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Table of Contents

Original Articles

| How does agomelatine affect contraction in rat myocardial tissue? Raviye ÖZEN KOCA, Zülfikare Işık SOLAK GÖRMÜŞ, Hatice SOLAK, Gülnur AKDOĞAN | 669-675 |
|--|---------|
| The impact of dapagliflozin on FIB-4 index over 2 years in patients with type 2 diabetes mellitus Semra ÖZKABN Deniz GEZER | 676-682 |
| Risk factors for nonunion of ulnar styloid fractures associated with distal radius fractures Emre KAYA, Nurtaç Alper AKDEMİR, Ali GEÇER, Levent KONUKOĞLU | 683-688 |
| Midline mini-incision approach with superolateral facet joint quadrantectomy for extraforaminal disc herniations: A modified technique and outcomes Turgut KUYTIU Ahmet KARAOĞLU, Muhammet BAYAT, Serdar BAYRAM | 689-696 |
| The effect of swallowing disorder on quality of life in patients with Parkinson's disease Dilara BİNGÖL, Serkan BENGİSU, Zeynep TÜFEKÇİOĞLU, Ecem Nur DEMİRSOY, Haşmet HANAĞASI, Seyhun TOPBAŞ | 697-704 |
| The correlation between anxiety and depression levels with bulimic symptomatology and body mass index during COVID-19 quarantine measures: A 2-month follow-up study Ayşe ERDOĞAN KAYA, Çağlar TURAN, Yavuz Selim OĞUR, Nurullah YAVAŞ, Atila EROL | 705-713 |
| Are systemic and topical tranexamic acid superior to each other in bleeding control in coronary bypass surgery? Füsun GÖZEN, Fikret MALTEPE | 714-721 |
| Factors influencing difficult and failed intubation in patients undergoing gynecologic oncology surgery: a retrospective cohort study Seyyid Furkan KINA, Zeynep KOÇ, Damla USALAN, Atakan SEZGİ, Savaş ALTINSOY, Julide ERGİL | 722-731 |
| The utilization of the large unstained cell (LUC) parameter in lymphoid, haematopoietic and related tissue's malignant neoplasms Gamze GÖK, Serpil ERDOĞAN, Erbay ASUTAY, Gülsen YILMAZ, Özcan EREL, Fatma MERİÇ YILMAZ | 732-740 |
| Analysis of validity and reliability of the risk assessment form for children Melike TEKİNDAL Nurullah ÇALIŞ, Aslı SABAN Tarık TUNCAY, İbrahim Kürşat ERGÜT, Mustafa AGAH TEKİNDAL | 741-752 |
| Comparison of preoperative and postoperative frailty in elderly following gastrointestinal cancer surgery Gorkem OZDEMİR, Alper SÖZÜTEK | 753-761 |
| The impact of suicide rates on admissions to emergency medical services and the role of education and employment $Erkan\ BO\ GA$ | 762-768 |

| AI as a patient educator: Evaluating ChatGPT's role in disseminating information on herpes zoster ophthalmicus Seçil YİGEN İRİTAŞ, İlter İRİTAŞ | 769-775 |
|--|---------|
| Evaluation of the effect of rectus sheath block and transversus abdominis plan block on sevoflurane and fentanyl consumption in laparoscopic cholecystectomy: A randomized controlled study Ecem KELEŞ, Ahmet GÜLTEKİN, Ilker YILDIRIM, Cavidan ARA Birol TOPÇU | 776-785 |
| Comparison of ultrasound-guided joint reduction with traditional methods in the emergency center Semih ERİTEN, Vedat İZCİ, Serdar MENEKŞE | 786-793 |
| Factors influencing fistula formation following perianal abscess treatment Amil HUSEYNOV, Sevim Nuran KUŞLU ÇİÇEK | 794-799 |
| The relationship between knowledge of cardiovascular disease risk factors and health anxiety among caregivers of patients undergoing open-heart surgery Nazan DOLAPOĞLU, Ahmet DOLAPOĞLU, Sinan ALTUNÖZ, Emin BARBARUS | 800-808 |
| Meta-Analysis | |
| The efficacy of benzydamine on cancer treatment-induced oral mucositis: A systematic review of randomised controlled trials Dilek GÜMÜŞ, Zeynep YILMAZ, Fuzuli TUĞRUL | 809-820 |
| Reviews Artificial intelligence, machine learning, and radiomics in lung cancer classification Hatice ELMAS, Aysun Hatice UĞUZ, Abdullah Fahri ŞAHİN, Fahriye Seçil TECELLİOĞLU, Lutz WELKER | 821-827 |
| Case Reports Management of giant popliteal artery aneurysm using in situ saphenous vein bypass: A case report Gündüz YÜMÜN, Hakan HAŞİMOĞLU | 828-831 |

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Medical Physiology

How does agomelatine affect contraction in rat myocardial tissue?

Raviye Özen Koca¹, Zülfikare Işık Solak Görmüş¹, Hatice Solak², Gülnur Akdoğan¹

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ABSTRACT

Objectives: Cardiovascular diseases and depression are frequently seen together. Despite the developments in the treatment efficacy of agomelatine, a widely used antidepressant, its safety profile on cardiac tissue has not been sufficiently investigated. The aim of this study was to evaluate effects of agomelatine on contraction in rat myocardial tissue in depression and anxiety conditions frequently encountered in cardiovascular diseases and after cardiac surgery.

Methods: Myocardial tissue sections were removed from 12 male Wistar Albino rats divided into control and agomelatine groups. The tissues were placed in the isolated organ bath system. Maximum contraction was achieved by applying 10^{-1} M adrenaline to both groups. When the contraction plateaued, the same volume of vehicle as agomelatine were applied to the Control group. Agomelatine cumulative doses ($10^{-8} - 10^{-4}$ M) were applied to the agomelatine group. The resulting isometric contraction forces were recorded by the isolated organ bath system. The statistical analyses of the study were performed with the R 4.3.1 program.

Results: A significant increase in the tension of the tissues was observed with adrenaline in both the Control and Agomelatine groups. In the Agomelatine group, the tension at 10^{-8} agomelatine dose was significantly lower compared to 10^{-1} M adrenaline dose (P<0.05), and tension at 10^{-6} agomelatine dose was significantly lower compared to 10^{-7} agomelatine dose (P<0.05).

Conclusions: Agomelatine produced a dose-dependent suppressed contractile response in myocardial tissue. This suggests that it may have positive effects on increased blood pressure, positive inotropic effect and hypertensive state, which can occur in cardiovascular diseases and are also common in depression. Agomelatine may have a more favorable side effect profile than other antidepressants in cardiovascular disease states.

Keywords: Agomelatine, antidepressant, cardiovascular disease, contraction, myocardium

ood disorders often emerge in young adulthood. Anxiety and depression have been found to be associated with cardiovascular diseases (CVD) in young adults [1]. Unrecognized anxiety presents a significant challenge in cardiology.

It may be essential to examine anxiety and its various subtypes in relation to the onset and progression of CVD. Anxiety disorders seem to elevate the risk of developing CVD and serve as an indicator of poor prognosis in individuals with existing CVD, regardless of

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the presence of depression. Understanding anxiety is crucial for uncovering the mechanisms behind cardiopathogenesis, formulating new treatment approaches, and implementing clinical interventions for those at risk of or already diagnosed with CVD [2]. Depression and anxiety frequently occur together in individuals with CVD. People with CVD are at a greater risk of experiencing depression compared to the general population. Likewise, individuals suffering from depression have an elevated likelihood of developing CVD over time and face higher mortality rates. Among CVD patients, those who also struggle with depression tend to have worse clinical outcomes than those without it. More severe depression is associated with an increased risk of death and other cardiovascular complications. Given how common depression is among CVD patients, there is likely a two-way connection, where CVD contributes to depression, and depression, in turn, worsens CVD and its prognosis. Since both depression and anxiety play a significant role in overall well-being, addressing them is essential in CVD management [3].

The effects of depression on the cardiovascular system can be listed as positive chronotropic effect, increased blood pressure, cardiac arrhythmia, platelet aggregation and negative effects on inflammation. It has been determined that antidepressants used in the treatment of depression cause a decrease in risk of coronary heart disease [4].

It has been reported that pineal gland dysfunction is involved in the pathogenesis of psychiatric disorders and that depression is associated with low melatonin levels. The fact that many antidepressant drugs increase norepinephrine and serotonin levels and thus increase melatonin levels is seen as evidence of the depression-melatonin relationship. It has also been thought that melatonin, released during night, may play an important role in balancing high blood pressure because it reduces blood pressure, heart rate [5]. In addition, physiological deficiency of melatonin can increase hypoxia and oxidative damage. The importance of melatonin use in heart diseases caused by oxidative damage can be emphasized. In an in vivo study conducted by Lee et al. [6], it was determined that intravenous melatonin administration prevented ventricular tachycardia, fibrillation and premature ventricular contraction.

Recent findings have shown that effects of mela-

tonin on cardiovascular system. Melatonin causes vasodilation in peripheral vascular beds. Melatonin levels have been found to be low at risk of sudden death [7].

Agomelatine (Ago), a new melatonergic antidepressant drug, has good therapeutic effects on mood disorders and insomnia. Recent studies have shown the neuroprotective function of Ago, including its antiapoptotic and antioxidative effects. Ago is a 5-hydroxytryptamine receptor 2C (5HT2C) receptor antagonist and melatonin receptor (MT1-MT2) agonist. Melatonin also has protective properties in providing physiological conditions for the cardiovascular system [8]. Depression is a common comorbid disease in cardiac patients. Despite the developments in the treatment efficacy of Ago, a widely used antidepressant, its safety profile on cardiac tissue has not been sufficiently investigated. Detailed animal studies may be guiding in determining the cardiovascular side effects associated with the use of the drug. The aim of this study was to evaluate whether Ago, an antidepressant widely used in cardiovascular diseases and in depression and anxiety frequently encountered after cardiac surgery, affects the physiological properties (inotropy and chronotropy) of rat myocardium in a dose-dependent manner.

METHODS

Twelve male Wistar Albino rats aged 12 weeks (250-300 gr) were included in the study. The rats were kept in an environment with 12 hours of light and darkness, 24°C room temperature and 55-60% humidity. The animals were given standard rat food and fresh water ad libitum throughout the experiment. After a seven-day acclimation period, study groups were formed.

For isolated organ bath studies, experimental animals were decapitated under anesthesia and myocardial tissue sections were separated and immediately placed in Krebs-Henseleit solution. The content of the Krebs-Henseleit solution to be used in the experiments is as follows: NaCl, KCl, MgSO₄, KH2PO₄, CaCl₂, NaHCO₃, glucose.

