statistical analysis of the study			
	Group 1 (mean±std.dev)	Group 2 (mean±std.dev)	P value
Plaque index	.43±.05	.55±.07	.291*
Gingival index	.26±.03	.50±.06	.008*
Probing depth	1.23±.04	1.43±.09	.113*
*Mann-Whitney U test			

DISCUSSION

Dental implants have been widely recognized in the scientific community since their introduction at the Toronto Conference in 1982, where early studies reported implant stability rates of 81% in the maxilla and 91% in the mandible (15). Over time, research has established key criteria for implant success, including the absence of radiolucency, implant mobility, pain, and infection. Long-term clinical studies have further explored factors affecting implant survival, particularly the impact of marginal bone loss on implant longevity.

A retrospective study conducted by Chrcanovic et al. in Sweden analyzed implant outcomes over a 20-year follow-up period. The findings revealed a significant correlation between marginal bone loss and implant failure, with the majority of failures (62%) occurring within the first three years of placement. Additionally, implants exhibiting bone loss greater than 3 mm had a survival rate of 87.8%, indicating that excessive bone loss may compromise implant stability. These findings emphasize the importance of early detection and intervention to minimize marginal bone loss, particularly in the critical early years post-placement. Furthermore, the study highlighted that short-term failure rates were more prominent, reinforcing the need for long-term observational studies to better understand the progression of bone loss and its implications for implant success (16).

Fransson et al. emphasized that the primary objective of implant therapy is to maintain tissue integrity, which is closely linked to the preservation of adequate bone support. Their findings highlight marginal bone loss as a key determinant of implant success, underscoring its clinical significance in long-term stability (17).

Similarly, a study conducted by Schou et al. assessed patients over a 5 to 10-year follow-up period, categorizing them based on their history of periodontitis. The results

indicated that while bone loss was more pronounced in patients with both prostheses and implants, the observed difference, although statistically significant, was only 0.5 mm. Notably, this minor variation was deemed clinically insignificant for individuals with a prior history of periodontitis, suggesting that while periodontitis may influence bone remodeling, it does not necessarily translate into a clinically meaningful impact on implant outcomes (18).

Marginal bone loss around both natural teeth and dental implants is influenced by multiple factors, including biological aging, mechanical stress, and systemic conditions. Similar to natural teeth, implants also experience progressive bone remodeling over time, which is often considered a physiological process associated with aging. However, in edentulous areas, bone resorption may occur at a different rate, particularly around implants, due to altered biomechanical loading and changes in bone metabolism. A study by Bryant et al. evaluated patients with long-term edentulism as well as those who received implants shortly after tooth extraction. Their findings indicated that bone loss progressed more rapidly in patients who underwent implant placement following short-term tooth loss, suggesting that the absence of a natural dentition for an extended period may allow for a more gradual adaptation of bone to mechanical forces. Additionally, implants placed in the basal bone demonstrated a lower rate of bone resorption compared to those placed in the alveolar bone, emphasizing the role of implant location in long-term bone stability (19-22).

Our findings are in partial agreement with recent systematic reviews and meta-analyses evaluating the impact of implant surface characteristics on peri-implant tissue health. For instance, Hussein A. et al. (23) reported that machined surface implants showed a trend toward reduced marginal bone loss and significantly lower probing pocket depths, although no significant differences were observed

in implant failure rates compared to rough surfaces. Similarly, in our study, the implants with a more aggressive neck design and rougher surface (Type 2) demonstrated significantly higher gingival index values, suggesting an increased inflammatory response. However, no significant differences were found in terms of marginal bone loss or plaque index. These results collectively underscore that while rough surfaces may support osseointegration, their influence on soft tissue health—especially gingival inflammation—should not be underestimated.

Two types of implants were evaluated in our study. As stated in previous studies, neck resorption in implants is a physiological event. Many factors affect the survival life of the implant. Therefore, the specific difference of the implants we used is that their neck structures are different. Implants with an aggressive neck part irritate the tissues surrounding the implant more after resorption and cause more inflammation. In addition, more resorption was observed in aggressive implants, although it was not statistically significant. We think that this is due to the thinner thickness in the neck region. We think that bone nutrition is weakened in aggressive implants.

Today, implant systems have different surface designs and the effect of these surfaces on the osseointegration process is still being investigated. Although long-term clinical studies have shown that different surface modifications provide successful results, the development of these surfaces is usually based on various in vivo and in vitro tests. However, most of these tests are non-standard experiments and include differences in the cell populations and animal models used. This makes it difficult to fully understand the biological interaction of implant surface properties with bone (14). The surface roughening techniques of the implant types compared in our study are different; Type 1 implants have HSA (Hybrid Sandblasting and Acid Etching) surface treatment, while Type 2 implants were processed with AB/AE (Acid Etching + Aluminum Oxide Sandblasting) method. It has been reported in the literature that hydrophilic micro-rough surfaces accelerate osseointegration, and further clinical studies are needed to better understand the effect of implant surface design on early bone attachment and long-term stability. In the future, standardized research to better understand tissue and cell interactions with implant surfaces may contribute significantly to early loading protocols and long-term implant success.

While this study provides valuable insights into the effects of implant design on peri-implant tissue health, several limitations also need to be recognized. Firstly, the sample size was relatively small (n=50 implants), which may limit the generalizability of the findings. A larger cohort with a more diverse patient population could provide a more comprehensive understanding of the long-term effects of implant morphology. Secondly, bone loss was evaluated clinically by probing and no radiographic imaging was used, which may limit the precision in detecting subtle crestal bone changes. Third, the study only included implants that

were entirely surrounded by native bone without any grafting procedures, and all participants were systemically healthy individuals. While this homogeneity reduces confounding factors, it may also limit the generalizability of the findings to broader clinical populations. Additionally, demographic data such as patient age, gender, implant placement site, and whether the implants were single or part of a splinted unit were not recorded or analyzed, and thus could not be included in subgroup comparisons. These omissions should be considered in the interpretation of our findings and addressed in future studies.

CONCLUSION

In this study, peri-implant bone loss and soft tissue conditions were evaluated in two different implant designs during a 12-month follow-up period. While no significant difference was found between implant types in terms of bone loss, gingival index was observed to be significantly higher in Type 2 implants, which may be related to increased inflammatory response due to implant neck design. This finding emphasizes the role of implant morphology on peri-implant tissue health and long-term stability. The importance of periodontal care increases especially in implants with more aggressive neck structures. Future studies should evaluate the effects of additional variables such as occlusal forces, bacterial biofilm formation and systemic factors on peri-implant tissue dynamics and implant longevity more comprehensively.

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REFERENCES

1. Hong DGK, Oh JH. Recent advances in dental implants. *Maxillofac Plast Reconstr Surg*. 2017;39:33.
2. Shemtov-Yona K, Rittel D. An overview of the mechanical integrity of dental implants. *Biomed Res Int*. 2015;2015:547384.
3. McCracken M. Dental implant materials: commercially pure titanium and titanium alloys. *J Prosthodont*. 1999;8:40-3.
4. Liu X, Chen S, Tsoi JKH, Matinlinna JP. Binary titanium alloys as dental implant materials—a review. *Regen Biomater*. 2017;4:315-23.
5. Zhang L, Chen LY. A review on biomedical titanium alloys: recent progress and prospect. *Advanced Engineering Materials*. 2019;21:1801215.
6. Duong HY, Roccuzzso A, Stahli A, et al. Oral health-related quality of life of patients rehabilitated with fixed and removable implant-supported dental prostheses. *Periodontol* 2000. 2022;88:201-37.

7. Lin CY, Chen Z, Pan WL, Wang HL. Is history of periodontal disease still a negative risk indicator for peri-implant health under supportive post-implant treatment coverage? A systematic review and meta-analysis. *Int J Oral Maxillofac Implants*. 2020;35:52-62.
8. Roccuzzo A, Imber JC, Salvi GE, Roccuzzo M. Peri-implantitis as the consequence of errors in implant therapy. *Periodontol* 2000. 2023;92:350-61.
9. Romandini M, Lima C, Pedrinaci I, et al. Clinical signs, symptoms, perceptions, and impact on quality of life in patients suffering from peri-implant diseases: a university-representative cross-sectional study. *Clin Oral Implants Res*. 2021;32:100-11.
10. Ravidà A, Galli M, Siqueira R, et al. Diagnosis of peri-implant status after peri-implantitis surgical treatment: proposal of a new classification. *J Periodontol*. 2020;91:1553-61.
11. Schwarz F, Derks J, Monje A, Wang HL. Peri-implantitis. *J Clin Periodontol*. 2018;45:246-66.
12. Amerio E, Mainas G, Petrova D, et al. Compliance with supportive periodontal/peri-implant therapy: a systematic review. *J Clin Periodontol*. 2020;47:81-100.
13. Eke PI, Dye BA, Wei L, et al. Self-reported measures for surveillance of periodontitis. *J Dent Res*. 2013;92:1041-7.
14. Rupp F, Liang L, Geis-Gerstorfer J, et al. Surface characteristics of dental implants: a review. *Dent Mater*. 2018;34:40-57.
15. Silness J, Loe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand*. 1964;22:121-35.
16. Loe H, Silness J. Periodontal disease in pregnancy. I. prevalence and severity. *J Periodontol*. 1963;32:612-7.
17. Coli P, Jemt T. On marginal bone level changes around dental implants. *Clin Implant Dent Relat Res*. 2021;23:159-69.
18. Chrcanovic BR, Kisch J, Albrektsson T, Wennerberg A. A retrospective study on clinical and radiological outcomes of oral implants in patients followed up for a minimum of 20 years. *Clin Implant Dent Relat Res*. 2018;20:199-207.
19. Fransson C, Tomasi C, Pikner SS, et al. Severity and pattern of peri-implantitis-associated bone loss. *J Clin Periodontol*. 2010;37:442-8.
20. Schou S, Holmstrup P, Worthington HV, Esposito M. Outcome of implant therapy in patients with previous tooth loss due to periodontitis. *Clin Oral Implants Res*. 2006;17:104-23.
21. Hugoson A, Laurell L. A prospective longitudinal study on periodontal bone height changes in a Swedish population. *J Clin Periodontol*. 2000;27:665-74.
22. Carlsson GE, Bergman B, Hedegård B. Changes in contour of the maxillary alveolar process under immediate dentures. A longitudinal clinical and x-ray cephalometric study covering 5 years. *Acta Odontol Scand*. 1967;25:45-75.
23. Hussein A, Shah M, Atieh MA, et al. Influence of implant surfaces on peri-implant diseases - a systematic review and meta-analysis. *Int Dent J*. 2025;75:75-85.



Distribution of Occupational Accident Cases Presenting to the Emergency Department by Time, Age and Injury Region

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Abstract

Aim: Occupational accidents cause many deaths, injuries, loss of labour force and a serious financial burden for the health system. The aim of this study was to investigate the demographic information and injury characteristics of occupational accident cases admitted to the emergency department.

Material and Method: Data were obtained by retrospectively reviewing the files of 1868 occupational accident cases admitted to the emergency department.

Results: Of the 1868 patients included in the study, 91.9% were male. Most admissions were made in August ($p<0.05$), on Mondays (17% and $p<0.05$) and between 10.00-12.00 am ($p<0.05$). Most of the cases came from the organized industrial zone ($p<0.05$). The most common type of injury was penetrating ($p<0.05$) and the most common injury sites were upper extremities and face ($p<0.05$).

Conclusion: It was determined that most of the occupational accidents occurred in the summer season, on Mondays in August and in the morning hours. Upper extremities and face were most commonly affected. Penetrating type injuries are most common. Precautions and trainings on this subject will reduce these deaths and injuries.

Keywords: Occupational accident, emergency service, injury

INTRODUCTION

According to the World Health Organisation (WHO), occupational accidents are defined as unplanned, unknown and uncontrolled events that cause injury to people, damage to machines and equipment, and halt production for a period of time (1). The International Labour Organization (ILO), on the other hand, defines it as 'an unplanned, unexpected event that leads to a specific damage or injury' (2). According to the Social Security Institution of the Republic of Türkiye, it is defined as "an event that occurs in one of the cases listed in the Law No. 5510 in the working life of the person and makes the insured physically or mentally disabled" (3). Every year, 270 million occupational accidents occur worldwide and result in 1,1 million deaths (4). Occupational accidents cause many deaths, injuries, loss of workforce

and a serious financial burden for the health system. Although technological advances, mechanisation and occupational health and safety studies have provided great improvements in the prevention of occupational accidents, it is observed that large industrial enterprises and mining accidents are still at high levels due to the huge increase in the proportion of working people in the last century (5). The first evaluation and intervention of the victims after occupational accidents are performed in emergency services, an occupational accident report is prepared and notification is mandatory.