The isolated organ bath is defined as a system that includes the basic conditions that can sustain the vitality of isolated tissues under in vitro conditions. The isolated organ bath system includes: amplifier, chambers, isometric power converter, thermostatic circula-

Eur Res J. 2025;11(4):669-675 Özen Koca et al



Fig. 1. Protocol for isometric contraction recording. After 10⁻¹ M adrenaline-induced maximal contraction, vehicle was added to Control (n=6) and cumulative agomelatine doses (10⁻⁸–10⁻⁴ M) to the treatment group (n=6) at 10-minute intervals.

tion pump, O₂-CO₂ mixture tube, recording unit, liquid and gas transport apparatus. In the isolated organ bath system, Krebs solution is used to maintain the vitality of tissues. Krebs-Henseleit solution is a solution that provides the physiological conditions in vivo to a certain extent in vitro. Its content allows smooth muscle cells to maintain their contractile properties at an optimal level in vitro.

In the current project; 10 ml organ bath chambers heated at 37°C and containing normal Krebs-Henseleit solution were continuously gassed with a mixture of 95% O₂ and 5% CO₂. Myocardial tissue sections obtained from the experimental animal were placed in the glass chambers in the isolated organ bath by applying 1 gr tension and then isometric contractions were recorded. This tension level was kept constant for all samples. Contractions of the tissues in the setup were recorded by following the amplitude and frequency of contractions with the isometric power converter and amplifier connection (BIOPAC MP36). The Krebs solution containing the tissues was renewed at 15-minute intervals.

The tissues taken from the experimental animals were divided into 2 groups as Group 1 (Control Group, n=6) and Group 2 (Agomelatine Group, n=6). After the tissues were hung, 10-1 M adrenaline was added to spontaneous isometric contractions and maximum contraction was achieved When the contraction reached a plateau, the same volume of vehicle as

agomelatine was added to the chambers of the Control group at 10-minute intervals and 10⁻⁸, 10⁻⁷, 10⁻⁶, 10⁻⁵, 10⁻⁴ M doses of Ago was added to the chambers of the Agomelatine group at 10-minute intervals. Muscle tension parameters were assessed 10 minutes before adrenaline was added, 10 minutes after adrenaline was added and after each dose of drug (Fig. 1) [9, 10].

Statistical Analysis

The statistical analyses of the study were performed with the R 4.3.1 program. Mean±standard error of mean (Mean±SEM) was calculated for numerical variables. P<0.05 was accepted as significant. Tukey-Kramer correction was used when statistical analyses were performed when necessary.

RESULTS

Contractions of rat myocardial tissue in isolated organ bath were recorded and statistically evaluated (Figs. 2 and 3). When the tension values recorded at Time3 (P<0.05), Time4 (P<0.05), Time5 (P<0.05), Time6 (P<0.001) and Time7 (P<0.005) were compared between the groups, significant differences were detected (Fig. 4).

The time-dependent change of the measured tensions showed significant difference between the groups (P<0.001). There were significant differences



Fig. 2. Control group. At the time indicated by the arrows, adrenaline has been added to the chamber.

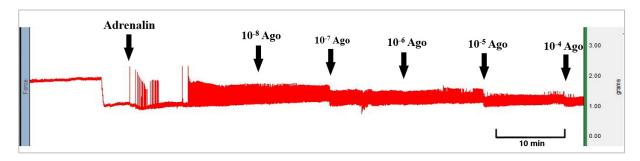


Fig. 3. Agomelatine group. Drugs were added to the chambers at the times indicated by the arrows.

between the tension values changing with time within the group (the tension values recorded at Time1 and Time2 (P<0.001), Time2 and Time3 (P<0.05), Time3 and Time4 (P<0.05), Time4 and Time5 (P<0.05), Time5 and Time6 (P<0.05) are significantly different from each other.

When the time-dependent changes in tension values were compared in pairs within the group, a significant difference was found between Time1 and Time2 in the control group (P<0.005). A significant difference was found between Time1 and Time2 (P<0.005), between Time2 and Time3 (P<0.05), and between Time4 and Time5 (P<0.05) in the agomelatine group (Fig. 4).

DISCUSSION

In the present study, the dose-dependent effects of agomelatine, an antidepressant commonly used in depression and anxiety conditions frequently encountered in cardiovascular diseases, on contraction in rat myocardial tissue were evaluated. Contraction forces of rat myocardial tissue were examined in an isolated organ bath system.

Ago was synthesized from melatonin as a melatonin analog among antidepressant agents [11]. Ago is a melatonergic agonist and 5HT2C antagonist [12]. Findings obtained in recent years have shown that effects of melatonin on cardiovascular system are recep-

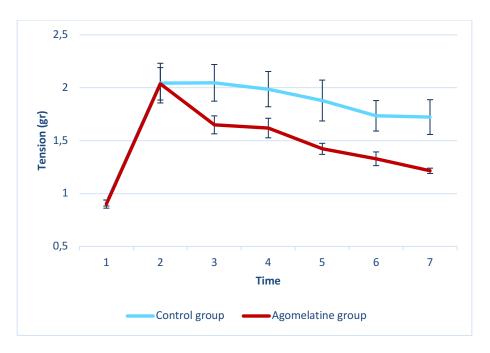


Fig. 4. Tension changes in rat myocardial tissues in response to adrenaline and agomelatine in isolated organ bath. Time 1: baseline; Time 2: 10^{-1} M adrenaline; Times 3–7: cumulative doses of agomelatine (10^{-8} to 10^{-4} M) were administered to the Agomelatine group, and vehicle to the Control group. Significant differences between groups were observed at Time 3, 4, and 5 (P<0.05), and at Time 6 and 7 (P<0.005). Time-dependent changes in tension values were significantly different between groups (P<0.001).

tor or non-receptor mediated. Melatonin causes vaso-constriction in cerebral arteries. Melatonin levels were found to be low in coronary heart disease patients at risk of myocardial infarction [13].

In a study, the possible healing effects of Ago on lipopolysaccharide-induced endothelial and cardiac damage were investigated. Lipopolysaccharide was shown to induce inflammation, oxidative stress, and apoptosis in cardiac and endothelial tissues. Ago improved all these parameters with its antioxidant, anti-inflammatory, and antiapoptotic activities [14]. In a different study, Ago significantly reduced hypertension-induced memory, endothelial function, nitrosative stress, mitochondrial dysfunction, inflammation, and brain damage disorders via MT1/MT2 and 5HT2C receptors [15].

Ago is a pharmaceutical compound that acts as an agonist for melatonin receptors with specific affinity for the MT1 and MT2 receptor subtypes. To evaluate the effect of this compound on contraction, various tissue contractions have been evaluated in different studies. The complex interaction between Ago and the modulation of estrous cycles, pregnancy periods, litter numbers and uterine contractions has been investigated in a study. Ago has been shown to inhibit spontaneous and oxytocin-induced myometrial contractions in a dose-dependent manner [16].

The results of the studies examining the effects of Ago on the contractions of the tissues belonging to the cardiovascular system are quite limited. Singh et al. [15] showed that 24-day Ago administration at a dose of 2 and 4 mg/kg can alleviate the suppressed relaxation of rat thoracic aortic tissue due to renovascular hypertension. In another study, Nurullahoğlu-Atalık et al. [17] stated that Ago caused a dose-dependent nitric oxide-mediated inhibition on intact rat thoracic aortic tissue contraction. In the current study examining its effect on cardiac contraction, Ago was shown to cause a significant inhibition in the increased tension of myocardial tissue induced by adrenaline, compared to the control, after each dose added. This reveals that the inhibitory effect of Ago on muscle contraction, which is also supported by other studies, is also effective in cardiac tissue. On the other hand, following the significant increase in the tension force of the tissues in both the Control (P<0.005) and Agomelatine (P<0.005) groups with adrenaline; the fact that the tension at Time3 was lower compared to Time2 (P<0.05) and the

tension at Time5 was lower compared to Time4 (P<0.05) in the Agomelatine group suggests that the inhibitory effect of Ago may be dose-dependent. This result is important, as there is no other study proving this effect of Ago on cardiac tissue. When the current study and other limited research results are evaluated together, it is clear that Ago produces a dose-dependent suppressed contractile response in both cardiac and vascular tissue. This suggests that it may cause positive effects on increased blood pressure, positive inotropic effect and hypertensive status, which can occur in cardiovascular diseases and are also common in depression.

In the study conducted in the isolated rat heart model to examine the effects of Ago on myocardial ischemia reperfusion injury (MIRI), rat hearts were isolated and subjected to 30 minutes of ischemia and then 120 minutes of reperfusion to induce MIRI. Ago (10, 20 or 40 mg/kg) was injected intraperitoneally into the rats 1 hour before heart isolation. It was observed that Ago significantly improved cardiac function and alleviated pathological changes in the ischemic myocardium [18].

A different study was conducted to investigate the protective effects of Ago, a melatonin receptor agonist, against cadmium-induced toxicity. Ago significantly inhibited the cadmium-induced elevation of serum cardiac enzymes. Ago restored the structure of cardiac myofibrils and seminiferous tubules [19].

The cardioprotective effect of Ago on isoproterenol-induced myocardial damage and the role of nitric oxide in cardioprotection were investigated. Serum cardiac enzymes and cardiac tissue oxidative stress parameters were evaluated. It was observed that isoproterenol significantly increased serum cardiac enzymes and there was a significant increase in oxidative, inflammatory and nitrosative stress in myocardial tissue. Pretreatment with Ago significantly reversed these profound isoproterenol myocardial damaging effects. These results revealed that Ago protects against isoproterenol-induced myocardial damage through its antioxidant, anti-inflammatory and anti-apoptotic effects [20]. In experimental studies on parameters related to oxidative stress in rats, Ago was shown to have an antioxidant function similar to melatonin. In a study, electrocardiographic, biochemical and nuclear imaging data show that pretreatment with Ago attenuates doxorubicin-induced cardiotoxicity similar to

melatonin [21].

The data obtained for Ago indicate that it may have cardioprotective effects. The data from the studies conducted reinforce the conclusion that this protective effect of Ago is due particularly to its antioxidant effect. In the present study, the dose-dependent inhibition caused by Ago in the increased tissue contraction of the myocardium due to adrenaline is similar to the results of the decrease in vascular tissue tension shown by a limited number of similar studies. The partial dose-dependent reduction of the increase in the contractile response induced by adrenaline through Ago addition suggests that the use of this drug may have a positive effect in cardiovascular diseases associated with conditions such as depression and anxiety, where cardiac inotropic/chronotropic response is considerably increased. On the other hand, while studies have shown that nitric oxide is a possible mediator in the vascular tissue for the inhibitory effect of Ago on contraction [17], it is not clear which mechanism may play a role in cardiac tissue. In addition, while it is thought that the improvement caused by Ago in damaged cardiac tissue functions is due to its antioxidant, anti-inflammatory, and antiapoptotic effects [14], the mechanism of the inhibitory effect it caused on adrenaline-induced increased tissue contraction in healthy hearts in the current study is also unknown. In this context, more detailed studies are needed to elucidate the pathways through which Ago affects cardiac tissue contraction.

Limitations

These results may not fully reflect the effects observed directly in living organisms. The effect of agomelatine was evaluated only under laboratory conditions, which may vary depending on different physiological factors in the body. The results obtained with different dose intervals of agomelatine or longer treatment periods may be different. The molecular mechanism by which ago may inhibit myocardial mechanical activity has not been investigated.

CONCLUSION

The healing and positive effects of agomelatine, which have been demonstrated in limited studies, have been

shown on cardiac tissue in cases of CVD. In the present study, it has been shown that Ago has an inhibitory effect on contraction in the increased increased tissue contraction of the myocardial tissue contraction induced by adrenaline. This suggests that the use of this drug does not pose a risk for mood disorders such as depression and anxiety and various cardiovascular diseases characterized by an increase in cardiac inotropic/chronotropic response, and may even lead to positive effects. Data from long-term studies in larger populations will be valuable for the use of Ago.

Ethical Statement

This study was approved by the Necmettin Erbakan University KONUDAM Experimental Medicine Application and Research Center Animal Experiments Local Ethics Committee (Decision no. 2025-002, date: 16.01.2025).

Authors' Contribution

Study Conception: RÖK, ZISG, HS; Study Design: RÖK, ZISG; Supervision: ZISG; Funding: RÖK, HS, ZISG; Materials: RÖK, GA; Data Collection and/or Processing: RÖK, GA; Statistical Analysis and/or Data Interpretation: RÖK, GA; Literature Review: RÖK; Manuscript Preparation: RÖK, GA and Critical Review: RÖK, ZISG.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Internal Medicine

The impact of dapagliflozin on FIB-4 index over 2 years in patients with type 2 diabetes mellitus

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ABSTRACT

Objectives: Dapagliflozin belongs to the sodium-glucose co-transporter 2 inhibitor drug group used in the treatment of type 2 diabetes. This study aimed to investigate the effects of dapagliflozin and simultaneous dapagliflozin+pioglitazone therapy on the FIB-4 index, associated with liver inflammation and fibrosis, at the end of the first and second years.

Methods: This retrospective study, conducted between 01.01.2017 and 01.01.2020, included 386 patients using dapagliflozin alone (DAPA Group) and 122 patients using dapagliflozin in combination with pioglitazone (DAPA+PIO Group). ALT, AST, and FIB-4 index were compared at baseline, at week 52, and at week 104. **Results:** The DAPA group consisted of 243 females (63%) and 143 males (37%) with a mean age of 59.8±6 years. The DAPA+PIO group consisted of 61 females (50%) and 61 males (50%) with a mean age of 58.3±5 years. No significant differences were observed between the groups in ALT, AST, hemoglobin levels, and platelet counts at the baseline, at the 52nd week, and at the 104th week (P>0.05). Statistically significant decreases in fasting blood glucose and HbA1C levels were observed in both groups at baseline, week 52, and week 104 (P<0.001). Furthermore, both groups exhibited no statistically significant changes in the FIB-4 index during the first and second years compared to baseline (P>0.05).

Conclusions: Dapagliflozin, either alone or in combination with pioglitazone, did not alter the FIB-4 index associated with liver fibrosis and inflammation over 1 and 2 years in patients with type 2 diabetes. Despite experimental evidence indicating its potential to reduce liver fibrosis, clinical data remain inconclusive. Future prospective studies with longer durations are necessary for a clearer understanding.

Keywords: Type 2 diabetes mellitus, dapagliflozin, pioglitazone, liver, FIB-4 index

n individuals with type 2 diabetes mellitus (T2DM), there is an uptick in metabolic dysfunction- associated steatotic liver disease (MASLD) due to insulin resistance and obesity [1, 2]. Even with liver enzymes within the normal range, it is estimated that up to half of those with T2DM also have MASLD [2]. Both T2DM and Non-alcoholic Fatty Liver Disease (NAFLD) pose risks of progressing to steatohep-

atitis, liver fibrosis, cirrhosis, and cancer [1]. Furthermore, MASLD is independently linked to an increased risk of cardiovascular disease and death [1, 3, 4]. MASLD is a metabolic condition closely associated with type 2 diabetes. A recent meta-analysis reported that 55.5% of patients with type 2 diabetes had MASLD, and 17% of them had advanced hepatic fibrosis [5]. Per the latest American Diabetes Associa-

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tion guidelines, individuals with prediabetes or T2DM and increased liver enzymes should undergo screening for liver fibrosis using non- invasive methods [6]. Non-invasive imaging tests for detecting MASLD are relatively costly, so assessing fibrosis through non-invasive biomarkers is more advisable [1, 7]. The European Association for the Study of Diabetes, the European Association for the Study of Obesity, and the European Association for the Study of the Liver have sanctioned non-invasive, validated biomarkers amalgamating metabolic and hepatic parameters commonly used in clinical practice [1]. The most widely used biomarkers for fatty liver include the Fatty Liver Index (FLI) and the MASLD Liver Fat Score (NLFS), while for liver fibrosis, the NAFLD Fibrosis Score (NFS) and the Fibrosis-4 (FIB-4) Index are commonly employed [8-11].

The FIB-4 index, initially devised for staging liver disease in HIV-HCV co-infected individuals, has since found application in others with liver disease [12]. It is a score computed using age, aspartate aminotransferase, and platelet count, routinely examined in nearly all patients with liver disease [13]. Studies have demonstrated the efficacy of pioglitazone in reducing fatty liver disease [14]. Dapaglifozin is an oral antidiabetic used in the treatment of T2DM. It works by specifically binding to SGLT-2 in the renal proximal tubule, inhibiting glucose reabsorption via this pathway and increasing urinary glucose excretion [15]. In addition to their glucosuric effect, SGLT-2 inhibitors provide weight loss and reduce body fat. They also have a positive effect on MASLD on the liver by reducing blood pressure, inflammation, and oxidative stress, reducing hyperuricemia, and correcting insulin [15,16]. One experimental study showed that dapagliflozin attenuated hepatic steatosis via the adenosine monophosphate-activated protein kinase (AMPK)-the mechanistic (or mammalian) target of rapamycin (mTOR), promoted autophagy and increased fatty acid oxidation in both in vitro and in vivo models [17].

Dapagliflozin, an SGLT-2 inhibitor, has been proven to diminish fibrosis and hepatic steatosis in a 24-week follow-up study involving patients with liver fibrosis [18]. There is one study showing that in patients with diabetes treated with dapagliflozin, there was a significantly greater reduction in both abdominal visceral adipose tissue and subcutaneous adipose tissue volume with dapagliflozin compared to placebo

[19]. There are experimental studies showing that different SGLT-2 inhibitors also improve histologic hepatic steatosis or steatohepatitis in obese mice or rats with T2DM [20, 21]. Only two prospective clinical trials have investigated the effect of SGLT-2 inhibitors on hepatic steatosis in patients with T2DM and NAFLD, but the anti-fibrotic effect of SGLT-2 inhibitors has not been studied in these patients [22, 23].

The objective of our study was to scrutinize the impact of dapagliflozin and combined dapagliflozin-pioglitazone treatment on liver enzymes and the FIB-4 index, associated with fibrosis. Our study encompasses results from a 104-week follow-up, and there's no existing research in the literature examining the effect of dapagliflozin on the FIB-4 index over 2 years.

METHODS

Study Participants

This retrospective investigation encompassed 508 individuals diagnosed with type 2 diabetes mellitus, who underwent monitoring at the Internal Medicine Clinic of from January 1, 2017 to January 1, 2020. The required sample size for the study was determined using the G Power software (v 3.1.9.7), resulting in the inclusion of 508 patients, with an effect size of f:0.1, alpha:0.01, and power:0.99. Among the participants, 386 received dapagliflozin alone, while 122 received pioglitazone concurrently with dapagliflozin. Data on fasting blood glucose, white blood cell count, platelet count (PLT), hemoglobin, alanine transaminase (ALT), and aspartate transaminase levels (AST) were gathered at week 0, week 52, and week 104 following the initiation of dapagliflozin and pioglitazone, utilizing the hospital's electronic information system. Patient comorbidities and demographic details were extracted from their medical records.

The FIB-4 index of each harvest was calculated. The formula for FIB-4index is: Age ([yr] \times AST [U/L]) / ((PLT [10(9)/L]) \times (ALT [U/L])(1/2)) [13]. The initial body mass index (BMI) values of each patient were calculated by dividing their weight in kilograms by the square of their height in meters.

The study excluded diabetic patients using alternative diabetes medications and insulins, those on antithrombotic drugs, individuals taking medications

impacting platelet count, patients with any hematologic disease, those with chronic liver disease, and individuals using herbal supplements potentially affecting liver function. Patients with alcohol consumption were also excluded because it affects liver enzymes.

Thyroid functions (fT3, fT4, TSH), renal functions (BUN, creatinine, protein in spot urine) were normal in all patients. Patients taking antihyperlipidemic drugs were excluded because they affect liver function tests. Patients over 65 years of age were excluded due to an inaccurate calculation of the FIB-4 Index.

Laboratory Procedures

The study assessed fasting blood glucose, alanine transaminase, and aspartate transaminase levels, along with hemogram parameters in both groups, utilizing an Abbott Architect 16200 automatic analyzer (Abbott Inc., Princeton, NJ, USA).

Statistical Analysis

A specialized statistical software (SPSS for Windows version 22, IBM Corporation, Armonk, NY, USA) was employed to analyze the collected data. Analytical methods, including the Shapiro-Wilk test or Kolmogorov-Smirnov, and visual approaches, such as probability plots and histograms, were utilized to ascertain the normal distribution of variables. Categori-

cal parameters are expressed as number (n) and percentage (%), while demographic data and other parameters are presented as the median and interquartile range (IQR). The Mann-Whitney U test determined significant differences between the DAPA and DAPA+PIO groups. Changes over time in evaluated parameters were assessed using the Friedman test, and the Wilcoxon test was applied to determine the significance of pairwise differences. A total type-1 error level of 5% was set for statistical significance.