Occupational accidents affect the young adult male population in the society. It has been reported that they occur mostly in the summer season and between 08:00-12:00 hours during the day. Victims are most frequently admitted from the construction sector and heavy industry

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and the upper extremities are most commonly affected. Blunt traumas and glass cuts are reported as the most common mechanism of injury.

Occupational accidents are classified in different ways such as blunt, penetrating etc. depending on the severity of the injury, type of injury and type of accident (3). In our country, occupational accidents are always evaluated primarily in emergency departments because of their forensic aspects and necessary interventions are performed and an occupational accident report is kept. For this reason, occupational accidents constitute an important part of traumatised patients presenting to the emergency department. In a study, it was reported that approximately 20% of all adult patients admitted to the emergency department due to injury were admitted due to occupational accidents (6).

Occupational accidents are an important cause of mortality and morbidity all over the world. Many studies have been conducted in the world in the last 50 years to reduce these accidents. Work Health and Safety Services (WHS) was established to solve problems related to occupational accidents, to provide safe and healthy environments in all work-related processes and to ensure the health and safety of employees (1).

According to the 2012-2021 data of the Turkish Social Security Institution (SSI), it is reported that the rate of increase in occupational accidents in Türkiye has decreased, but there has not been a significant decrease in mortality rates (7). Türkiye ranks 8th with a high number of accidents compared to EU countries within the scope of occupational accidents with a loss of 4 or more working days, unfortunately, it is by far ahead in terms of fatal occupational accidents. According to 2014 data, while 1.626 fatal occupational accidents occurred in Türkiye, only 589 fatal occupational accidents occurred in France, which follows Türkiye (8).

The aim of this study was to determine the frequency of occupational accidents admitted to the emergency department of Kırşehir Training and Research Hospital, the distribution according to age, season, day and hour, and the types of injuries and the distribution of injury sites.

MATERIAL AND METHOD

This study was conducted by retrospectively examining the patient files that were applied to the Emergency Department of Kırşehir Ahi Evran University Training and Research Hospital due to occupational accidents between 01.10.2020 and 01.10.2022 and for which a occupational accident report was opened. The study was carried out with the permission of Kırşehir Ahi Evran University Faculty of Medicine Ethics Committee (Ethic number: 2022-02/20, Date: 25.01.2022). The demographic data of the patients, types of injuries, injury sites, whether there were bone fractures, whether treatment or consultation

was required and how they ended were recorded in the previously prepared case report forms. The statistical analyses of the study were performed using Statistical Package for Social Sciences version 28.0 software for Windows (IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp., USA). The frequencies of the variables are given as n (%). Chi-square test was used to compare the distributions of categorical variables.

RESULTS

A total of 1868 patients who met the criteria were included in the study. Of these patients, 1716 (91.9%) were male and 152 (8.1%) were female. When the distribution of patients included in the study by age was examined, the number of patients in the 15-24 age range was 391 (20.9%), the number of patients in the 24-35 age range was 704 (37.7%), the number of patients in the 35-54 age range was 726 (38.9%) and the number of patients in the 55 and over age range was 47 (2.5%) (Table 1).

Table 1. Distribution of patients admitted to the emergency department due to occupational accidents by age group

Age groups	%	n
15-24	20.9	391
24-35	37.7	704
35-54	38.9	726
55+	2.5	47

*: Chi-square test

When the distribution of occupational accident cases by season was examined, it was found that the highest number of cases occurred during the summer months, with 524 patients (28.1%). The second highest number of cases occurred in the autumn, with 469 patients (25.2%). The number of patients presenting in the spring was 464 (24.9%), and the number of patients presenting in the winter was 411 (23.4%). When the distributions were examined separately by summer months, it was understood that the highest number of applications was made in August (10.1%). When the distributions of cases by month were examined, a statistically significant relationship was determined ($p=0.009$) (Table 2).

Table 2. Distribution of patients admitted to the emergency department due to occupational accidents according to seasons

Months	n	%
Summer (June, July, August)	524	28.1
Autumn (September, October, November)	469	25.2
Spring (March, April, May)	464	24.9
Winter (December, January, February)	411	23.4
p*	0.009	

*: Chi-square test

When we look at the time of day when patients apply, we see that the cases are concentrated between 10:00-12:00 and this distribution was found to be significant as a result of the statistical analysis ($p<0.001$), (Table 3).

Table 3. Distribution of the application times of patients who applied to the emergency department due to occupational accidents

Hours	n	%
08:00-10:00	229	12.3
10:00-12:00	300	16.1
12:00-14:00	229	12.3
14:00-16:00	249	13.3
16:00-18:00	212	11.3
18:00-20:00	140	7.5
20:00-22:00	132	7.1
22:00-24:00	100	5.4
24:00-02:00	103	5.5
02:00-04:00	73	3.9
04:00-06:00	54	2.9
06:00-08:00	47	2.5
p*	0.000	

*: Chi-square test

When the distribution of applications by day of the week was examined, it was found that the most frequent application was made on Monday and this distribution was found to be statistically significant ($p<0.001$), (Table 4).

Table 4. Distribution of days for patients who presented to the emergency department due to occupational accidents

Application days	n	%
Monday	317	17.0
Tuesday	294	15.7
Wednesday	305	16.3
Thursday	274	14.7
Friday	282	15.1
Saturday	220	11.8
Sunday	176	9.4
p*	0.000	

*: Chi-square test

When the distribution of patients according to their work field was examined, it was seen that the most applications came from the organized industrial zone, and this distribution was found to be statistically significant ($p<0.001$) (Table 5).

Table 5. Distribution of work fields among patients who presented to the Emergency Department due to occupational accidents

Field of study	n	%
Agriculture	11	0.6
Small tradesmen	81	4.3
Small industry	9	0.5
Organized industry	1211	64.8
Government office	203	10.9
Other	353	18.9
p*	0.000	

*: Chi-square test

When the types of injuries of the patients were examined, it was found that penetrating injuries were significantly more common than other types of injuries among the injury mechanisms ($p<0.001$). When the distribution of the patients according to the injury sites was examined, it was found that 816 patients (43.5%) had injuries in the upper extremities, 556 patients (28.8%) in the lower extremities, 296 patients (15.8%) in the head and neck region and 79 patients (4.3%) in the thorax. In line with this information, the types of injuries suffered by the patients and the distribution of the injury sites are statistically significant ($p<0.001$). While 1808 of the patients were discharged from the emergency room, 57 patients were hospitalized and treated, and 3 patients died.

DISCUSSION

Occupational accidents have become a significant public health problem in all societies (9). According to the data of the International Labor Organization worldwide, an average of 50 million people are exposed to occupational accidents every year in industrial production (10). In addition to having negative effects on the health of individuals, occupational accidents also cause loss of workforce, thus posing a serious burden on individuals, the health system, and the national economy. Today, technological developments, increased production, and competition have further increased the risks to the health and occupational safety of employees. Occupational accidents can result in mortality, as well as disabilities that lead to permanent disability. Occupational accidents and the resulting material and moral losses also reach significant dimensions in terms of the national economy (10).

In our study, we determined that the ratio of emergency room visits due to occupational accidents to all emergency room visits was 0.48%. Ulutaşdemir et al., in their study with 133 occupational accident cases, stated that occupational accident applications constituted 0.2% of all applications to the emergency department (11). In a study conducted by Karakurt et al., it was stated that 1.2% of applications to the emergency department were workplace-related accidents (12). The reason why this rate was below 1% in our study may be that our city is not a large industrial center and the number of employment in heavy industry is low.

91.9% of the patients in our study were male. Studies conducted in our country reported that patients applying to the emergency department due to occupational accidents were predominantly male (10,13). This rate was reported as 81.6% in another study (6). When gender distributions were examined, the obtained data were consistent with the literature. This may be due to the fact that male employment is higher than female employment and that men tend to work in heavier and more dangerous jobs than women. When the seasonal distribution of occupational accidents was examined, it was seen that the most frequent applications were in the summer season. In some studies on this subject, it has been reported that occupational accidents increase due to the fact that occupational branches such as construction and agriculture are more

active in the summer months (4,12). In a study conducted by Ulutaşdemir et al. on 133 occupational accident applications, it was stated that occupational accidents occur most frequently in May (12%) (9). In another study, similar to our study, it was stated that the highest number of applications occur in the summer months (13). Karakurt et al. (12) reported that most occupational accidents occur in December, while Dizdar et al. (14) reported that occupational accidents increase in June, July and August. It is likely that occupational accidents increase in May, June and July due to the warming of the weather and the resulting intensification of production and employment in many occupations. According to the data of the Turkish Statistical Institute (TÜİK), occupational accidents are reported to occur more frequently in the first hours of work. According to the occupational accident data of TÜİK between 2003-2005, it has been reported that accidents occur most frequently in the first 3 hours after the start of work (7). In a study conducted by Dağlı and Serinken, the distribution of accidents during the day was examined and it was reported that they occurred most frequently in the morning hours (08:00-10:00) and around noon (14:00-16:00) (10). In our study, we found that occupational accidents occurred most frequently between 10:00-12:00, frequently within the first 4 hours after starting work. When the distribution of occupational accidents among the days of the week was examined, we found that the highest number of applications was on Monday. According to ILO data, the most frequent applications are made on Mondays (7). Ulutaşdemir and his colleagues stated in their study that occupational accidents occur most frequently on Mondays (37.8%) (11).

Approximately one third of occupational accident-related deaths in our country occur in the construction sector, followed by the manufacturing sector. In a study conducted by Çelik and his colleagues covering 654 patients, they reported that the highest number of applications were made by industrial and construction workers (15). In our study, in relation to the current employment situation in the region, the most frequent application was made by workers working in the industrial site. It is very clear that the different data in the literature are related to the industrialization situation of the region where the study was conducted, the widespread economic activities and employment areas.

In our study, it was observed that the most common type of injury was penetrating injuries and the most common injury site was the upper extremities and head-neck region. Similarly, in the study of Dağlı et al., the most frequently injured site was the upper extremities (65.3%) (10). Ulutaşdemir et al. also reported the most upper extremity injuries with a rate of 61.7% (11). Kadioğlu et al. reported that the most injuries were in the upper extremity region with 46% among the injury sites (13). When the mortality rate in occupational accidents was examined in our study, it was found as 0.2%. In various studies, mortality rates in occupational accidents vary between 1% and 4.9% (16,17). The reason for this lower rate (0.2%) in our study may be

the lack of heavy industry facilities in Kırşehir province and the fact that injuries are often mild.

CONCLUSION

Occupational accidents are an important public health issue both globally and within our country. This study found that occupational accidents were most common during the summer months, particularly in August, and most frequently occurred on Mondays and in the morning. Occupational accidents are most frequently observed as localized penetrating injuries, and anatomically, they are most frequently observed in the upper extremity and head-neck region. In this study, we believe that precautions to be taken and training to be provided regarding occupational accidents will reduce these deaths and injuries. The data of this study was obtained by conducting a 2-year case scan in a small province of Türkiye. However, since all cases were brought to a single hospital, it reflects the sample well.

This study is based on the Specialization Thesis in Medicine titled "Analysis of Occupational Accident Cases Presenting to the Emergency Department of Kırşehir Ahi Evran University Training and Research Hospital".

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REFERENCES

1. İnce H, İnce N, Ozyildirim BA. Occupational accidents and forensic medicine in Türkiye. J Clin Forensic Med. 2006;13:326-30.
2. Investigation of Occupational Accidents and Diseases: A Practical Guide for Labour Inspectors. International Labour Office, Geneva, Switzerland, 2015. <https://www.ilo.org/> access date 25.02.2015.
3. Akı E. 6331 sayılı iş sağlığı ve güvenliği kanunu ve çalışma yaşamına etkileri. Dokuz Eylül Üniversitesi Hukuk Fakültesi Dergisi. 2013;15:3-24.
4. Ozkan S, Kiliç S, Durukan P, et al. Occupational injuries admitted to the emergency department. Ulus Travma Acil Cerrahi Derg. 2010;16:241-7.
5. Ceylan H. Türkiye'deki iş kazalarının genel görünümü ve gelişmiş ülkelerle kıyaslanması. International Journal of Engineering Research and Development. 2011;3:18-24.
6. Leonard DR, Suruda AJ, Cook LJ, et al. Distinctive emergency department usage for injury for workers' compensation cases in Utah in 1996. J Occup Environ Med. 1999;41:686-92.
7. Ceylan H, Kaplan A. Fatal Occupational Accidents in Turkey from a City and Country Perspective. Kent Akademisi. 2024;17:231-54.