RESULTS

Among the 508 participants in the study, 386 individuals were prescribed dapagliflozin as the sole antidiabetic therapy, while 122 were concurrently prescribed pioglitazone with dapagliflozin. The DAPA group comprised 243 females (63%) and 143 males (37%), with an average age of 59.8±6 years, receiving dapagliflozin exclusively. The DAPA+PIO group, consisting of 61 females (50%) and 61 males (50%) with an average age of 58.3±5 years, utilized pioglitazone concurrently with dapagliflozin. No significant age difference was observed between the two groups (P=0.127). BMI values of the patients were between 20-29.3 and were similar between the two groups (P=0.742). Furthermore, Table 1 provides details on

Table 1. Demographic characteristics and clinical findings in the DAPA and DAPA+PIO Group

| Parameters | | DAPA Group | DAPA+PIO Group |
|-------------------------|--------|-------------|----------------|
| | | (n=386) | (n=122) |
| Gender | Female | 243 (63%) | 61 (50%) |
| | Male | 143 (37%) | 61 (50%) |
| Age (years) | | 59.8±6 | 58.3±5 |
| Hypertension | No | 212 (54.9%) | 67 (54.9%) |
| | Yes | 174 (45.1%) | 55 (45.1 %) |
| Hyperlipidemia | No | 276 (71.5%) | 78 (64.5 %) |
| | Yes | 110 (28.5%) | 43 (35.5 %) |
| Coronary artery disease | No | 355 (92%) | 116 (95.1%) |
| | Yes | 31 (8%) | 6 (4.9%) |
| Cerebrovascular disease | No | 383 (99.2%) | 121 (99.2%) |
| | Yes | 3 (0.8%) | 1 (0.8%) |

Data are shown as mean±standard deviation or n (%). DAPA group=Group receiving dapagliflozin alone, DAPA+PIO Group=Group receiving pioglitazone simultaneously with dapagliflozin

Table 2. Comparison of blood parameters at baseline, week 52, and week 104 in the DAPA group and the DAPA+PIO group

| Parameters Parameters | Weeks | DAPA Group (n=386) | DAPA+PIO Group (n=122) | P value |
|--|----------|--------------------------------|--------------------------------|---------|
| DMI (leg/m²) | Baseline | ` / | , | 0.742 |
| BMI (kg/m²) ALT (IU/L) | Baseline | 24.9 (23.8-26.5) 20 (15-27) | 24.6 (23.8-26.3) 19 (15-31) | 0.742 |
| ALI (IU/L) | Week 52 | 21 (16-30) | | 0.376 |
| | Week 104 | 20 (15-27) | 20 (14-26) 19 (15-26) | 0.148 |
| | P value | 0.170 | 0.125 | 0.911 |
| AST (IU/L) | Baseline | 18 (14-24) | 19 (14-25) | 0.731 |
| ASI (IU/L) | Week 52 | 19 (15-25) | 19 (15-24) | 0.731 |
| | Week 104 | 19 (15-25) | 20 (15-26) | 0.300 |
| | P value | 0.257 | 0.656 | 0.323 |
| White blood cell (10 ³ /mm ³) | Baseline | 7.8 (6.5-9.2) | 7.9 (6.8-9.9) | 0.213 |
| white blood cen (10 /mm) | Week 52 | 8.0 (6.7-9.6) | 7.9 (6.8-9.9) | 0.213 |
| | Week 104 | 8.3 (6.8-10.0) | 8.0 (6.8-9.9) | 0.788 |
| | P value | 0.004* | 0.695 | 0.788 |
| Homoglobin (g/dI) | | | | 0.279 |
| Hemoglobin (g/dL) | Baseline | 13.6 (12.5-14.7) | 13.8 (12.4-15.2) | 0.378 |
| | Week 52 | 13.8 (12.6-15.0) | 13.6 (12.3-15.0) | 0.641 |
| | Week 104 | 13.7-12.7-15.0) | 13.6 (12.4-15.0) | 0.743 |
| DI-4-1-4-()4109/1 | P value | 0.278 | 0.628 | 0.610 |
| Platelets (×10 ⁹ /mL) | Baseline | 270 (229-320) | 266 (227-311) | 0.610 |
| | Week 52 | 273 (226-317) | 266 (214-315) | 0.467 |
| | Week 104 | 269 (227-317) | 262 (220-310) | 0.519 |
| TIED AA I | P value | 0.188 | 0.589 | 0.600 |
| FIB-4 index | Baseline | 0.92 (0.68-1.21) | 0.84 (0.62-1.20) | 0.699 |
| | Week 52 | 0.93 (0.70-1.27) | 0.87 (0.70-1.28) | 0.965 |
| | Week 104 | 0.95 (0.73-1.22) | 0.97 (0.69-1.30) | 0.847 |
| | P value | 0.124 | 0.150 | 0.154 |
| Fasting blood sugar (mg/dL) | Baseline | 213 (157-276) | 226 (169-290) | 0.154 |
| | Week 52 | 178 (137-247) | 169 (142-243) | 0.843 |
| | Week 104 | 181 (141-238) | 191 (131-231) | 0.816 |
| | P value | <0.001* | <0.001* | |
| HbA1c (%) | Baseline | 9.2 (7.9-10.6) | 9.6 (8.4-10.9) | 0.074 |
| | Week 52 | 8.5 (7.4-9.6) | 8.4 (7.3-9.5) | 0.611 |
| | Week 104 | 8.3 (7.2-9.8) | 8.1 (7.1-9.3) | 0.257 |
| | P value | <0.001* | <0.001* | |
| LDL (mg/dL) | Baseline | 115 (91-143) | 111 (89-133) | 0.108 |
| | Week 52 | 109 (86-131) | 101 (80-126) | 0.066 |
| | Week 104 | 106 (85-130) | 100 (80-130) | 0.254 |
| | P value | <0.001* | <0.001* | |
| Triglyceride (mg/dL) | Baseline | 181(140-268) | 199 (143-300) | 0.237 |
| | Week 52 | 175 (136)-262) | 182 (134-300) | 0.675 |
| | Week 104 | 174 (130-256) | 175 (125-250) | 0.510 |
| | P value | <0.001* | <0.001* | |

Data are shown as median (interquartile range). DAPA group=Group receiving dapagliflozin alone, DAPA+PIO Group=Group receiving pioglitazone simultaneously with dapagliflozin. AST=Aspartate Aminotransferase, ALT=Alanine Aminotransferase, BMI=Body Mass Index, LDL=low density lipoprotein

^{*}P<0.05 (Comparison between pre and post treatment), Friedman test

patient comorbidities.

A noteworthy disparity in white blood cell levels emerged between week 52 and week 104 in the DAPA group (P=0.004). A pairwise comparison disclosed a substantial increase in white blood cell count within the DAPA group after the first year compared to the baseline (P=0.003). In the DAPA+PIO group, no significant difference in white blood cell counts was noted in the first and second years compared to the baseline (P=0.695). Levels of ALT, AST, hemoglobin, and platelets were assessed at the baseline, in the 52nd week, and in the 104th week for both the DAPA and DAPA+PIO groups, revealing no significant differences between the two groups (P>0.05). HbA1C, fasting blood glucose, triglyceride and LDL levels of patients decreased significantly at 1 and 2 years compared to baseline (P<0.001). Additionally, there were no statistically significant alterations in the FIB-4 index for both groups during the initial and second years compared to the baseline (P>0.05). For detailed statistical outcomes, please consult Table 2.

DISCUSSION

Our study is the first in the literature to retrospectively investigate the effect of dapagliflozin onliver fibrosis with a 2-year follow-up using the FIB-4 index. In our study, we did not observe a statistically significant change in the FIB-4 index compared to the baseline in the first and second years for the group receiving dapagliflozin alone or dapagliflozin and pioglitazone concomitantly.

There are few studies in the literature examining the effect of dapagliflozin on the FIB-4 index. The results of this study are also controversial. In the comparison study of dapagliflozin and teneligliptin, the FIB-4 index showed similarity between the two groups, with no statistically significant difference found [24]. Dapagliflozin 5 mg was used in this study and the patients had BMI over 23. In a separate study, pioglitazone and dapagliflozin exhibited no notable impact on the FIB-4 index in type 2 diabetic patients at the 24-week follow-up [25]. The doses of pioglitazone and dapagliflozin used in this study are unclear, and the study patients consisted of patients with BMI 23 and above. An experimental study involving 11 patients with diabetes and NASH demonstrated that da-

pagliflozin reduced the FIB-4 index [26]. A recent meta-analysis suggested that standard treatment doses of SGLT-2 inhibitors may not be adequate to reduce liver fibrosis and fatty liver in NASH patients. However, it was acknowledged that the study results might have been influenced by the use of these drugs in high doses, potentially increasing the likelihood of side effects and reducing patient tolerability [27]. In our study, no change in the FIB-4 index was observed between the group using only dapagliflozin and the group using dapagliflozin-pioglitazone concomitantly at the 104-week follow-up. Our research is the initial one in the literature to evaluate the impact of dapagliflozin on the FIB-4 index, examining liver fibrosis over 104 weeks. Similar to other studies, the present study demonstrated that the use of dapagliflozin alone or concurrently with pioglitazone did not impact the FIB-4 index in the liver over two years.

In our study, patients were selected from those receiving 10 mg dapagliflozin. Other studies used dapagliflozin doses of 5-10mg. We do not know whether the difference in the drug doses used affects the FIB-4 index because there are no available studies.

Our study was performed in patients with a BMI 20-29.3. Considering the weight loss and adipose tissue reducing effects of dapagliflozin, we think that the fact that the BMI of the patients was in the normal range may have affected the results of the study. In addition, our patient population included patients taking antihypertensive drugs, which may have affected the study results. Therefore, new large prospective studies in obese individuals are needed.

Previous studies have indicated significant reductions in AST, ALT, and GGT in the dapagliflozin group after 24 weeks [18]. Some studies have suggested that dapagliflozin lowers ALT and AST levels [28, 29]. A recent meta-analysis, including 43 randomized controlled trials, indicated that serum ALT levels decreased by 0.21 IU/L (95% CI 0.33-0.10) following treatment with SGLT2 inhibitors [30]. However, this study also included SGLT-2 inhibitors other than dapagliflozin. In our study, no change was noted in ALT and AST levels after 2 years of dapagliflozin use. These results may be attributed to the absence of a 2year follow-up study for dapagliflozin use in the literature. Long-term studies are necessary to elucidate this matter. In our study, dapagliflozin was found to cause a statistically significant increase in white blood cell

counts starting from the 1st year during the 2-year follow-up (P=0.004). Since no studies on this subject were identified in a comprehensive literature review, we cannot comment on whether these results hold clinical importance. We believe that these results may become clearer with new studies to be conducted in the future.

Limitations

Our study presents several notable limitations. The first one is the retrospective design of the study. The second important limitation is that the effect of weight loss on FIB-4 index, ALT and AST levels could not be evaluated considering the height and weight of the patients. Although the patients had body mass index data at the beginning of the study, BMI data at the 1st and 2nd follow-up years could not be obtained. The third important limitation is that antihypertensives and additional medications used for coronary artery disease may also affect liver function. The last important limitation is the lack of previous liver imaging.

CONCLUSION

In patients with type 2 diabetes, dapagliflozin alone did not modify the FIB-4 index, associated with liver fibrosis and inflammation, in 1 year and 2 years compared to concurrent dapagliflozin use with pioglitazone. Although experimental studies show that dapagliflozin improves liver fibrosis, the matter has not yet been clarified in clinical studies. There is no 2-year follow-up study in the literature. Therefore, this needs to be elucidated in new prospective studies.

Ethical Statement

This study was approved by the Mersin University Clinical Research Ethics Committee (Decision no. 2023/861, date: 13.12.2023). Since the study was retrospective, written informed consent was not required.

Authors' Contribution

Study Conception: SÖ; Study Design: SÖ, DG; Supervision: SÖ, DG; Funding: SÖ; Materials: SÖ; Data Collection and/or Processing: SÖ, DG; Statistical Analysis and/or Data Interpretation: SÖ; Literature Review: DG; Manuscript Preparation: SÖ and Critical Review: SÖ, DG.

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Orthopaedics and Traumatology

Risk factors for nonunion of ulnar styloid fractures associated with distal radius fractures

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ABSTRACT

Objectives: A major complication of ulnar styloid fractures (USFs) associated with displaced distal radius fractures (DRFs) is nonunion, which can result in pain and instability of the distal radioulnar joint (DRUJ). This study aimed to identify the risk factors influencing the healing of USFs in cases of displaced DRFs, when treated using different methods - either surgically with plate-screw fixation, or conservatively with closed reduction and a plaster cast.

Methods: A total of 41 patients with USFs associated with DRFs, treated either surgically or conservatively, were retrospectively evaluated. Fractures were classified based on the treatment modality (surgical/conservative), demographic data, and radiographic characteristics. The Fernandez classification system was used to categorize DRFs. USF displacement was stratified into two groups: displacement >2 mm and <2 mm. Union and nonunion rates were compared across all parameters.

Results: Of the 41 cases included, 12 DRFs were managed surgically with plate-screw fixation, while 29 were treated conservatively with closed reduction and casting. Union was achieved in 35 cases, whereas nonunion was observed in 6. A statistically significant correlation was found between USF displacement >2 mm and nonunion. No significant association was observed between nonunion and other variables, including treatment modality, age, sex, laterality, or fracture classification.

Conclusions: The development of nonunion in USFs accompanying DRFs is not significantly influenced by treatment modality, age, sex, fracture classification, or side of involvement. However, a displacement of the USF greater than 2 mm is associated with a significantly increased risk of nonunion.

Keywords: Ulnar styloid fractures, distal radius fractures, fracture healing, radioulnar joint, risk factors

lnar styloid fractures (USFs) are observed in approximately 70% of DRFs [1, 2]. The ulnar styloid serves as the ulnar attachment site for the triangular fibrocartilage complex (TFCC), a critical structure for the stability of the DRUJ. Extending from the sigmoid notch of the radius to the base of the

ulnar styloid, the TFCC helps maintain the anatomical relationship between the distal radius, the ulnar head, and the proximal carpal row. Consequently, nonunion of USFs may compromise DRUJ stability, resulting in pain and impaired clinical outcomes [3-5].

DRFs represent the most frequently encountered

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fractures of the upper limb, and among the complications seen with accompanying USFs, nonunion is the most common. This study aims to investigate the factors associated with nonunion of USFs in patients with displaced DRFs.

METHODS

This study was conducted retrospectively with approval from the institutional ethics committee (HNEAH-GAEK/KK/2924/150). It included patients treated at our clinic between 2017 and 2020 for USFs associated with displaced DRFs, managed either surgically with plate-screw fixation or conservatively with closed reduction and casting. Radiographic data were retrieved and evaluated using the Picture Archiving and Communication System (PACS). All surgical interventions were performed by orthopedic surgeons trained at the same institution, utilizing a standardized surgical approach within a consistent clinical setting.

Patients who achieved complete union of the DRF were subsequently contacted for follow-up, during which the incidence of USN was evaluated. The minimum follow-up duration was 12 months. The diagnosis of nonunion was based on the absence of bony trabeculation across the fracture line on anteroposterior and lateral wrist radiographs obtained at six months post-treatment.

Radiographic assessment at the final follow-up included measurements of radial height, volar tilt, radial inclination, and ulnar variance. Patients presenting with distal radius malalignment, such as radial shortening or altered volar tilt, were excluded from the study. Additional exclusion criteria included loss of fracture reduction, a history of prior wrist fractures, or concomitant ipsilateral upper extremity fractures.

USFs were anatomically classified as either base or tip fractures. Displacement was stratified as greater than or less than 2 mm. Demographic data (age, sex, and laterality), radiographic measurements, and nonunion status were recorded for each patient. DRFs were classified according to the Fernandez classification system. Treatment modalities included conservative management with closed reduction and casting, or surgical intervention using plate-screw osteosynthesis. All clinical and radiographic parameters, along

with healing outcomes (union vs. nonunion), were statistically analyzed and compared.

Statistical Analysis

Descriptive statistics were presented as mean, standard deviation, median, minimum, maximum, frequencies, and percentages. The Kolmogorov-Smirnov test was employed to assess the normality of data distribution. Independent quantitative variables were analyzed using the independent samples t-test or the Mann-Whitney U test, depending on the distribution. Categorical variables were compared using the chisquare test, and the Fisher's exact test was applied when expected frequencies were insufficient for the chi-square test assumptions. All analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). A post hoc power analysis demonstrated that the sample size of 41 patients was sufficient to detect statistically meaningful differences with a power level exceeding 80%.

RESULTS

A total of 41 patients were included in the study, with a mean age of 50 years (range: 27-66). Of the participants, 16 (39%) were male and 25 (61%) were female. The fracture involved the right wrist in 19 (46.3%) cases and the left in 22 (53.7%) cases. The mean follow-up duration was 15.6 months, with a minimum of 12 months and a maximum of 18 months (Table 1).

Among the USFs, 13 (31.7%) were classified as tip fractures and 28 (68.3%) as base fractures. DRFs (DRFs) were categorized according to the Fernandez classification: 29 (70.7%) cases were type I, 1 (2.4%) case type II, 10 (24.4%) cases type III, and 1 (2.4%) case type IV. Surgical fixation with plate and screws was performed in 12 (29.3%) patients, while 29 (70.7%) patients were managed conservatively with closed reduction and casting. Radiographic assessment confirmed complete anatomical healing of the distal radius in all cases.

The effect of radiologic and demographic parameters on union and nonunion was evaluated (Table 2). A statistically significant correlation was found between USF displacement >2 mm and nonunion. No significant association was observed between

nonunion and other variables, including treatment modality, age, sex, laterality, or fracture classification.

DISCUSSION

The most common complication associated with USFs is nonunion. This condition may lead to increased stress and strain on the DRUJ, manifesting as pain during forearm rotation, ulnar deviation, or translational joint movements. Additionally, symptoms may result from associated TFCC tears or mechanical irritation

caused by the unhealed bone fragment. USFs accompany approximately 6% to 70% of DRFs [1, 2]. However, the clinical relevance of USF displacement in terms of treatment planning and long-term functional outcomes remains a subject of debate. In a prospective study involving 272 patients, May *et al.* [3] reported that USFs with displacement greater than 2 mm were associated with DRUJ instability in 166 cases. Consistent with these findings, our study demonstrated a significantly higher nonunion rate in cases with USF displacement exceeding 2 mm.

Several studies in the literature have addressed the

Table 1. Radiographic and demographic parameters of the patients

| | Median (min-max) | Mean±SD | n (%) |
|----------------------------------|-------------------|----------|------------|
| Age (years) | 50.0 | 49.3±9.7 | |
| | 27.0-66.0 | | |
| Sex | | | |
| Male | | | 16 (39.0%) |
| Female | | | 25 (61.0%) |
| Follow-up time (months) | 7.0 (4.0-11.0) | 7.4±1.5 | |
| Ulnar styloid fracture size (mm) | | | |
| >2 | | | 34 (82.9%) |
| <2 | | | 7 (17.1%) |
| Ulnar styloid fracture | | | |
| Tip | | | 13 (31.7%) |
| Base | | | 28 (68.3%) |
| Classification (Fernandez) | | | |
| I | | | 29 (70.7%) |
| II | | | 1 (2.4%) |
| III | | | 10 (24.4%) |
| IV | | | 1 (2.4%) |
| Treatment | | | |
| Plate | | | 12 (29.3%) |
| Conservative | | | 29 (70.7%) |
| Side | | | |
| Right | | | 19 (46.3%) |
| Left | | | 22 (53.7%) |
| Union | | | 35 (85.4%) |
| Nonunion | | | 6 (14.6%) |

n=number, SD=standard deviation, min=minimum, max=maximum

Table 1. The effect of radiologic and demographic parameters on union and nonunion

| | Union | | None | union | P value |
|----------------------------------|---------------------|------------|---------------------|-----------|---------------------|
| | mean±SD (median) | n (%) | mean±SD (median) | n (%) | |
| Age (years) | 50.5±9 (50) | | 42.3±11 (38) | | 0.057^{t} |
| Sex | | | | | |
| Male | | 13 (37.1%) | | 3 (50.0%) | 0.551x2 |
| Female | | 22 (62.9%) | | 3 (50.0%) | |
| Follow-up time (months) | 7.2 ± 1.5 (7) | | 8.2±1.7 (8) | | 0.234 ^m |
| Ulnar styloid fracture size (mm) | | | | | |
| >2 | | 33 (94.3%) | | 1 (16.7%) | |
| <2 | | 2 (5.7%) | | 5 (83.3%) | $< 0.001^{x^2}$ |
| Ulnar styloid fracture | | | | | |
| Tip | | 11 (31.4%) | | 2 (33.3%) | 1.000^{x2} |
| Base | | 24 (68.6%) | | 4 (66.7%) | |
| Classification (Fernandez) | | | | | |
| I | | 24 (68.6%) | | 5 (83.3%) | |
| II | | 1 (2.9%) | | 0 (0%) | |
| III | | 9 (25.7%) | | 1 (16.7%) | |
| IV | | 1 (2.9%) | | 0 (0%) | 0.651x2 |
| Treatment | | | | | |
| Plate | | 10 (28.6%) | | 2 (33.3%) | |
| Conservative | | 25 (71.4%) | | 4 (66.7%) | 1.000 ^{x2} |
| Side | | | | | |
| Right | | 18 (51.4%) | | 1 (16.7%) | |
| Left | | 17 (48.6%) | | 5 (83.3%) | 0.115^{x2} |