8. Şen M, Dursun S, Murat G. Work accidents in Turkey: an evaluation in the context of the European Union Countries. *International Journal of Society Researches*. 2018;9:1169-90.
9. Bedel C, Armağan HH, Oğuzlar FÇ, et al. Occupational accidents presenting to the emergency department. *Genel Tıp Derg*. 2021;31:12-7.
10. Dağlı B, Serinken M. Occupational injuries admitted to the emergency department. *JAEM*. 2012;11:167-71.
11. Ulutaşdemir N, Tanır F, Dokur M, Uysal E. Analysis of the patients admitted to emergency department of a private hospital due to work accidents. *Sakarya Med J*. 2015;5:193-8.
12. Karakurt U, Satar S, Acikalin A, et al. Analysis of occupational accidents admitted to the emergency medicine department. *JAEM*. 2013;12:19-23.
13. Kadioğlu E, Karaman S, Arık Ö. Demographic analysis of patients applying to the emergency department due to workplace accident. *Gazi Osman Paşa Üniversitesi Tıp Fakültesi Derg*. 2016;8:163-73.
14. Dizdar MG, Asırdizer M, Yavuz MS. Celal Bayar Üniversitesi Hastanesi acil servisine başvuran göz travması olgularının değerlendirilmesi. *Adli Tıp Dergisi*. 2008;8:14-20.
15. Celik K, Yilmaz F, Kavalci C, et al. Occupational injury patterns of Turkey. *World J EmergSurg*. 2013;8:57.
16. Sayhan MB, Sayhan ES, Yemenici S, Oguz S. Occupational injuries admitted to the emergency department. *J Pak Med Assoc*. 2013;63:179-84.
17. Kalemoglu M, Keskin Ö, Yıldırım İ. Acil servise başvuran travmatik iş kazalarının incelenmesi. *Nobel Med*. 2006;2:21-3.



Bibliometric Analysis of Published Articles on Bruxism

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Abstract

Aim: This study aims to perform a bibliometric analysis of bruxism-related research published between 2005 and 2024. By evaluating publication trends, citation impact, key contributors, and keyword networks, the study seeks to provide insights into the intellectual structure of the field and highlight emerging research directions.

Material and Method: Data for this bibliometric analysis were extracted from the Web of Science database. The inclusion criteria consisted of original research articles published in English between 2005 and January 2025. The search term 'bruxism' was used to identify relevant publications. VOSviewer software was employed for network mapping to examine collaborations among authors, institutions, and countries. Citation metrics, keyword frequency, and journal distribution were analyzed to assess the academic impact of bruxism research.

Results: A total of 2,874 relevant articles were identified, demonstrating a significant increase in bruxism-related research over the last two decades. The United States, Brazil, and Japan emerged as leading contributors. Frank Lobbezoo was identified as the most prolific author, while the Journal of Oral Rehabilitation published the highest number of articles. Keyword analysis revealed that 'bruxism,' 'sleep bruxism,' and 'temporomandibular disorders,' were the most frequently studied topics.

Conclusion: The growing volume of bruxism research highlights its significance across multiple disciplines, including dentistry, neurology, and sleep medicine. Future studies should focus on standardizing diagnostic criteria, exploring genetic predispositions, and leveraging technological innovations for improved clinical outcomes.

Keywords: Bruxism, bibliometric analysis, Web of Science

INTRODUCTION

Bruxism is a parafunctional activity characterized by the involuntary grinding or clenching of teeth, occurring either during wakefulness or sleep (1). This condition has been extensively studied due to its complex etiology, which involves physiological, psychological, and neurological components. Bruxism is not only a condition that leads to dental wear but also a complex disorder associated with neurological and psychological factors. Its interdisciplinary nature requires a comprehensive approach involving dentistry, neurology, and sleep medicine. (2). It has been recognized as a contributing factor to dental wear, headaches, orofacial pain, and sleep disturbances, ultimately impacting the quality of life of affected individuals (3).

Over the last two decades, there has been a substantial increase in research focusing on bruxism, driven by advancements in diagnostic methodologies, such as polysomnography and electromyography, and an improved

understanding of its underlying mechanisms (4). The use of bibliometric analysis in this field has become crucial for mapping the academic landscape, assessing publication trends, citation metrics, influential authors, and inter-institutional collaborations. Such analyses provide valuable insights into the evolution of bruxism research, identifying emerging topics and key contributors in the field.

This study aims to conduct a thorough bibliometric analysis of research articles related to bruxism published between 2005 and 2024. It seeks to assess various bibliometric indicators, including annual publication trends, citation impact, leading researchers and institutions, and the distribution of research across different journals. Additionally, keyword analysis will be conducted to highlight dominant research themes and identify shifts in scientific focus over time. The ultimate goal of this study is to elucidate the intellectual structure of bruxism research, aiding future researchers in identifying knowledge gaps and potential directions for further investigation.

CITATION

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MATERIAL AND METHOD

Study Design

In this bibliometric analysis study, the methodological flow of studies with similar research designs were followed (5). The data were obtained from the Web of Science (WoS) (Thomson Reuters, Philadelphia, PA, USA) database by TB on January 25, 2025. As the data were obtained from a single database, duplication was inherently avoided.

WoS is a leading citation database and contains records of articles from the highest impact journals worldwide. It has ten indexes containing information gathered from thousands of scholarly journals, books, book series, and conferences. Science Citation Index-Expanded (SCI-E) is a large database of approximately ten thousand journals with high-impact citations. It is the latest journal citation system and database offered by the WoS, covering many fields, including arts, humanities, and social sciences (6). The H-index was introduced by Jorge Hirsch from the University of California in the USA in 2005. It is one of the bibliometric data in the scientific world. While the number of publications a researcher has made and the citations made to these publications are important, Hirsch's invention created a balance between the number of publications produced and the number of citations received. For example, if an author has 10 articles and 6 of these 10 articles have received six or more citations, the H-index value for that researcher is accepted as 6 (7).

The inclusion criteria were determined as follows: (I) English language articles, (II) published between January 2005 and January 2025, (III) original articles category according to WoS indexing. The search term 'bruxism' was typed into the search bar in the WoS database. Data on the determined articles were obtained using the 'create citation report' and 'analyse results', exported in tab-delimited file format, and transferred to VOSviewer, a freely-available software for bibliometric analysis (www.vosviewer.com) (8). Web mapping was performed to identify the links and density between the characteristics of articles including authors, institutions, countries, scientific categories, keywords, journals, and publication years. On the network map, a larger sized ring and a thicker line between the nodes represent a greater network and strength of links between the queried items.

Since the data used in this study is completely public, it does not require ethics committee approval. Clinical trial number: not applicable.

RESULTS

The search for the term 'bruxism' resulted in 4,091 documents in the all fields category at all times. The title of 1,302 documents, the abstract of 2,210 documents, and the keywords of 1,887 documents contained the term 'bruxism'. Excluding the abstracts, letters, editorials, book chapters, and amendments there were 3,525 documents containing the term 'bruxism'. After excluding non-original, early access articles and not in English 2,874 articles remained.

While the number of articles containing the term 'bruxism' was 44 in 2005, this number increased to 221 in 2024. There has been a significant increase in articles about bruxism over the years. 2022 appears to be the year with the most articles about bruxism. Figure 1 reveals the trend in articles containing the term 'bruxism' over the last 20 years.

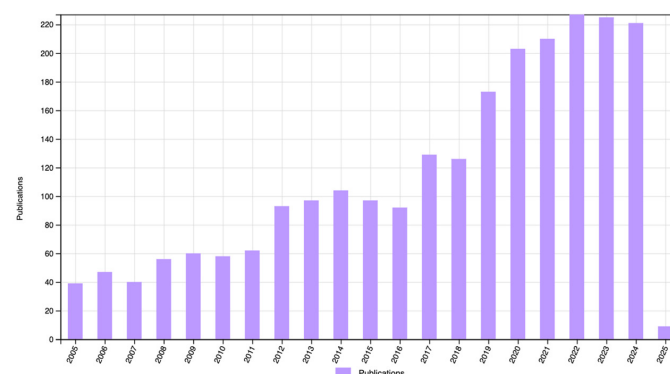


Figure 1. Articles containing the term 'bruxism' between 2005 and 2025

While the number of citations to articles containing the term 'bruxism' was 742 in 2005, this number increased to 7,402 in 2024 (Figure 2).

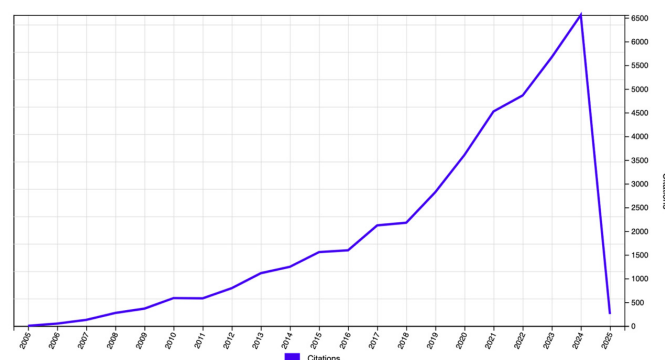


Figure 2. Citations of articles containing the term 'bruxism' between 2005 and 2025

The country with the most articles containing the term 'bruxism' was the United States of America with 444 articles. It was followed by Brazil with 372 articles and the Japan with 288 articles (Figure 3).

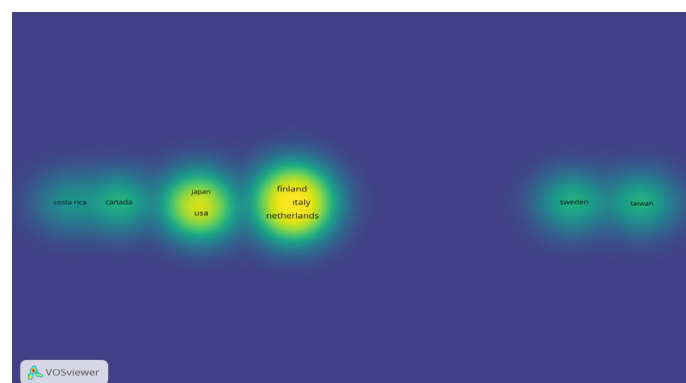


Figure 3. Country density mapping

The author with the most articles about bruxism in total was Frank Lobbezoo with 115 articles. Daniel Manfredini is in second place with 93 articles and Gilles J. Lavigne is in third place with 72 articles (Figure 4).

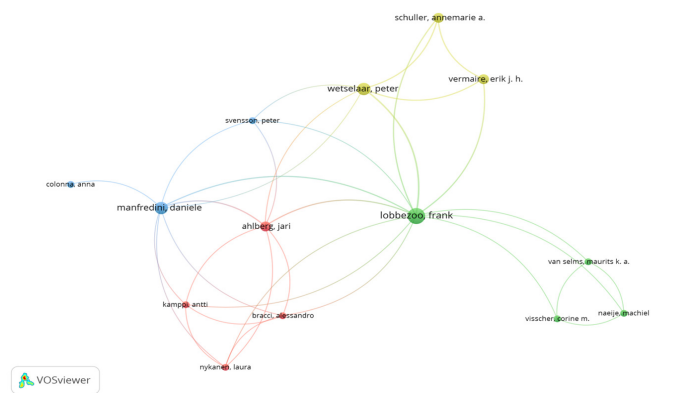


Figure 4. Author network mapping

The institutions with the most articles about bruxism were the Academic Center for Dentistry Amsterdam, and Vrije Universiteit Amsterdam with 142 publications, followed by University of Amsterdam with 115 articles (Figure 5).

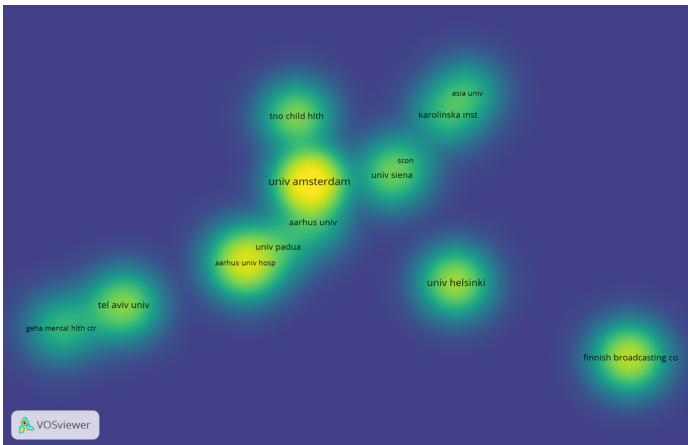


Figure 5. Institution network mapping

When the keywords of the articles about bruxism were examined, it was seen that the most frequently used keywords were 'bruxism', 'sleep bruxism', and 'temporomandibular disorders'. Keyword network mapping is demonstrated in Figure 6.