^{*}t test / m Mann-Whitney U test / x2 Chi-square test (Fisher's exact test)

impact of USF displacement and nonunion on clinical outcomes. Ayalon *et al*. [4] observed that the presence of USFs correlated with poorer functional scores and increased wrist pain in a cohort of 315 patients. Yılmaz *et al*. [5] reported reduced supination strength while Belloti *et al*. [6] found higher levels of wrist pain and worse DASH scores. Daneshvar *et al*. [7] noted more persistent pain, slower improvement in grip strength, and limited wrist flexion over time. Walenkamp *et al*. [8], in a prospective study of 312 cases, found significantly lower PRWE scores in the early recovery period.

The causes of pain related to USF nonunion have been explored extensively. Lindau *et al.* [9] reported a significantly higher incidence of TFCC injuries in DRFs accompanied by USFs, emphasizing their influence on clinical outcomes. Abid *et al.* [10] also linked poor clinical results in USFs to TFCC tears. Other authors have attributed persistent wrist pain to extensor carpi ulnaris tendon impingement caused by fibrous tissue at the site of nonunion [11-14]. Tsukazaki and Iwasaki [15] identified 17 USF nonunions in 109 patients, noting ulnar instability in 13. Nakamura *et al.* [16] achieved favorable outcomes with surgical fixa-

tion. On the other hand, the literature reported that USFs accompanying DRFs resulted symptomatic and were treated surgically. Hauck *et al.* [12] reported successful results in 20 symptomatic cases of USF nonunion treated surgically. Although some studies suggest that nonunion does not significantly affect outcomes, limitations in methodology weaken these conclusions. We believe that nonunion can have a negative impact on clinical outcomes and that prospective studies involving MRI or wrist arthroscopy will clarify the relationship between fracture healing and wrist pain.

Previous studies have reported no significant association between demographic factors and ulnar styloid nonunion in cases of DRFs. In line with previous research, our findings showed no correlation between age, sex or affected limb and the occurrence of nonunion. Similarly, the Fernandez classification of DRFs had no apparent effect on the rate of nonunion. The influence of treatment modality on ulnar styloid healing has also been investigated. Ayalon *et al.* [4] found no significant difference in nonunion rates or functional outcomes between the conservative and surgical management of DRFs.

Limitations

The retrospective design and relatively small sample size, particularly in the nonunion group, are the main limitations of this study. Additionally, functional outcomes and advanced imaging were not evaluated, which may limit the assessment of clinical impact.

CONCLUSION

Age, gender, side, and fracture classification have no effect on the development of nonunion in USFs associated with DRFs. Whether the treatment is surgical or conservative does not influence the risk of ulnar styloid nonunion. The risk of nonunion is significantly higher in cases with fracture displacement greater than 2 mm. These findings suggest that displacement magnitude should be a key consideration in clinical decision-making and follow-up planning for patients with associated USFs.

Ethical Statement

This study was approved by the Haydarpaşa Nu-

mune Training and Research Hospital Non-Interventional Clinical Research Ethics Committee. (Decision no. HNEAH-GAEK/KK/2924/150, Date: 19.11.2024).

Authors' Contribution

Study Conception: EK, NAA; Study Design: EK, LK; Supervision: EK, LK; Funding: N/A; Materials: N/A; Data Collection and/or Processing: EK, AG; Statistical Analysis and/or Data Interpretation: AG, NAA; Literature Review: LK, EK; Manuscript Preparation: EK, LK and Critical Review: EK, AG.

Conflict of interest

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Neurosurgery

Midline mini-incision approach with superolateral facet joint quadrantectomy for extraforaminal disc herniations: A modified technique and outcomes

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ABSTRACT

Objectives: Extraforaminal disc herniations constitute 3-12% of all lumbar disc herniations. In the literature, many surgical procedures have been described for extraforaminal disc herniations, including roughly medial and lateral approaches. In our study, we discussed the clinical results of cases in which we applied the super-olateral quadrantectomy (resection of the super-olateral quarter of the facet joint) technique described in the literature but modified by us, and we made conclusions about the technique. Patient outcomes were evaluated using the Macnab criteria: excellent, good, fair, and poor.

Methods: Between 2019 and 2023, 72 patients who were operated on with the diagnosis of single-level extraforaminal lumbar disc herniation and underwent superolateral facet joint quadrantectomy via mini incision-midline approach in our clinic were retrospectively analyzed.

Results: Preoperative Visual Analog Scale scores were 4-10 (mean: 8.5±2.17). Postoperative scores were 0-1 (mean: 0.3±0.1). According to the Macnab classification, 37 (51.39%) of the patients were evaluated as excellent, and 27 (37.50%) in the third postoperative month. Postoperative follow-up dynamic radiographs showed no instability in patients at the end of the 1st year. There were no perioperative complications in any of the cases.

Conclusions: The modified technique that we have described offers the potential advantages of preserving the facet joint capsule and reducing the size of the incision.

Keywords: Extraforaminal disc herniation, superolateral quadrantectomy, combined approach, mini-incision

xtraforaminal disc herniations constitute 3-12% of all lumbar disc herniations [1-3]. This group includes protruded discopathies extending beyond the neural foramen [4]. However, in some cases, lumbar disc herniation is found simultaneously in foraminal and extraforaminal localization [5]. This is often one of the causes of persistent or recurrent leg pain after micro-decompression of the extraforaminal disc alone [5, 6].

In the literature, many surgical procedures have been described for extraforaminal disc herniations, roughly medial and lateral approaches [6, 7]. Medial or midline approaches include laminectomy, laminotomy, hemilaminectomy, and subtotal or total facetectomy. In almost all of these approaches, access to the extraforaminal region requires significant bone resection and major facet joint removal. This leads to instability and permanent low back pain [6].

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Lateral paraspinal approaches and endoscopic techniques are superior since they do not require bone resection [8, 9]. However, these procedures are more complicated, especially at the L5-S1 level, due to the distance's specific narrow and oblique anatomical structure [10]. Another disadvantage of lateral approaches is the difficulty in reaching the foraminal disc component and the preforaminal bulging, which occurs just before the intervertebral foramen, the opening where spinal nerves exit the spinal column, and which often causes permanent irritation of the associated root. In these cases, an additional medial approach is required [6].

Dereymaeker et al. [6] briefly described the superolateral facet joint quadrantectomy. A 4 to 5-cm incision is made targeting the disc space of the herniated level. The aponeurosis is cut using a cautery, and the multifidus is released from the spinous process on one side using a curved chisel until the articular bone is exposed. The facet joint, which is located slightly more cranial to the disc space, is then exposed, and fluoroscopic control is performed. Under microscopic view, the facet capsular ligament of the facet joint and especially the mamilloaxicular ligament at the L2 and L3 level, as well as the medial branch of the posterior ramus are cauterized, and the superolateral quadrant of the facet joint is removed with a high-speed drill. The ligamentum flavum is opened with blunt dissection, and the root is followed to the level where it exits the foramen, and the free fragment is removed. In case of additional preforaminal bulging or herniation, decompression with a classic medial approach may be performed [6]. We have been using the same technique for about five years. However, our technique offers potential advantages, such as preserving the facet joint capsule and reducing incision size, compared to the technique described by Dereymaeker et al. [6].

In classical paramedian lumbar disc herniations, it is possible to perform single-distance microdiscectomy microscopically using a 3-5 cm skin incision [4]. However, a longer incision is required for lateral extension in the midline approach defined for extraforaminal lumbar discopathies with a preforaminal component [4]. In extraforaminal disc cases, if the midline approach is to be used, it is necessary to extend laterally from the midline and simultaneously reveal the facet joint. This extension increases the incision approximately two times. However, a shorter

skin incision has advantages such as aesthetics, less skin integrity disruption, and less infection risk.

Our study discussed the clinical outcomes of patients with single-distance extraforaminal (with or without multicomponent content) lumbar disc herniation operated on with this technique between 2019 and 2023.

METHODS

The study was started with Bursa Yüksek Ihtisas Education and Research Hospital ethics committee approval with protocol number 2024-TBEK 2024/04-09. Between 2019 and 2023, 72 patients who were operated on with the diagnosis of single-level extraforaminal lumbar disc herniation and underwent superolateral facet joint quadrantectomy via mini-in-

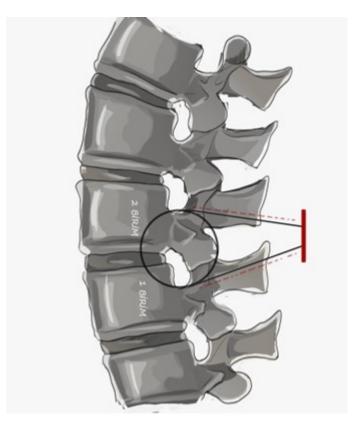


Fig. 1. Lateral view of the lumbar region. A midline, vertical, linear mini skin incision was made. 2/3 of the incision was made on the upper part of the distance and 1/3 on the lower part. A cone-shaped approach was made from the skin to the base to create a sufficient field of view at the base. The thick red line represents the skin incision, the dashed thin red lines represent the cone-shaped approach, and the black circle represents the field of view at the base.

cision midline approach in our clinic were retrospectively analyzed. Age, gender, body mass index, preoperative symptoms, and examination findings were documented. Preoperative lumbar magnetic resonance imagings (MRIs) and follow-up lumbosacral dynamic radiographs were re-examined to determine the levels of intervention and the anatomical compartments of disc herniation and instability findings. The clinical status, length of skin incision, instability, peri-postoperative complications, and follow-up periods were determined according to modified Macnab criteria which are used to evaluate the success of spinal surgery based on pain relief and functional improvement. It categorizes post-surgical outcomes into four levels: "Excellent" means no pain, no restriction of mobility; "Good" indicates occasional non-radicular pain, relief of presenting symptoms; "Fair" signifies some improved functional capacity, still handicapped and/or unemployed; and "Poor" intends continued objective symptoms of root involvement. Based on the data, there were inferences about the technique's clinical advantages and possible disadvantages.

Surgical Technique

All patients were operated on under endotracheal general anesthesia. After general anesthesia, the patients were positioned together with the anesthesia team. The head of the patients who were turned to the prone position was placed in the gelatin headrest, mainly in the neutral midline or rarely on the side, and it was ensured that the eyes were not under pressure in the gelatin headrest. The abdomen and chest were not under pressure in the lumbar frame. In female patients, whether the breasts were free in the frame was checked to prevent necrosis in the breasts.

Subsequently, a vertical, linear mini skin incision was made to the targeted distance after necessary field cleaning, covering, and distance determination with a scope. 2/3 of the incision was made on the upper part of the distance and 1/3 on the lower part (Fig. 1). The aponeurosis was incised with a scalpel, and the paravertebral muscle was unilaterally dissected from the spinous process to the facet joint by using blunt mini spoons and dry sponges. A cone-shaped approach was made from the skin to the base, and a much smaller

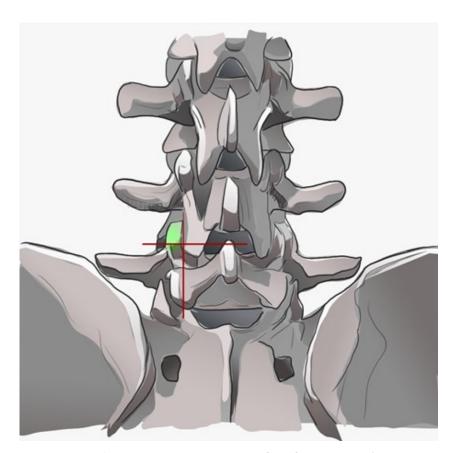


Fig. 2. Superolateral quadrantectomy (The upper outer quadrant of the facet marked in green was removed as described in the technique).

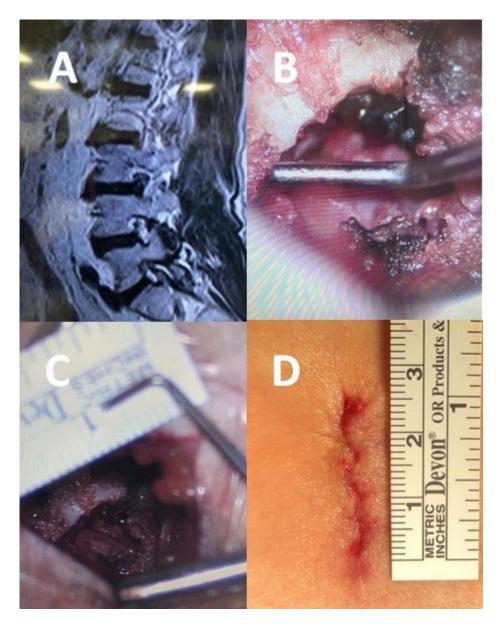


Fig. 3. (A) Lumbar MRI sagittal section, L3-4 right extraforaminal disc herniation, preoperative image. (B and C) Superolateral quadrantectomy of the facet joint. (D) Approximately 2.5 cm long skin incision.

skin incision was made to create sufficient visualization at the base (Fig. 1). After palpation of the facet joint, the microscope was brought to the surgical field with a repeat scope control to verify the distance. All cases were operated under xenon light using a HOX Leica M530 OHX microscope. In the superolateral quadrant of the facet joint, the joint capsule was incised with a number 11 scalpel and scraped upwards with a dissector. The facet capsule was not coagulated in any case. Cautery was not used at any stage of the operation. Then, the superolateral quadrant of the facet

joint was removed with the help of thin Kerrison rongeurs (Figs. 2 and 3). (It is essential not to coagulate the facet capsule before this stage and not disrupt the facet joint's nutrition, ³/₄ of which will be preserved). The lower ligamentum flavum was lifted with the help of a hook and removed with the help of Kerrison rongeurs. The free fragment was found and removed following the upper root to the exit point. Microdiscectomy was performed laterally to the distance in necessary cases.

In many cases, the root may appear completely

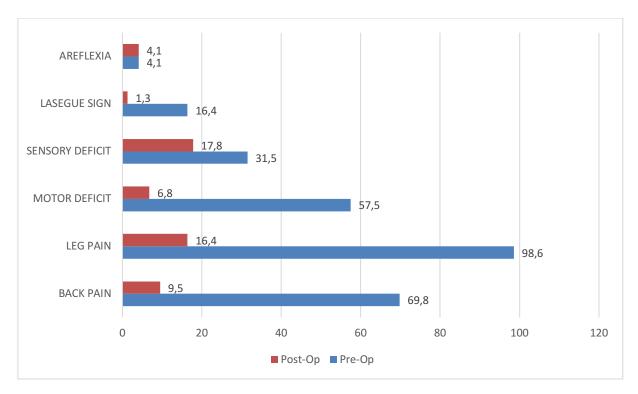


Fig. 4. Results of the McNemar test of motor deficit, sensory deficit, back pain, leg pain, Lasegue's sign, and areflexia comparing the preoperative to postoperative situation. The blue bars represent the preoperative situation and the red bars the postoperative situation. Numerical values indicate the percentage of patients in the study cohort.

flattened secondary to compression, giving the capsule the impression of a disc fragment. Therefore, clear visualization of the root by following the root up to the level of exit from the tectal sac may prevent possible root damage. After removing the disc fragment, the axilla and base of the root were checked with the help of a hook to check whether there were other fragments and whether the root was decompressed entirely. After bleeding control and washing, the folds were closed according to the anatomy.

Statistical Analysis

SPSS 15.0 for Windows statistical package program was used for statistical analyses. Continuous variables are presented as mean±standard deviation or median, categorical variables are presented as numbers and percentages. The conformity of the data to normal distribution and homogeneity of variances were examined using Levene test and Kolmogorov-Smirnov test. Motor deficit, sensory deficit, back pain, leg pain, Lasegue sign and areflexia were compared with the preoperative and postoperative status using the McNemar test. The results are shown graphically. Test results will be considered significant if P<0.05.

RESULTS

There were 40 (55.6%) females and 32 (44.4%) males. The age range was 38-72 years (mean: 50.43 ± 13.54 years) in women and 38-64 years (mean: 53.34±9.71 years) in men. Body mass index was 21-39 kg/m2 (mean: 26.98±2.94 kg/m2). The intervened distances were 41 (56.94%) L4-5, 16 (22.22%) L5-S1, 11 (15.28%), L3-4, and 4 (5.56%), L2-3 distances. In 41 (56.94%) cases, discopathy was observed on the left and 31 (43.06%) on the right. Incision length was 2.5-5.1 cm (mean: 3.6±1.47 cm). Preoperative symptom duration was 2-30 days (mean: 11.75±5.76 days); 13 patients had only motor deficits, 29 patients had both motor and sensorial deficits, and three patients had both motor and sensorial deficits and unilateral areflexia (Fig. 4). In 12 cases, the Lasegue test was positive unilaterally. The follow-up period was 12-24 months (mean: 14.20±4.67 months) (Table 1). Preoperative Visual Analog Scale (VAS) scores were 4-10 (mean: 8.5±2.17). Postoperative VAS scores were 0-1 (mean: 0.3±0.1). According to the Macnab classification, 37 (51.39%) of the patients were evaluated as excellent, 27 (37.50%) as good, and 8 (11.11%) as fair

Table 1. Patient characteristics

| | Data |
|---------------------------------------|------------------|
| Gender (male/female) | 32/40 |
| Age (years) | 51.72 ± 9.02 |
| BMI (kg/m^2) | 26.98 ± 2.94 |
| Level | |
| L2-L3 | 4 |
| L3-L4 | 11 |
| L4-L5 | 41 |
| L5-S1 | 16 |
| Preoperative Symptoms | |
| Back pain | 51 |
| Leg pain | 72 |
| Presence of motor deficit | 42 |
| Presence of sensory deficit | 23 |
| Lasegue sign | 12 |
| Areflexia | 3 |
| Postoperative neuropathic pain | |
| Presence | 8 |
| Absence | 64 |
| Incision length (cm) | 3.66 ± 1.47 |
| Pre-Op Symptom Duration (days) | 11.75±5.76 |
| Follow-up period (months) | 14.20±4.67 |

Data are shown as mean±standard deviation or number (n).

in the third postoperative month. Postoperative followup dynamic radiographs showed no instability in patients at the end of the 1st year. There were no perioperative complications in any of the cases. However, neuropathic pain was observed in the early postoperative period in 8 cases. Of the eight patients with neuropathic pain, 6 of them were relieved at the end of the 1st year with medical treatment.

In 63 cases, the root was pushed upward and laterally secondary to the compressing disc fragment from the axilla under the peduncle, whereas in 9 cases, a free fragment was seen that entered under the root instead of the axilla, extended laterally, and pushed the root medially and to the ceiling. Microdiscectomy was not performed in 23 cases, in which only sequestered fragments were observed. In 35 cases, microdiscectomy was performed laterally after removal of the free fragment.

In 24 cases with preforaminal bulging or hernia-

tion, paramedian microdiscectomy was performed by performing a classic medial opening in the same field after the lateral approach, lifting and preserving the medial ligamentum flavum after laminotomy.

DISCUSSION

In most lumbar disc herniations, the disc herniation protrudes mediolaterally into the spinal canal. However, the situation is different in extraforaminal lumbar disc herniations. Disc prolapse and nerve compression are at the exit of the intervertebral foramen and lateral to it. Since the compression is towards the cranial end, the axilla of the upper root, the clinical symptoms are caused by the compression of the upper root [5].

Lateral and medial procedures have been described in the surgical treatment of extraforaminal lumbar disc herniation [5, 6, 8, 9, 11]. When medial procedures are analyzed, interlaminar midline interventions are generally described, including laminectomy, laminotomy, hemilaminectomy, and subtotal or total facetectomy. However, case reports of spinal instability after total facetectomy are not few [5]. In the lateral paraspinal approach, reaching the extraforaminal and foraminal regions is possible without bone resection. Studies comparing lateral and medial approaches have reported that lateral interventions give far better results [9, 11]. However, the lateral approach must be revised at anatomically more challenging levels, such as the L5-S1 level [8].