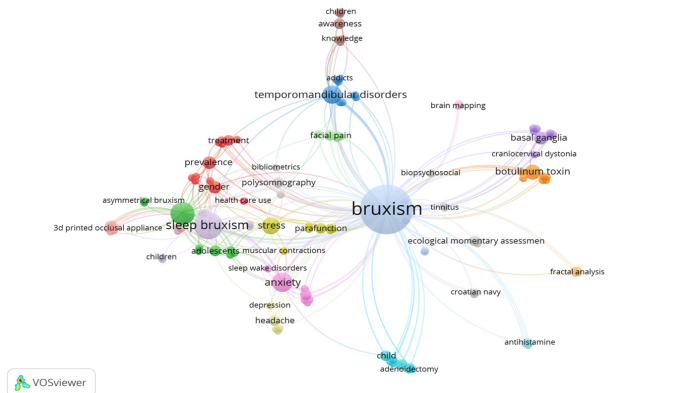


Figure 6. Keyword network mapping

The most cited articles on bruxism are shown in Table 1. The first two articles appear to have been written by Frank Lobbezoo, the author with the most articles on bruxism, and were published in the Journal of Oral Rehabilitation.

Of the 2874 articles published on bruxism, 1566 were published in the field of dentistry oral surgery medicine, 352 in the field of neurosciences neurology, and 230 in the field of general internal medicine (Figure 7).

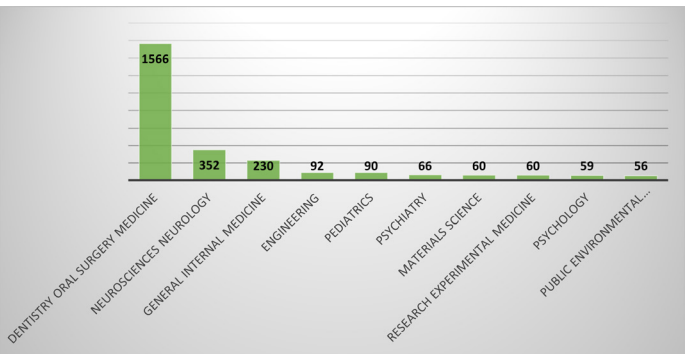


Figure 7. Top 10 categories containing the term 'bruxism'

The 10 journals that published the most articles on bruxism are shown in Table 2. Journal of Oral Rehabilitation ranks first with 260 articles.

Table 1. The 10 most cited articles containing the term 'bruxism'				
Article	First author	Journal name	Year	Total citation
Bruxism Defined and Graded: An International Consensus (9)	Frank Lobbezoo	Journal of Oral Rehabilitation	2013	773
International Consensus on the Assessment of Bruxism: Report of a Work in Progress (10)	Frank Lobbezoo	Journal of Oral Rehabilitation	2018	728
Longevity of Posterior Composite Restorations: Not Only a Matter of Materials (11)	Flavio Demarco	Dental Materials	2012	677
Epidemiology of Restless Legs Symptoms in Adults (12)	Phillips, Brian	Archives of Internal Medicine	2000	552
Sleep Bruxism: Validity of Clinical Research Diagnostic Criteria in a Controlled Polysomnographic Study (13)	Gilles J. Lavigne	Journal of Dental Research	1996	522
Restless Legs Syndrome and Sleep Bruxism - Prevalence and Association Among Canadians (14)	Gilles J. Lavigne	Sleep	1994	512
Risk Factors for Sleep Bruxism in the General Population (15)	Maurice M Ohayon	Chest	2001	339
Biological and Technical Complications and Failures With Fixed Partial Dentures (FPD) on Implants and Teeth After Four to Five Years of Function (16)	Urs Bragger	Clinical Oral Implants Research	2001	321
Development of Parasomnias From Childhood to Early Adolescence (17)	Luc Laberge	Pediatrics	2000	243
Quantitative Study of Bite Force During Sleep Associated Bruxism (18)	Kesikue Nishigawa	Journal of Oral Rehabilitation	2001	232

Table 2. The 10 journals that published the most articles about bruxism

Journal name	Article number	Percentage
Journal of Oral Rehabilitation	260	9.05
Cranio The Journal of Craniomandibular Sleep Practice	139	4.84
Journal of Prosthetic Dentistry	67	2.33
Journal of Clinical Medicine	65	2.62
Clinical Oral Investigations	55	1.91
International Journal of Prosthodontics	53	1.84
Acta Odontologica Scandinavica	46	1.60
Bmc Oral Health	42	1.46
Journal of Orofacial Pain	41	1.43
Sleep and Breathing	39	1.36

DISCUSSION

The findings of this bibliometric analysis reveal a growing academic interest in bruxism, demonstrated by a consistent increase in publications over the past two decades. The upward trend in research output, particularly noticeable after 2010, can be attributed to an enhanced awareness of bruxism’s impact on oral health and general well-being, as well as improvements in diagnostic and assessment techniques. The increasing volume of research underscores the importance of bruxism as a multidisciplinary issue that spans dental, medical, and psychological fields.

A detailed examination of the most cited publications indicates that international consensus reports on bruxism classification and assessment have significantly influenced the field (9-11). Notably, researchers such as Frank Lobbezoo (9,10) and Gilles J. Lavigne (13,14) have made substantial contributions, with their work receiving widespread recognition. These studies emphasize the necessity for standardized diagnostic criteria and evidence-based methodologies to ensure the reliability and reproducibility of bruxism-related research. The prevalence of systematic reviews and meta-analyses among the most cited articles further highlights the need for rigorous, well-designed studies to guide clinical practice and policymaking.

Geographical analysis suggests that the United States, Brazil, Japan, and several European nations are at the forefront of bruxism research, contributing the highest number of publications. This trend aligns with the presence of well-established research institutions and funding support in these regions. Institutional collaborations have played a pivotal role in advancing the field, with multidisciplinary teams from various specialties—ranging from dental sciences to neurology—driving innovation and expanding our understanding of bruxism.

Keyword network analysis reveals several recurring themes in bruxism research, including "sleep bruxism," "stress," "temporomandibular disorders," "muscle activity," and "polysomnography." These keywords reflect the

evolving nature of bruxism studies, with increasing emphasis on its relationship with sleep disorders, neurophysiological mechanisms, and psychological factors (19). Furthermore, the association between bruxism and comorbid conditions such as obstructive sleep apnea and anxiety disorders has gained significant attention in recent years (20).

Recent studies have also explored the impact of technological advancements in diagnosing and managing bruxism (21,22). Wearable devices and smartphone applications equipped with electromyographic sensors have been introduced as potential tools for real-time monitoring and assessment. These innovations could enhance the accuracy of bruxism diagnosis and facilitate early interventions, reducing the risk of long-term complications.

Moreover, the role of genetic predisposition in bruxism is an emerging research avenue. Preliminary studies have suggested a potential hereditary component, indicating that genetic markers may play a role in an individual's susceptibility to developing bruxism (23). Further exploration in this area could lead to personalized treatment strategies and improved preventive measures tailored to individuals with a higher genetic risk.

Despite significant advancements, several challenges remain in bruxism research. One major limitation is the heterogeneity in diagnostic criteria across different studies, leading to inconsistencies in reported prevalence rates and treatment outcomes. A unified framework for diagnosis and classification is necessary to improve the comparability of findings and ensure more reliable conclusions (21). Additionally, most studies rely on self-reported data or clinical examinations, which may not always provide accurate representations of bruxism severity (24). The integration of objective, technology-driven assessment tools into routine clinical practice could enhance diagnostic accuracy.

Another critical aspect that requires further investigation is the long-term impact of bruxism on oral and systemic health. While the role of bruxism in dental wear,

temporomandibular disorders, and orofacial pain is well documented (25,26), its potential implications for systemic conditions such as cardiovascular diseases and metabolic disorders remain unclear. Given the known associations between sleep disorders and systemic health (27), future studies should explore whether chronic bruxism contributes to broader physiological dysfunctions.

Although VOSviewer is an effective tool for network visualization, it has certain limitations, such as its reliance on co-occurrence data, which may overlook nuanced relationships between publications.

Future research directions should focus on interdisciplinary collaboration to develop a more holistic understanding of bruxism. Integrating findings from neuroscience, behavioral sciences, and biomechanics could yield a comprehensive approach to diagnosis and treatment. Additionally, longitudinal studies with large sample sizes are essential to validate existing findings and establish standardized treatment protocols.

CONCLUSION

In conclusion, this bibliometric analysis provides a comprehensive overview of the academic landscape surrounding bruxism research. It highlights key contributors, emerging trends, and critical areas that require further exploration. As the field continues to advance, interdisciplinary collaborations and technological innovations will be instrumental in shaping future research directions. Addressing existing knowledge gaps and refining diagnostic and therapeutic methodologies will ultimately lead to better clinical outcomes and an improved quality of life for individuals affected by bruxism. Future studies should focus on large-scale cohort investigations exploring the genetic predisposition to bruxism, which could pave the way for personalized treatment strategies.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: Since the data used in this study is completely public, it does not require ethics committee approval.

REFERENCES

1. Matusz K, Maciejewska-Szaniec Z, Gredes T, et al. Common therapeutic approaches in sleep and awake bruxism - an overview. *Neurol Neurochir Pol.* 2022;56:455-63.
2. Lavigne GJ, Khoury S, Abe S, et al. Bruxism physiology and pathology: an overview for clinicians. *J Oral Rehabil.* 2008;35:476-94.
3. Manfredini D, Serra-Negra J, Carboncini F, Lobbezoo F. Current concepts of bruxism. *Int J Prosthodont.* 2017;30:437-8.
4. Minakuchi H, Fujisawa M, Abe Y, et al. Managements of sleep bruxism in adult: a systematic review. *Jpn Dent Sci Rev.* 2022;58:124-36.
5. Üçer H, Kaya E. Bibliometric analyses of publications in the field of restless legs syndrome. *Acta Neurol Belg.* 2023;123:465-74.
6. Yang L, Tu S, Feng L, et al. Bibliometric analysis of multiple sclerosis nursing research based on Web of Science. *Ann Palliat Med.* 2021;10:7551-9.
7. De Groote SL, Raszewski R. Coverage of Google Scholar, Scopus, and Web of Science: a case study of the h-index in nursing. *Nurs Outlook.* 2012;60:391-400.
8. Arruda H, Silva ER, Lessa M, et al. VOSviewer and Bibliometrix. *J Med Libr Assoc.* 2022;110:392-5.
9. Lobbezoo F, Ahlberg J, Glaros AG, et al. Bruxism defined and graded: an international consensus. *J Oral Rehabil.* 2013;40:2-4.
10. Lobbezoo F, Ahlberg J, Raphael KG, et al. International consensus on the assessment of bruxism: report of a work in progress. *J Oral Rehabil.* 2018;45:837-44.
11. Demarco FF, Corrêa MB, Cenci MS, et al. Longevity of posterior composite restorations: not only a matter of materials. *Dent Mater.* 2012;28:87-101.
12. Phillips B, Young T, Finn L, et al. Epidemiology of restless legs symptoms in adults. *Arch Intern Med.* 2000;160:2137-41.
13. Lavigne GJ, Rompré PH, Montplaisir JY. Sleep bruxism: validity of clinical research diagnostic criteria in a controlled polysomnographic study. *J Dent Res.* 1996;75:546-52.
14. Lavigne GJ, Montplaisir JY. Restless legs syndrome and sleep bruxism: prevalence and association among Canadians. *Sleep.* 1994;17:739-43.
15. Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. *Chest.* 2001;119:53-61.
16. Brägger U, Aeschlimann S, Bürgin W, et al. Biological and technical complications and failures with fixed partial dentures (FPD) on implants and teeth after four to five years of function. *Clin Oral Implants Res.* 2001;12:26-34.
17. Dai Y, Halabicky OM, Ji X, Liu J. Childhood lead exposure and sleep problems in adolescents: a longitudinal cohort study. *Int Arch Occup Environ Health.* 2024;97:959-70.
18. Nishigawa K, Bando E, Nakano M. Quantitative study of bite force during sleep associated bruxism. *J Oral Rehabil.* 2001;28:485-91.
19. Kuang B, Li D, Lobbezoo F, et al. Associations between sleep bruxism and other sleep-related disorders in adults: a systematic review. *Sleep Med.* 2022;89:31-47.
20. Beddis H, Pemberton M, Davies S. Sleep bruxism: an overview for clinicians. *Br Dent J.* 2018;225:497-501.
21. Raja HZ, Saleem MN, Mumtaz M, et al. Diagnosis of bruxism in adults: a systematic review. *J Coll Physicians Surg Pak.* 2024;34:1221-8.
22. Thomas DC, Manfredini D, Patel J, et al. Sleep bruxism: the past, the present, and the future-evolution of a concept. *J Am Dent Assoc.* 2024;155:329-43.

23. Oliveira JMD, Coelho MS, Pereira RPL, et al. Genetic polymorphisms and bruxism: a scoping review. *Sleep Med.* 2024;124:554-75.
24. Solis ACO, Corchs F, Duran ÉP, et al. Self-reported bruxism in patients with post-traumatic stress disorder. *Clin Oral Investig.* 2024;28:152.
25. Bronkhorst H, Kalaykova S, Huysmans MC, et al. Tooth wear and bruxism: a scoping review. *J Dent.* 2024;145:104983.
26. Romero-Reyes M, Bassiur JP. Temporomandibular disorders, bruxism and headaches. *Neurol Clin.* 2024;42:573-84.
27. Jaspan VN, Greenberg GS, Parihar S, et al. The role of sleep in cardiovascular disease. *Curr Atheroscler Rep.* 2024;26:249-62.



The Effects of Chronic Neck Pain on Spinal Posture, Spinal Mobility and Handgrip Strength in Older Adults

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Abstract

Aim: The objective of the study was to compare spinal posture, spinal mobility, and handgrip strength between the participants aged 65 and over with and without Chronic Neck Pain (CNP).

Material and Method: A total of 35 participants aged 65 and over, 17 older people with a diagnosis of CNP (CNP group) and 18 older people without CNP (control group), were included in this cross-sectional study. The Spinal Mouse device was used to measure spinal posture for the positions of vertebral column and spinal mobility for the movements in sagittal and frontal planes for the vertebral column. Handgrip strength was measured with a hand dynamometer.

Results: The mean age of the CNP group and the control group were 69.88 ± 4.66 years and 71.50 ± 4.61 years ($p > 0.05$), respectively. There were significant differences in right and left handgrip strength between the CNP group and the control group, respectively ($p = 0.008$, $p = 0.022$). According to the spinal posture values, the mean length of the vertebral column in CNP group was higher than the controls ($p = 0.028$). In addition, the lumbar and pelvic inclination angles were different between the groups in maximum flexion positions ($p = 0.040$ and $p = 0.027$, respectively). According to the spinal mobility values, the mean pelvic inclination angle was lower in the CNP group than the controls from the upright position to the flexion movement ($p = 0.023$). In addition, the lumbar and pelvic inclination angles were lower in the CNP group than the controls from the maximum extension to the maximum flexion movement ($p = 0.017$ and $p = 0.013$, respectively).

Conclusion: This study showed that the length of the vertebral column and the grip strength were higher in the older adults with CNP than the controls. According to the spinal posture, the lumbar angle and pelvic inclination angle were lower in the older adults with CNP than the controls. According to the spinal mobility, the pelvic inclination and lumbar angles in the older adults with CNP were lower than the controls.

Keywords: Chronic neck pain, handgrip strength, spinal posture, spinal mobility, spinal curvature

INTRODUCTION

Neck pain is characterized as discomfort in the cervical region persisting for at least one day, potentially accompanied by reflective pain in one or both upper limbs. Typically, the prognosis for neck pain indicates a favorable trend towards improvement during the initial six weeks following onset. There is a tendency for certain individuals who suffer from neck pain to develop chronic or persistent symptoms. Like other musculoskeletal disorders, neck pain is categorized based on the duration of the symptoms as acute (up to 6 weeks), subacute (6 to 12 weeks), and chronic (>12 weeks) (1).

Chronic neck pain (CNP) is a common problem in society

arising from various etiological factors. Stress, insufficient sleep, poor posture and sitting positions, excess weight, and trauma are all risk factors for persistent neck pain (2). CNP ranks fourth globally in terms of causing disability and accounts for 10–20% of primary care visits. Due to degenerative changes in the joints and intervertebral disc collapse, it is more prevalent in older people (3).

Considering that the population aged 65 and over in Türkiye is 8,722,806, there are more than 200,000 people with CNP in this age group in our country (4,5). The considerable economic strain associated with CNP arises from the expenses of treatment, reduced productivity, and a decrease in the labor force (6). In particular, resistance exercises and posture training positively affect CNP (7-10).

CITATION

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In literature, it was shown that hand grip strength is influenced by multiple factors such as age, gender, body mass index, leisure activities, occupation, upper extremity muscular strength, pain, nutritional status, sensory impairment, and cognitive decline. Additionally, several conditions, including carpal tunnel syndrome and cervical radiculopathy, were linked to a reduction in hand grip strength. Hand grip strength is also adversely affected by neck pain (11).

Alterations in postural control among individuals with Chronic Neck Pain (CNP) vary according to the underlying cause of their condition. Within diverse neck pain syndromes, specific and characteristic deficits in posture regulation can be observed and assessed. It is hypothesized that differences in postural stability and performance arise from varying degrees of disruption either in the afferent proprioceptive information transmitted to the central nervous system or in the subsequent central processing and integration of these sensory inputs (12).

From a functional perspective, CNP is a common musculoskeletal issue that can adversely impact hand grip strength, spinal posture, spinal mobility, and spinal curvature. This study aimed to compare the hand grip strength, spinal posture, spinal mobility, and spinal curvature between individuals aged 65 or over with and without CNP.

MATERIAL AND METHOD

Patients with CNP (patient group) who applied to the Physiotherapy and Rehabilitation Unit, Izmir Aliaga State Hospital, and individuals without CNP (control group) who met the inclusion criteria were included in this cross-sectional study. Ethical approval was obtained from İzmir Bakırçay University Ethics Committee for the study (2022/642, date: 22.06.2022).

The inclusion criteria were (1) being 65 years and over, (2) being diagnosed with CNP, (3) having CNP at least 12 weeks for the patient group; (1) being 65 years and over, (2) having no previous history of neck pain for the control group. The exclusion criteria were (1) having reading-comprehension problems, (2) having any orthopedic or neurological diseases or cognitive disorders, (3) having any head and cervical spine injury or surgery, and (4) having a score below 24 according to Mini-Mental State Examination (MMSE) for both the patient and the control groups.

Outcome Measures

Demographic information of the participants including age, gender, height, and body weight was recorded. All evaluations were applied to all the participants once by the same researcher.

The severity of the neck pain in patients diagnosed with CNP was evaluated using the Visual Analogue Scale (VAS). The VAS has a horizontal line that is 100 mm length. At each end of the line are word descriptors representing symptom severity from 0 (no symptoms/pain) to 10 (very severe symptoms/pain). The patient marked the point on the line that they believe reflects their perception of the current situation. The VAS score was calculated by measuring the

distance from the beginning point on the left side of the line to the point marked by the patient (13).

The Spinal Mouse® (Idiag M360, Volkswill, Switzerland), a non-invasive and computer-assisted device, was used to evaluate spinal posture and spinal mobility. Before the measurement, the spinal processes of the spine from C7 to S3 were marked while the individual was standing. During the evaluation, measurements were obtained by moving the Spinal Mouse device from top to bottom along the spine. During recording, the device recorded the distances and positions of the vertebrae in the x, y, and z planes. The intra-rater reliability (>0.8) and inter-rater reliability (0.95) of the Spinal Mouse device were documented previously (14,15). Spinal posture in the sagittal plane was evaluated in the upright posture, maximum flexion, and maximum extension positions, while in the frontal plane, it was assessed in upright posture, maximum left lateral flexion, and maximum right lateral flexion positions. The movements between the related positions evaluated spinal mobility in sagittal and frontal planes. Thoracic angle (°), lumbar angle (°), sacral angle (°), pelvic inclination angle (°), and length (mm) of the vertebral column data were calculated using a software program (IDIAG M360pro 7.7.0, Switzerland) to determine the spinal posture and spinal mobility of the participants in each position and movement. Positive values represent anterior posture (kyphosis) or flexion movement for the sagittal plane and right-side posture for the frontal plane, whereas negative values represent posterior posture (kyphosis) or extension movement for the sagittal plane and left-side posture for the frontal plane.

The upper extremity grip strength of the participants was evaluated using a handheld dynamometer (Lafayette Professional Hand Dynamometer, 5030L1, USA). Participants were assessed for right- and left-hand grip strength in a sitting position, with the arm fully adduction position and the elbow at 90 degrees flexion position. The best value obtained from three consecutive measurements was recorded (16,17).

Statistical Analysis

The G*Power program was used to determine the number of participants enrolled in the study. Cohen's d effect size was 1.02 in a study comparing thoracic kyphosis angle for spinal posture in sagittal plane upright position in older adults (18). Accordingly, we calculated the sample size to complete the study with a minimum of 34 participants in total, ensuring at least 17 participants in each group with 80% power, $\alpha=0.05$ error probability, and Cohen's d effect size of at least "1.02".

Data analysis was conducted with the IBM SPSS 20.0 statistical software program. Data were expressed as mean and standard deviation. The Shapiro-Wilk test was used to perform normal distribution analysis for continuous variables, and it was determined that all data showed normal distribution. Therefore, the Student's t-test was used for statistical analysis in independent two-group comparisons. $p<0.05$ probability value was considered statistically significant.

RESULTS

A total of 35 older adults participated in this study. Seventeen older adults were diagnosed with CNP, whereas 18 did not have such a diagnosis. The mean VAS score of the older adults diagnosed with CNP was 6.82±1.54 cm.

There was no statistically significant difference among the

participants regarding age, height, weight, and BMI (Table 1). Regarding age, height, weight, and BMI, the subjects did not show any statistically noteworthy variation (Table 1). While the mean left-hand grip strength was 26.88±7.07 kg and 33.78±9.58 kg, respectively (p=0.222), the mean right-hand grip strength was 27.53±8.49 kg and 36.11±9.6 in the CNP group and the control group, respectively (p=0.008).

Table 1. Demographic information			
	CNP group (n=17) (mean±SD)	Control group (n=18) (mean±SD)	p
Age (year)	69.88±4.66	71.50±4.61	0.31
Heigh (m)	1.64±0.95	1.61±0.96	0.51
Weight (kg)	79.29±11.20	75.06±9.32	0.23
BMI (kg/m²)	29.59±4.67	28.76±3.99	0.57
CNP: chronic neck pain, BMI: body mass index			

According to the spinal posture values in the sagittal plane, the mean length of the vertebral column was higher in the CNP group than the control group in the upright position (p=0.028). The lumbar and pelvic inclination angles were lower in the CNP group than the

control group in maximum flexion positions (p=0.040 and p=0.027, respectively). In addition, the absolute value of the pelvic inclination angle was lower in the CNP group than the control group in the maximum flexion position (p=0.030) (Table 2).

Table 2. Comparison of the spinal posture and spinal mobility results					
Spinal posture	Position	Data	CNP Group (n=17) (mean±SD)	Control Group (n=18) (mean±SD)	p
Sagittal	Upright	Thoracic (°)	58.29±14.13	54.50±12.44	0.405
		Lumbar (°)	-26.00±18.79	-20.11±16.98	0.337
		Sacral (°)	13.65±12.495	7.89±12.75	0.187
		Pelvic inclination (°)	6.35±6.480	3.67±4.86	0.173
		Length (mm)	506.53±40.84	446.89±99.64	0.028*
	Maximum flexion	Thoracic (°)	54.47±13.00	53.72±9.90	0.849
		Lumbar (°)	2.53±17.99	12.94±9.88	0.040*
		Sacral (°)	61.71±12.854	62.61±20.96	0.879
		Pelvic inclination (°)	75.94±12.11	86.83±15.50	0.027*
		Length (mm)	520.06±51.878	494.11±44.22	0.120
	Maximum extension	Thoracic (°)	41.47±15.005	39.22±19.29	0.704
		Lumbar (°)	-20.12±23.593	-27.06±23.02	0.385
		Sacral (°)	4.53±11.609	-.17±15.73	0.325
		Pelvic inclination (°)	-7.12±9.51	-15.06±11.05	0.030*
		Length (mm)	475.65±35.976	450.00±42.49	0.063
Frontal	Upright	Thoracic (°)	0.76±3.66	4.17±5.51	0.040*
		Lumbar (°)	-0.47±4.57	-1.44±4.89	0.547
		Sacral (°)	.76±3.527	0.22±3.36	0.643
		Inclination (°)	0.47±1.06	0.22±1.92	0.643
		Length (mm)	504.24±48.37	466.94±35.64	0.014*
	Maximum left lateral flexion	Thoracic (°)	-12.18±7.88	-8.89±5.54	0.161
		Lumbar (°)	-7.53±5.52	-7.33±7.65	0.932
		Sacral (°)	-7.06±5.66	-11.61±7.55	0.053
		Pelvic inclination (°)	-16.18±6.51	-19.89±6.03	0.089
		Length (mm)	507.47±41.93	476.50±37.28	0.027*
	Maximum right lateral flexion	Thoracic (°)	14.94±8.69	22.72±6.94	0.006*
		Lumbar (°)	9.53±8.92	11.50±8.50	0.508
		Sacral (°)	3.06±5.65	3.67±5.36	0.746
		Pelvic inclination (°)	13.71±7.50	18.17±6.68	0.072
		Length (mm)	510.47±45.14	484.89±35.25	0.070*
CNP: chronic neck pain, *p<0.05					

Table 2. Comparison of the spinal posture and spinal mobility results

Spinal mobility	Movement	Data	CNP Group (n=17) (mean±SD)	Control Group (n=18) (mean±SD)	p
Sagittal	From upright position to maximum flexion	Thoracic (°)	-3.82±7.07	-0.78±10.04	0.310
		Lumbar (°)	26.53±19.21	34.17±12.00	0.165
		Sacral (°)	48.06±14.70	54.72±17.36	0.230
		Pelvic inclination (°)	69.59±15.88	83.17±17.57	0.023*
		Length (mm)	13.53±31.58	25.00±32.81	0.300
	From upright position to maximum extension	Thoracic (°)	-16.82±14.00	-12.50±18.21	0.439
		Lumbar (°)	0.12±20.70	-5.33±18.57	0.418
		Sacral (°)	-9.12±14.60	-5.83±14.77	0.513
		Pelvic inclination (°)	-13.47±7.23	-13.44±25.28	0.997
		Length (mm)	-30.88±24.47	-14.00±33.24	0.098
	From maximum extension to maximum flexion	Thoracic (°)	13.00±13.43	14.50±14.32	0.752
		Lumbar (°)	26.41±21.13	42.67±16.94	0.017*
		Sacral (°)	57.18±15.641	62.78±20.24	0.368
		Pelvic inclination (°)	83.06±19.84	101.89±22.41	0.013*
		Length (mm)	44.41±30.782	44.11±33.22	0.978
Frontal	From upright to maximum left lateral flexion	Thoracic (°)	-12.94±6.90	-13.06±8.21	0.965
		Lumbar (°)	-7.06±7.07	-5.89±7.43	0.637
		Sacral (°)	-7.82±6.16	-11.83±7.32	0.090
		Pelvic inclination (°)	-16.65±6.44	-20.11±5.28	0.090
		Length (mm)	3.24±22.55	9.56±19.34	0.379
	From upright to maximum right lateral flexion	Thoracic (°)	15.88±8.40	18.56±4.96	0.256
		Lumbar (°)	11.71±6.56	12.94±8.67	0.638
		Sacral (°)	2.18±5.81	3.44±3.63	0.442
		Pelvic inclination (°)	15.06±5.64	17.94±6.82	0.183
		Length (mm)	5.35±22.08	19.06±26.04	0.104
	From maximum left flexion to maximum right flexion	Thoracic (°)	28.82±10.466	31.61±8.82	0.399
		Lumbar (°)	18.76±8.197	18.83±12.21	0.985
		Sacral (°)	10.00±7.632	15.28±7.95	0.054
		Pelvic inclination (°)	31.71±10.687	38.06±11.25	0.097
		Length (mm)	2.12±24.349	9.50±21.17	0.345

CNP: chronic neck pain, *p<0.05

When the spinal posture values in the frontal plane were compared, the mean thoracic angle and the vertebral column length were higher in the CNP group than the control group in maximum left lateral flexion ($p=0.040$ and $p=0.014$, respectively). Additionally, the mean thoracic angle was lower in the CNP group than the control group in the maximum right lateral flexion ($p=0.006$) (Table 2).

According to the spinal mobility values in the sagittal plane, the mean pelvic inclination angle was lower in the CNP group than the control group from the upright position to the flexion movement ($p=0.023$). In addition, the lumbar and pelvic inclination angles were lower in the CNP group than the control group from the maximum extension to the maximum flexion movement ($p=0.017$ and $p=0.013$, respectively). There was no statistical difference between the CNP group and the control group in any spinal mobility values in the frontal plane ($p>0.05$) (Table 2).

DISCUSSION

According to the spinal posture results of this study, the length of the vertebral column in older adults diagnosed with CNP was higher than the age-matched control group

in most of the positions, while the lumbar angle, pelvic inclination angle, and thoracic angle were lower. In addition, the pelvic inclination and lumbar angles in older adults diagnosed with CNP were lower than the age-matched control group in a few movements for spinal mobility. Moreover, the grip strength in older adults diagnosed with CNP was lower than the age-matched control group.

In CNP, decreased grip strength may occur for various reasons, such as muscle pain, weakness, circulatory disorders, and nerve compression. Loss of muscle strength, numbness, and tingling sensations due to decreased blood circulation or restricted neural transmission may cause difficulty in performing gross and fine motor functions in the hands (11). Tutar et al. reported that CNP significantly reduces grip strength measured by a handheld dynamometer in adults (19). Our study, which includes older adults, supports literature in this respect. It was known that the primary causes of CNP are myofascial pain and mechanical pain linked to improper posture (19). For this reason, the main reason for the difference in grip strength between older adults with and without CNP may be due to problems in spinal posture and spinal mobility.

Spinal mouse measurements are useful for measuring spinal posture and spinal mobility in situations with cost and time constraints. In a study conducted on adults with and without CNP, evaluating spinal posture and mobility with a spinal mouse, the thoracic angle was higher, and spinal mobility was lower in the adults with CNP than the adults without CNP (18). Another study conducted with adults revealed that CNP negatively affects the upper thoracic angle, and it was also emphasized that the presence of neck discomfort is more accurately predicted by the upper thoracic angle than the cranio-vertebral angle (20). Regarding thoracic angle and spinal mobility results, our study is consistent with the literature and indicates that the area affected by CNP is not only limited to the thoracic region but also includes the lumbar region. From these findings, it can be concluded that CNP causes changes in not only the thoracic but also the lumbar spine in the long term because the poor or compensated posture of the spine can exert significant pressure on the surrounding muscles and ligaments, hence impacting spinal stability. It can also cause tension and fatigue in the surrounding structures, often leading to more pain (21). The results of our study also showed that pelvic inclination in the maximum flexion and maximum extension position, from the upright to flexion movement, and from maximum extension to maximum flexion movement of the older adults with CNP were lower than the older adults without CNP. This situation reveals the restrictive effect of CNP, which generally becomes more severe as spine position and movement progresses. According to the results of our study, older adults with CNP may tend to perform more limited spinal movements compared to the older adults without CNP.

The relationship between vertebral column length and CNP is not well-established in current literature. The correlation between vertebral column length and neck pain is multifactorial, encompassing factors such as posture, biomechanics, spinal health, and muscular function (22,23). The development of neck pain can be influenced by the length of the vertebral column, especially the cervical spine. While variations in vertebral column length can influence posture and biomechanics, there is limited direct evidence linking overall vertebral length to the development or severity of CNP. Abnormalities in the cervical spine's curvature, such as a reduction or loss of the normal lordotic curve, have been linked to neck pain (24). Posture can be influenced by the cervical spine's length and alignment. Pain may result from misalignment or strain on the muscles and ligaments of the neck if the vertebral column is longer or shorter than the average. In our study, the vertebral column length was higher in older adults with CNP than without CNP in all positions except the maximum flexion position. A longer vertebral column may result in increased stress on the neck muscles and discs, particularly when there is poor posture, which can contribute to neck pain. Vertebral column length may be a predictor of CNP. However, further studies are needed on this topic.

This study has some limitations that the spinal posture and spinal movement of the cervical region and fine motor skills could not be evaluated. Further studies are needed to examine the comparisons of the results via pinch meter for fine motor skills and advanced imaging modalities for spinal posture and spinal mobility in older adults with and without CNP.

In addition to the changes in the thoracic region, the fact that CNP shows changes in the lumbar region, such as decreased lordosis angle and mobility, can be seen as a strength of our study. The restrictive effect of CNP on flexion and extension movements should be considered in the approach and treatment of these patients.

CONCLUSION

This study demonstrated that the length of the vertebral column and the grip strength were higher in the older adults diagnosed with CNP than the older adults without CNP; however, the lumbar angle, pelvic inclination angle, and thoracic angle were lower in the older adults diagnosed with CNP than the older adults without CNP according to the spinal posture measurements. The pelvic inclination angle and lumbar angle in older adults with CNP were lower than in older adults without CNP, according to the spinal mobility measurements. We recommend that further studies should evaluate the length of the vertebral column, grip strength and, spinal posture and spinal mobility of all the vertebral column parts in older adults diagnosed with CNP to understand the pathophysiology of CNP and biomechanical effects on cervical region.

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REFERENCES

1. Verhagen AP. Physiotherapy management of neck pain. J Physiother. 2021;67:5-11.
2. Fandim JV, Nitzsche R, Michaleff ZA, et al. The contemporary management of neck pain in adults. Pain Manag. 2021;11:75-87.
3. Childress MA, Stueck SJ. Neck pain: initial evaluation and management. Am Fam Physician. 2020;102:150-6.
4. Turkish Statistical Institute (TÜİK). İstatistiklerle Yaşlılar, 2023. <https://data.tuik.gov.tr/Bulten/Index?p=İstatistiklerle-Yaşlılar-2023-53710#:~:text=T%C3%9C%C4%B0K%20Kurumsal&text=Ya%C5%9Fl%C4%B1%20n%C3%BCfus%20olarak%20kabul%20edilen,10%2C2'ye%20y%C3%BCkseldi> access date 28.02.2025.
5. Kazeminasab S, Nejadghaderi SA, Amiri P, et al. Neck pain: global epidemiology, trends and risk factors. BMC Musculoskelet Disord. 2022;23:26.

6. Jahre H, Grotle M, Smedbråten K, et al. Risk factors for non-specific neck pain in young adults. A systematic review. *BMC Musculoskelet Disord*. 2020;21:366.
7. Rasmussen-Barr E, Halvorsen M, Bohman T, et al. Summarizing the effects of different exercise types in chronic neck pain - a systematic review and meta-analysis of systematic reviews. *BMC Musculoskelet Disord*. 2023;24:806.
8. Kang T, Kim B. Cervical and scapula-focused resistance exercise program versus trapezius massage in patients with chronic neck pain: a randomized controlled trial. *Medicine (Baltimore)*. 2022;101:e30887.
9. Mendes-Fernandes T, Puente-González AS, Márquez-Vera MA, et al. Effects of global postural reeducation versus specific therapeutic neck exercises on pain, disability, postural control, and neuromuscular efficiency in women with chronic nonspecific neck pain: study protocol for a randomized, parallel, clinical trial. *Int J Environ Res Public Health*. 2021;18:10704.
10. Mendes Fernandes T, Méndez-Sánchez R, Puente-González AS, et al. A randomized controlled trial on the effects of "Global Postural Re-education" versus neck specific exercise on pain, disability, postural control, and neuromuscular features in women with chronic non-specific neck pain. *Eur J Phys Rehabil Med*. 2023;59:42-53.
11. Wollesen B, Gräf J, Schumacher N, et al. Influences of neck and/or wrist pain on hand grip strength of industrial quality proofing workers. *Saf Health Work*. 2020;11:458-65.
12. Michaelson P, Michaelson M, Jaric S, et al. Vertical posture and head stability in patients with chronic neck pain. *J Rehabil Med*. 2003;35:229-35. Erratum in: *J Rehabil Med*. 2007;39:744.
13. Heller GZ, Manuguerra M, Chow R. How to analyze the Visual Analogue Scale: myths, truths and clinical relevance. *Scand J Pain*. 2016;13:67-75.
14. Post RB, Leferink VJ. Spinal mobility: sagittal range of motion measured with the SpinalMouse, a new non-invasive device. *Arch Orthop Trauma Surg*. 2004;124:187-92.
15. Mannion AF, Knecht K, Balaban G, et al. A new skin-surface device for measuring the curvature and global and segmental ranges of motion of the spine: reliability of measurements and comparison with data reviewed from the literature. *Eur Spine J*. 2004;13:122-36.
16. Sipers WM, Verdijk LB, Sipers SJ, et al. The martin vigorimeter represents a reliable and more practical tool than the jamar dynamometer to assess handgrip strength in the geriatric patient. *J Am Med Dir Assoc*. 2016;17:466.e1-7.
17. Bohannon RW. Grip strength: an indispensable biomarker for older adults. *Clin Interv Aging*. 2019;14:1681-91.
18. Özer Kaya D, Toprak Çelenay Ş. An investigation of sagittal thoracic spinal curvature and mobility in subjects with and without chronic neck pain: cut-off points and pain relationship. *Turk J Med Sci*. 2017;47:891-6.
19. Tutar B, Boyan N, Oguz O. Effects of chronic neck pain on grip strength and psychomotor skills in adults. *J Oral Rehabil*. 2024;51:1989-96.
20. Lau KT, Cheung KY, Chan KB, et al. Relationships between sagittal postures of thoracic and cervical spine, presence of neck pain, neck pain severity and disability. *Man Ther*. 2010;15:457-62.
21. Yang S, Boudier-Revéret M, Yi YG, et al. Treatment of chronic neck pain in patients with forward head posture: a systematic narrative review. *Healthcare (Basel)*. 2023;11:2604.
22. Côté P, Cassidy JD, Carroll L. The factors associated with neck pain and its related disability in the Saskatchewan population. *Spine (Phila Pa 1976)*. 2000;25:1109-17.
23. Huang Z, Bai Z, Yan J, et al. Association between muscle morphology changes, cervical spine degeneration, and clinical features in patients with chronic nonspecific neck pain: a magnetic resonance imaging analysis. *World Neurosurg*. 2022;159:e273-84.
24. Grob D, Frauenfelder H, Mannion AF. The association between cervical spine curvature and neck pain. *Eur Spine J*. 2007;16:669-78.



Pterygoid Hamulus Bursitis: A Rare and Overlooked Cause of Orofacial Pain

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Abstract

Pterygoid hamulus bursitis (PHB) is an infrequently reported condition that presents with chronic orofacial pain, often misdiagnosed as temporomandibular disorders (TMDs) or other common craniofacial pain syndromes. This condition arises from inflammation of the bursa surrounding the pterygoid hamulus (PH), a small hook-like bone structure of the sphenoid bone. Anatomical variations such as elongation of the PH or repetitive mechanical irritation are among the primary causes of this rare pathology. Clinically, PHB manifests as pain radiating to the soft palate, throat, or temporomandibular joint area, accompanied by symptoms such as dysphagia or otologic discomfort. This comprehensive review examines the current understanding of PHB, including its anatomy, pathophysiology, clinical presentation, diagnostic challenges, and management strategies, based on the available literature and clinical evidence. Early recognition and appropriate management, including surgical intervention when necessary, are essential to alleviate symptoms and prevent long-term complications.

Keywords: Bursitis, facial pain, synovial bursa, temporomandibular joint, oral surgery

INTRODUCTION

Orofacial pain encompasses a spectrum of clinical conditions affecting the head, face, and neck, with etiologies ranging from dental pathologies to neuropathic disorders. Among these, non-dental causes, such as temporomandibular joint disorders (TMDs), Eagle syndrome, and neuralgias, often dominate the differential diagnosis (1). However, rarer causes like pterygoid hamulus bursitis (PHB) are frequently overlooked, primarily due to their nonspecific clinical features and limited awareness among clinicians. This underrecognition often delays diagnosis and prolongs patient suffering, as individuals endure persistent pain while undergoing ineffective treatments for misdiagnosed conditions (2).

The pterygoid hamulus (PH), though a relatively small anatomical structure, plays a significant role in oropharyngeal function and is prone to mechanical irritation. Anatomical variations, such as elongation or angulation of the PH, may lead to repetitive trauma of the surrounding soft tissues, resulting in inflammation of the synovial bursa enveloping the hamulus (3). This condition, termed PHB, is characterized by chronic orofacial pain

that is often referred to adjacent regions, including the temporomandibular joint, throat, or ear. These referred pain patterns contribute to the diagnostic complexity of PHB, as the symptoms overlap with those of more prevalent conditions such as TMDs, glossopharyngeal neuralgia, or masticatory myalgia (4).

Despite its rarity, PHB deserves attention due to its debilitating impact on patients' quality of life. Early and accurate diagnosis not only prevents unnecessary interventions but also ensures timely treatment, which may include conservative measures or surgical resection of the hamulus (5). This review synthesizes current knowledge about PHB, highlighting its anatomical and clinical features, diagnostic approach, and treatment strategies. By doing so, we aim to improve awareness among clinicians and provide a comprehensive resource for understanding and managing this uncommon yet significant condition.

Anatomy and Function of the Pterygoid Hamulus

The pterygoid hamulus is a hook-like bony projection that extends inferiorly from the medial pterygoid plate of the sphenoid bone. Measuring approximately 6-8 mm in length,

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it serves as a critical anatomical fulcrum for the tensor veli palatini muscle, which wraps around the hamulus before inserting into the soft palate (6). This unique anatomical configuration allows the tensor veli palatini muscle to tighten the soft palate during swallowing and speech, facilitating proper oropharyngeal function. In addition, the pterygoid hamulus provides an attachment point for the pterygomandibular raphe, a fibrous band connecting the buccinator and superior pharyngeal constrictor muscles, thereby contributing to the coordination of oral and pharyngeal musculature (7).

Variations in the morphology of the pterygoid hamulus,

such as elongation, irregular angulation, or roughened bony surfaces, can predispose individuals to chronic irritation of the surrounding tissues. These variations may be congenital or acquired, with the latter often resulting from repetitive microtrauma, overuse, or age-related changes (8). Over time, this irritation leads to inflammation of the synovial bursa enveloping the hamulus, culminating in PHB. The inflammation not only causes localized pain but also impacts the adjacent soft tissues and neurovascular structures, producing a constellation of symptoms that extend beyond the immediate anatomical site (9). Avarage length, angulation and interhamular distances calculated in the literature are shown in Table 1.

Table 1. Morphometric analysis of pterygoid hamulus			
Author	Avarage length	Avarage angulation	Avarage interhamular distance
Putz and Kroyer (7)	7.2mm	Saggital: 75 Frontal: 58	Between 26mm and 36.9 mm
Eyrich et al. (10)	L: 5mm R: 4.9mm	No data	Hamulus to median cut distance: L: 19.6 mm R: 19.9 mm
Orhan et al. (3)	L: 5.48±1.94 mm R: 5.40±2.00 mm	No data	No data
Komarnitki et al. (11)	6.88 mm	Sagittal: 35.3 Frontal: 22.47	No data
Krmpotić-Nemanić et al. (12)	Children: 3.6 mm Adults: 6.9 mm Elders: 5.0 mm	Children: 19.6 Adults: 35.9 Elders: 19.7	Children: 31 mm Adults: 38.9 mm Elders: 32.7 mm
mm: Milimeters			

Pathophysiology

The pathophysiology of PHB is complex, involving both mechanical and inflammatory components. At its core, PHB arises from chronic irritation or trauma to the bursa overlying the pterygoid hamulus, a hook-like bony projection at the medial pterygoid plate (13). This irritation can lead to inflammation of the bursa, resulting in pain and referred symptoms that radiate to surrounding anatomical structures.

The pterygoid hamulus serves as a functional pulley for the tensor veli palatini muscle, which tenses the soft palate and plays a critical role in swallowing and speech (14). Repetitive mechanical stress on the hamulus, such as from excessive muscle activity or trauma caused by adjacent tissues, contributes to bursal irritation. Prolonged or repeated inflammation may lead to fibrosis and thickening of the bursa, perpetuating the cycle of pain and dysfunction (15).

Anatomical variations, such as an elongated or abnormally shaped hamulus, exacerbate the condition by increasing mechanical stress on the overlying tissues (14). In such cases, even normal activities like chewing or speaking may provoke inflammation, leading to chronic symptoms. Additionally, systemic conditions such as rheumatoid arthritis or other inflammatory disorders may predispose individuals to bursitis by amplifying the inflammatory response (16).

The close anatomical relationship between the pterygoid hamulus and the greater palatine nerve explains the referred pain patterns commonly observed in PHB. Sensitization of the nerve fibers by chronic inflammation may lead to hyperalgesia, where normal stimuli are perceived as painful, or allodynia, where non-painful stimuli evoke pain (11). This neural component further complicates the condition and underscores the need for multidisciplinary management.

Etiology and Risk Factors

PHB is a multifactorial condition with various intrinsic and extrinsic factors contributing to its onset. Key etiological factors include:

- Anatomical Variations:**
An elongated or abnormally angulated pterygoid hamulus is a significant risk factor for PHB. Studies have shown that these anatomical variations increase the likelihood of mechanical irritation to the overlying bursa, particularly during mastication or speech (17).
- Repetitive Trauma:**
Activities involving repetitive or excessive movement of the soft palate, such as vigorous chewing, frequent swallowing, or even prolonged speaking, can lead to microtrauma and bursal irritation. Patients with habits like bruxism or clenching may also experience increased mechanical stress on the pterygoid hamulus (14).

3. Inflammatory Disorders:

Systemic inflammatory conditions such as rheumatoid arthritis or gout can predispose individuals to bursitis, including PHB. These disorders amplify the inflammatory response, making the bursa more susceptible to irritation and swelling (18).

4. Dental and Surgical Factors:

Dental procedures involving the posterior maxilla, such as extractions or implant placement, may inadvertently traumatize the pterygoid hamulus. Similarly, surgical interventions in the oropharyngeal region can lead to postoperative inflammation and subsequent PHB (14).

5. Age and Gender:

While PHB can occur at any age, studies suggest that older adults are more susceptible due to degenerative changes in soft tissues and increased likelihood of systemic inflammatory conditions (19). There is no strong gender predilection, though certain lifestyle factors may influence risk.

Diagnostic Challenges

Diagnosing PHB is particularly challenging due to its nonspecific symptomatology and the overlapping clinical features it shares with more common orofacial pain disorders (20). Patients with PHB often present with diffuse, poorly localized pain that radiates to the soft palate, throat, ear, or temporomandibular joint (TMJ) area, mimicking conditions such as TMDs, Eagle syndrome, or myofascial pain dysfunction (21). Additionally, the rarity of PHB, combined with limited awareness among clinicians, further delays its recognition, leading to misdiagnoses and ineffective treatment approaches.

One of the primary diagnostic hurdles is the absence of pathognomonic clinical signs. Most patients describe a dull, aching pain that worsens with activities involving the oropharynx, such as swallowing, chewing, or speaking (22). However, these symptoms are often attributed to more common disorders, particularly when accompanied by tenderness in the TMJ region or masticatory muscles. Misdiagnosis is further compounded by the lack of specific imaging findings in routine diagnostic modalities such as panoramic radiographs, which are often insufficient to visualize the pterygoid hamulus in detail (23).

Advanced imaging techniques, including cone-beam computed tomography (CBCT) and magnetic resonance imaging (MRI), have significantly improved the diagnostic accuracy for PHB. CBCT provides high-resolution images of the pterygoid hamulus, allowing precise evaluation of its morphology, elongation, and angulation (24). Meanwhile, MRI is invaluable for assessing soft tissue changes, such as inflammation of the surrounding bursa or adjacent muscles (25). Together, these imaging modalities enable clinicians to identify anatomical variations and inflammatory changes that confirm the diagnosis of PHB. However, the routine use of these tools in orofacial pain clinics is limited by their cost and accessibility, particularly in low-resource settings (26).

Clinical palpation remains a crucial aspect of the diagnostic process. Palpating the medial pterygoid region intraorally, with attention to tenderness or pain elicited around the hamulus, is often indicative of PHB (27). Despite its utility, this technique requires skill and familiarity with the anatomy of the pterygoid region, which may not be routinely performed in general dental or medical practice. As such, interdisciplinary collaboration between oral and maxillofacial surgeons, otolaryngologists, and radiologists is essential for accurate diagnosis.

Clinical Presentation

The clinical presentation of PHB is highly variable, reflecting the multifactorial nature of its pathophysiology and its impact on surrounding anatomical structures. Most patients report a gradual onset of pain, which may persist for months or even years before an accurate diagnosis is made (28). Pain is typically described as deep, dull, and aching, localized to the posterior region of the oral cavity or radiating to the ear, throat, or TMJ area (29). In some cases, patients experience intermittent sharp pain exacerbated by movements such as swallowing, speaking, or chewing.

Referred pain patterns are a hallmark feature of PHB and are attributed to the proximity of the pterygoid hamulus to key neurovascular structures. The greater palatine nerve and branches of the maxillary nerve may become sensitized, leading to radiating pain that mimics neuralgias or TMD-related disorders (30). Dysphagia, a sensation of fullness in the throat, or even otologic symptoms such as ear fullness or tinnitus are not uncommon, further complicating the clinical picture (31).

Physical examination findings often include tenderness upon palpation of the medial pterygoid region, which can be assessed intraorally (32). In advanced cases, palpation may reveal a bony prominence corresponding to an elongated pterygoid hamulus, and this finding, combined with patient-reported pain during palpation, strongly suggests PHB. Additionally, muscle spasms or hyperactivity in the surrounding masticatory muscles may be observed, particularly if the patient has been experiencing chronic pain. The main symptoms and associated complaints in the clinical studies are shown in Table 2.

Table 2. Symptoms and associated complaints		
Symptom	Number of cases	Percentage
Ear complaints	11	35.47%
TMJ complaints	14	45.1%
Dysphagia	13	41.9%
Tender on palpation	25	80.6%
Speech disturbance	4	12.9%

Treatment Strategies

Treatment of PHB is dictated by the severity of symptoms, underlying anatomical variations, and the presence of any contributing systemic factors. Management typically begins with conservative measures, focusing on alleviating inflammation and reducing mechanical irritation of the pterygoid hamulus.

Conservative Management

Nonsteroidal anti-inflammatory drugs (NSAIDs) are often the first line of treatment, providing symptomatic relief from pain and inflammation (33). Adjunct therapies such as topical analgesics, corticosteroid injections, or oral muscle relaxants may also be employed to reduce discomfort and improve function. Physical therapy techniques, including soft tissue massage and myofascial release, have been reported to alleviate muscle tension and reduce referred pain in patients with PHB.

For patients with persistent symptoms, splint therapy using custom-made oral appliances may be considered. These appliances aim to reduce mechanical strain on the pterygoid hamulus by altering occlusal forces and repositioning the jaw (34). While conservative measures are effective in many cases, they often provide only temporary relief, particularly in patients with significant anatomical abnormalities or chronic inflammation.

Surgical Management

In cases refractory to conservative treatment, surgical resection of the pterygoid hamulus may be indicated. This procedure involves careful excision of the elongated or angulated hamulus to eliminate the source of mechanical irritation. Surgical resection is performed under local or general anesthesia, with intraoral access minimizing postoperative morbidity and ensuring aesthetic outcomes.

Recent advancements in minimally invasive surgical techniques have further improved the prognosis for patients undergoing hamulus resection. Outcomes are generally favorable, with most patients experiencing significant pain relief and restoration of function within weeks of surgery. However, careful patient selection and thorough preoperative planning are essential to minimize complications and ensure optimal results. A short review the cases with treatment approaches are shown in Table 3.

Table 3. Literature review of pterygoid hamulus syndrome cases							
Author	Sex	Age	Side	Pain location	Duration	Conservative treatment	Surgical treatment
Shah et al. (21)	M	26	L	Craniofacial (Palatal, ear)		No	Yes
Prats-Sisquella et al. (22)	F	69	L	Craniofacial	4 months	Yes (Failed)	Yes (LA)
Maracineanu et al. (30)	M	41	R	Craniofacial (Ear, TMJ, lateral pharyngeal)	2years	Yes (Failed)	Yes (GA)
Elmonofy et al. (17)	F	55	L	Craniofacial (Ear, temporal)	>4 years	Yes (Failed)	Yes (LA)
Galvez et al. (24)	F	54	R	Local, oral	>10 years	Yes	No
Firdouse et al. (14)	F	17	L&R	Craniofacial (Ear, throat, temporal orbital)	>1 years	Yes (Failed)	Yes (GA)
Thukral et al. (17)	F	48	R	Craniofacial (Oropharynx to face)	6 months	Yes	No
Thukral et al. (17)	F	52	L	Craniofacial (Tooth 28, temporal)	N/A	Yes (Failed)	Yes (LA)
Thukral et al. (26)	F	57	L	Craniofacial (Neck, temporal, face)	6 months	No	Yes (LA)
Kende et al. (13)	M	45	L&R	Craniofacial (TMJ, palatal, pharyngeal)	2 years	No	Yes
Kende et al. (13)	M	23	L	Craniofacial (Ear, temporal)	2-3 years	No	Yes
Shetty et al. (4)	F	42	L&R	Craniofacial (Temporal, orbital)	3 years	No	Yes
Bandini et al. (31)	F	36	L&R	Craniofacial (Oropharynx)	6 months	Yes	No
Cho et al. (25)	F	62	L	Craniofacial (Oral, pharynx, ear)	10 years	Yes	Yes (GA)
Sattur et al. (27)	M	52	L	Local	1 year	Yes	No
Orhan et al. (3)	F	26	R	Craniofacial (Palate, oropharynx, TMJ)	9 months	No	Referred
Ramirez et al. (9)	F	43	L	Craniofacial (Ear, mandible, temporal)	N/A	Yes	No
Ramirez et al. (9)	F	52	L	Craniofacial-cervical (Neck, scalp)	N/A	Yes	No
Sasaki et al. (29)	M	47	L	Craniofacial (Oral, pharynx, temporal, frontal)	8 years	No	Yes (LA)
Eyrich et al. (10)	M	25	R	Craniofacial (Palate, TMJ)	>1 year	No	Yes (LA)
Shankland (5)	M	73	L&R	Craniofacial (Palate, oropharyngeal)	N/A	Yes	No
Shankland (5)	F	47	R	Craniofacial (Ear, face, neck, TMJ)	N/A	Yes	No
Shankland (5)	F	38	L&R	Craniofacial (Ear, mandible, throat)	N/A	Yes (Failed)	Yes (LA)
Kronman et al. (28)	F	70	R	Craniofacial (Jaws, face, orbital, neck, TMJ)	>20 years	No	Yes (LA)
Salins et al. (20)	F	50	L&R	Craniofacial (Palate, ear, zygoma)	2 years	Yes	No
Charbeneau et al. (32)	M	222	L	Local	N/A	No	No
Wooten et al. (23)	M	20	R	Local	2 weeks	No	No
Wooten et al. (23)	M	4	L&R	No (Only swelling)	1 week	No	No
Wooten et al. (23)	M	19	R	Local	N/A	Yes	No
M: male, F: female, L: left, R: right, LA: local anesthesia, GA: general anesthesia, N/A: not assessed							

Prognosis

The prognosis of PHB varies depending on the severity of symptoms, the presence of underlying anatomical variations, and the treatment approach employed. With accurate diagnosis and appropriate intervention, most patients experience significant relief from symptoms and an improved quality of life.

Short-Term Outcomes

In cases managed conservatively, short-term outcomes are generally favorable, with many patients reporting a reduction in pain and improved function within weeks of initiating therapy. However, recurrence rates are higher in patients with anatomical abnormalities or unresolved underlying conditions.

Long-Term Outcomes

Surgical intervention, particularly hamulus resection, offers excellent long-term outcomes for patients with refractory PHB. Studies indicate that over 90% of patients undergoing surgery achieve sustained pain relief and functional restoration (13). Potential complications, such as postoperative infection or scarring, are rare and can often be managed effectively with appropriate perioperative care.

Factors Influencing Prognosis

Several factors influence the prognosis of PHB, including the duration of symptoms prior to diagnosis, the presence of systemic inflammatory conditions, and the skill and experience of the treating clinician. Early diagnosis and a multidisciplinary approach are critical for optimizing outcomes and minimizing complications.

CONCLUSION

PHB remains an underdiagnosed cause of orofacial pain, with significant implications for patients' quality of life. Despite its rarity, PHB should be considered in the differential diagnosis of patients presenting with atypical orofacial pain, particularly when symptoms involve the posterior oral cavity or adjacent regions.

Advances in imaging and a growing understanding of the condition have improved diagnostic accuracy, enabling clinicians to identify PHB more effectively. Conservative management remains the first line of treatment, offering symptomatic relief for many patients. However, surgical intervention provides a definitive solution for cases unresponsive to conservative measures, with excellent long-term outcomes reported in the literature.

Future research should focus on standardizing diagnostic criteria, evaluating the efficacy of novel treatment modalities, and exploring the underlying pathophysiology of PHB in greater detail. By increasing awareness among clinicians and promoting interdisciplinary collaboration, the burden of misdiagnosis and delayed treatment can be significantly reduced.

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REFERENCES

1. Van Deun L, de Witte M, Goessens T, et al. Facial pain: a comprehensive review and proposal for a pragmatic diagnostic approach. *Eur Neurol*. 2020;83:5-16.
2. Giral CR, Diaz-Manchay R, Leon-Jimenez F. Fibromyalgia: the underdiagnosed disease of pain. *Reumatologia*. 2021;59:64.
3. Orhan K, Sakul BU, Oz U, Bilecenoglu B. Evaluation of the pterygoid hamulus morphology using cone beam computed tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;112:e48-55.
4. Shetty SS, Shetty P, Shah PK, et al. Pterygoid hamular bursitis: a possible link to craniofacial pain. *Case Rep Surg*. 2018;2018:5108920.
5. Shankland WE 2nd. Pterygoid hamulus bursitis: one cause of craniofacial pain. *J Prosthet Dent*. 1996;75:205-10.
6. Barchetta N, Oliveira R, Silveira V, Faig-Leite H. Clinical and morphofunctional aspects of pterygoid hamulus: literature review. *Braz Dent Sci*. 2015;18:5.
7. Putz R, Kroyer A. Functional morphology of the pterygoid hamulus. *Ann Anat*. 1999;181:85-8.
8. Shankland WE 2nd. Bursitis of the hamular process. Part II: Diagnosis, treatment and report of three case studies. *Cranio*. 1996;14:306-11.
9. Ramirez LM, Ballesteros LE, Sandoval GP. Hamular Bursitis and its possible craniofacial referred symptomatology: two case reports. *Med Oral Patol Oral Cir Bucal*. 2006;11:E329-33.
10. Eyrich GK, Locher MC, Warnke T, Sailer HF. The pterygoid hamulus as a pain-inducing factor. A report of a case and a radiographic study. *Int J Oral Maxillofac Surg*. 1997;26:275-7.
11. Komarnitki I, Skadorwa T, Chloupek A. Radiomorphometric assessment of the pterygoid hamulus as a factor promoting the pterygoid hamulus bursitis. *Folia Morphol (Warsz)*. 2020;79:134-40.
12. Krmpotić-Nemanić J, Vinter I, Marusić A. Relations of the pterygoid hamulus and hard palate in children and adults: anatomical implications for the function of the soft palate. *Ann Anat*. 2006;188:69-74.
13. Kende P, Aggarwal N, Meshram V, et al. The pterygoid hamulus syndrome - an important differential in orofacial pain. *Contemp Clin Dent*. 2019;10:571-6.
14. Firdouse A, Firdoose N, Ghousia S. An unusual clinical vignette of oro-pharyngeal discomfort: Pterygoid Hamulus syndrome. *Med Pharm Rep*. 2020;93:306-9.
15. Luis Baerga-Varela M, Raul A. Rosario-Concepción M. Knee Bursopathy. In: Frontera WR, Silver JK, Rizzo TD, eds. *Essentials of Physical Medicine and Rehabilitation*. 4th edition. Philadelphia: Elsevier; 2019;399-402.
16. Williams CH, Jamal Z, Sternard BT. Bursitis. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 24, 2023.

17. Elmonofy O, ELMinshawi A, Mubarak F. Pterygoid hamulus elongation syndrome. *Int J Surg Case Rep.* 2021;78:81-4.
18. Chatra PS. Bursae around the knee joints. *Indian J Radiol Imaging.* 2012;22:27-30.
19. Baker HP, Gutbrod J, Cahill M, Shi L. Optimal treatment of proximal humeral fractures in the elderly: risks and management challenges. *Orthop Res Rev.* 2023;15:129-37.
20. Salins PC, Bloxham GP. Bursitis: a factor in the differential diagnosis of orofacial neuralgias and myofascial pain dysfunction syndrome. *Oral Surg Oral Med Oral Pathol.* 1989;68:154-7.
21. Shah A, Guduba V, Tejaswini K, Kothari C. Elongated pterygoid hamulus: a case report. *Indian J Otolaryngol Head Neck Surg.* 2023;75:3830-3.
22. Prats-Sisquella B, Peeva NA, Jorba-Garcia A, et al. Hamular bursitis as a cause of orofacial pain. A case report. *J Clin Exp Dent.* 2023;15:e599-604.
23. Wooten JW, Tarsitano JJ, Reavis DK. The pterygoid hamulus: a possible source for swelling, erythema, and pain: report of three cases. *J Am Dent Assoc.* 1970;81:688-90.
24. Galvez P, Moreau N, Fenelon M, et al. Pterygoid hamulus syndrome: a case report. *J Oral Med Oral Surg.* 2020;26:42.
25. Cho JY, Cheon KY, Shin DW, et al. Pterygoid hamulus bursitis as a cause of craniofacial pain: a case report. *J Korean Assoc Oral Maxillofac Surg.* 2013;39:134-8.
26. Thukral H, Nagori SA, Rawat A, Jose A. Pterygoid hamulus bursitis: a rare intra-oral pain syndrome. *J Craniofac Surg.* 2019;30:e643-5.
27. Sattur AP, Burde KN, Goyal M, Naikmasur VG. Unusual cause of palatal pain. *Oral Radiol.* 2011;27:60-3.
28. Kronman JH, Padamsee M, Norris LH. Bursitis of the tensor veli palatini muscle with an osteophyte on the pterygoid hamulus. *Oral Surg Oral Med Oral Pathol.* 1991;71:420-2.
29. Sasaki T, Imai Y, Fujibayashi T. A case of elongated pterygoid hamulus syndrome. *Oral Dis.* 2001;7:131-3.
30. Maracineanu R, Motoc M, Talpos-Niculescu RM, et al. Medial deviation of the pterygoid hamulus as an uncommon cause of persistent oral and facial pain - a rare case report and literature review. *Cranio.* 2025;43:253-7.
31. Bandini M, Corre P, Huet P, Khonsari RH. A rare cause of oral pain: The pterygoid hamulus syndrome. *Rev Stomatol Chir Maxillofac Chir Orale.* 2015;116:380-3.
32. Charbeneau TD, Blanton PL. The pterygoid hamulus: a consideration in the diagnosis of posterior palatal lesions. *Oral Surg Oral Med Oral Pathol.* 1981;52:574-6.
33. Butts R, Dunning J, Pavkovich R, et al. Conservative management of temporomandibular dysfunction: a literature review with implications for clinical practice guidelines (Narrative review part 2). *J Bodyw Mov Ther.* 2017;21:541-8.
34. Friction JR. Management of masticatory myofascial pain. *Semin Orthod.* 1995;1:229-43.