The technique described by Dereymaeker *et al.* [6] is a medial approach with superolateral quadrantectomy to the facet joint and is much more advantageous than the other techniques described. It is a familiar method using anatomical landmarks in classical central or paracentral disc herniations. With this technique, the L5-S1 level can be easily reached, as in all other lumbar levels, and there is no need for extensive removal of the area, iliolumbar ligament, or peduncle [6].

Considering that extraforaminal disc herniation and foraminal, subarticular, paracentral, and central disc compression are also observed in some of these cases, it would be much more advantageous to use a technique that allows both lateral and medial approaches from the same access point instead of the lateral approach in cases involving additional compartments.

However, this technique's disadvantages are that the incision is much longer and the facet capsule is coagulated. The technique we have described is advantageous because it protects the facet joint capsule and reduces the skin incision by approximately half.

It is essential to preserve the anatomical structure as much as possible with a minimally invasive approach in any surgical intervention. From this point of view, it is essential to disrupt the skin integrity minimally and to protect the paraspinal muscles and facet joints as much as possible. Minimal disruption of skin integrity is essential regarding aesthetic appearance, patient psychology, postoperative pain secondary to the incision, and significantly minimizing the risk of infection. In contrast, protecting the underlying paraspinal muscles, facet joints, and the capsule that provides nutrition minimizes the risk of instability. In the study of Dereymaeker et al. [6], the rate of postoperative low back pain was reported as 13%, but this was reported as the value in week six. In our study, this rate was 9.7% in the postoperative third month. Our study's lower postoperative low back pain rate than in the original study may be because the facet joint capsule was not coagulated, and the incision was much shorter.

None of the patients operated on with this technique developed wound infection and instability. This may be because the facet joint is protected as much as possible, and the incision is much shorter. According to Macnab's classification, the rate of patients classified as "excellent" and "good" is 88.9%. In addition, the rate of patients with motor deficits recovered completely is around 88% (37 patients).

Limitations

Our study has some limitations. First, our study is a retrospective study with relatively few cases. The mean follow-up time of these cases was limited to approximately 14 months. This did not allow us to perform a long-term analysis. The lack of a comparative group of cases using traditional techniques also limits the ability to demonstrate the technique's advantages. However, our study is important in making a successful technique applied in extraforaminal lumbar discopathies even more advantageous. Prospective long-term studies planned compared to more extensive series may provide more transparent results. This study may be a source of inspiration for future studies.

CONCLUSION

In conclusion, the modified technique we have described offers the potential advantages of preserving the facet joint capsule and reducing the incision size.

Ethical Statement

This study was approved by the University of Health Sciences, Bursa Yüksek Ihtisas Training and Research Hospital, Medical Sciences Ethics Committee (Decision no. 2024-TBEK 2024/04-09, date: 17.04.2024).

Authors' Contribution

Study Conception: TK; Study Design: TK; Supervision: AK; Funding: TK; Materials: AK; Data Collection and/or Processing: TK; Statistical Analysis and/or Data Interpretation: TK; Literature Review: MB; Manuscript Preparation: TK and Critical Review: SB.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during the conduction or writing of this study.

Editor's note

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Public Health

The effect of swallowing disorder on quality of life in patients with Parkinson's disease

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ABSTRACT

Objectives: The aim of this study is to evaluate the severity of dysphagia in Idiopathic Parkinson's Disease (IPD) using both self-assessment and clinical assessment tools, to investigate the correlation between these methods, and to examine the effect of dysphagia on quality of life.

Methods: Patients diagnosed with IPD who applied to the Movement Disorders Clinic of the Neurology Department of Istanbul University Faculty of Medicine between 2020-2021 were included in the study. Dysphagia severity was assessed using the Eating Assessment Tool (EAT-10), Dysphagia Disability Index (DHI), and Gugging Swallowing Screening (GUSS). The effect of dysphagia on quality of life was assessed using the Turkish Swallowing Quality of Life Questionnaire (T-SWAL-QOL).

Results: A total of 38 patients, 24 (63.2%) of whom were male, were included in the study. There was a moderate correlation between GUSS and EAT-10 scores (r: -0.548; P<0.01). All areas of the quality of life questionnaire were negatively affected, with the most prominent problems being fatigue, sleep, and communication problems. The questionnaire scores showed a moderate correlation with EAT-10 scores (r: -0.583; P<0.01), a high correlation with DHI scores (r: -0.751; P<0.01)

Conclusions: This study demonstrates that dysphagia in IPD negatively impacts quality of life in several ways. The similar results obtained from self-assessment scales and clinical measures suggest that the clinician may include the results of self-assessment scales when screening for swallowing disorders.

Keywords: Dysphagia, swallowing disorder, Parkinson's disease, quality of life

diopathic Parkinson's disease (IPD) is a progressive neurodegenerative disease characterized by motor symptoms such as resting tremor, rigidity, bradykinesia, and postural instability, as well as nonmotor symptoms [1]. Dysphagia is a common symp-

tom in patients with IPD, and its prevalence varies between 11% and 82% depending on the stage, duration, and assessment method [2, 3]. It can limit or prevent safe oral feeding, reduce the patient's full capacity in society, and cause social, psychological, and economic

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problems for the individual [4]. Aspiration pneumonia, especially due to swallowing disorders, has been reported to be one of the leading causes of death in IPD [5]. Since it is not directly related to the stage of the disease and the perception of dysphagia usually develops much later, the presence of dysphagia should be investigated from the very early stages [2]. Health-related quality of life has been defined as "the patient's own perception and self-assessment of the effects of a disease and its consequences on his or her life" [6]. Quality of life is an important factor to be considered in the management of chronic, progressive and complex diseases such as IPD and is affected by a wide range of clinical features including both motor and non-motor symptoms in IPD (5). There are studies in the literature showing that swallowing disorders in IPD negatively affect quality of life; however, these studies evaluated swallowing disorders with screening scales and did not use clinical measurement tools applied by clinicians [7-10]. Although there are various studies in our country that include voice and swallowing evaluations in IPD, studies examining swallowing-related quality of life are limited [11, 12]. Dysphagia can be reported subjectively by patients or their caregivers, as well as objectively with instrumental tools. Since dysphagia is frequently seen in Parkinson's disease, it is important to determine whether the patient is at risk for dysphagia in order to determine whether instrumental evaluation is needed. In the literature, it is a matter of debate whether self-assessment scales provide accurate results in terms of detecting swallowing disorders in Parkinson's patients. For these reasons, in our study, swallowing severity in IPD was screened with clinical measurement tools as well as self-assessment scales and the effects of both methods on quality of life were investigated by looking at their relationships with each other. The aim of this study was to determine the reliability of using selfassessment methods and scales used by clinicians in screening swallowing disorders in Parkinson's patients as a practical screening for clinicians in the evaluation by examining the relationship between each other.

METHODS

Participants

This descriptive study included 38 consecutive pa-

tients who applied to the Movement Disorders Polyclinic of the Neurology Department of Istanbul University, Istanbul Faculty of Medicine between 2020-2021 and were diagnosed with Idiopathic Parkinson's disease according to the UK Brain Bank criteria [13]. In the study, all evaluations were performed with all patients during the "on" period of the drug cycle. The research plan was scientifically and ethically approved by the Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki (Date: 26.10.2021, Number: 1060). All subjects included in the study were informed about the purpose, duration, and evaluations to be performed. All subjects were included in the study after the "Informed Voluntary Consent Form" approved by the Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee was approved. The number of participants included in the study was limited to 38 people due to the ongoing Covid-19 pandemic and the decrease in the number of patients applying to the outpatient clinic.

Inclusion Criteria

Our study planned to include patients who did not have a diagnosis of dementia, did not have any additional neurological diseases (Stroke, ALS, Multiple Sclerosis, etc.), did not have other disorders that could affect swallowing function (e.g. head and neck cancer), had at least five years of education, and were diagnosed with Idiopathic Parkinson's Disease according to the UK Brain Bank criteria [13].

Demographic Data of the Sucjects

The name, surname, gender, age, educational status, and duration of illness of the patients who voluntarily participated in the study were questioned.

Data Collection

In order to clinically evaluate the severity of swallowing disorder, Gugging Swallowing Screening Test (GUSS), Dysphagia Handicap Index (DHI) and Eating Assessment Tool (EAT-10) scales were administered when the patients were alert in terms of motor findings. Dysphagia Handicap Index and EAT-10 scales measure the severity of swallowing disorder by the individual's answers to the questions in the scale. The Gugging Swallowing Screening Test scale involves a

speech and language therapist trained in swallowing to clinically evaluate the individual's swallowing with various consistencies. In addition to these scales, the T-SWAL-QOL, designed to assess swallowing-related quality of life, was administered to determine the effect of swallowing disorder and symptoms related to swallowing disorder on quality of life. The scales were administered in the examination room and took an average of 20 minutes for each participant. The researcher read the questionnaire items and answer options aloud to each patient to guarantee correct answers and reduce the possibility of misinterpretation due to low levels of education or visual impairments. The aim of this methodology was to increase the comprehensibility of the questionnaire and minimize the possibility of deceptive answers. By administering the questionnaires in the same way to each participant, consistency was maintained and any bias in the data collection process was avoided.

Scales Used

Eating Assessment Tool (EAT-10)

It measures the severity of swallowing disorder, quality of life and treatment effectiveness. The scale consists of 10 questions and the questions are scored between 0 and 4 (0=no problem, 4=severe problem). A total score of 3 or above indicates a risk for swallowing disorder. A higher total score indicates a higher severity of swallowing disorder. Turkish validity and reliability of the study was performed [14].

Dysphagia Handicap Index (DHI)

It is an assessment questionnaire consisting of 25 questions developed to evaluate the effects of swallowing disorder on the person's life and the severity of swallowing. The questions are divided into three groups. The aim of the groups is to evaluate the patient's swallowing quality from physical, emotional and functional perspectives. Turkish validity and reliability was performed by Çiyiltepe *et al.* [15]. Each question has three answers: "never", "occasionally" and "always". During scoring, "never" is scored as 0, "sometimes" as 2 and "always" as 4. As a result of the questionnaire, a score between 0-100 is obtained [15]. A higher total score indicates a higher severity of swallowing disorder.

Gugging Swallow Screening Test (GUSS)

It is one of the bedside swallowing screening tests with proven reliability and is used in clinical practice. A Turkish adaptation study of GUSS was also conducted by Umay et al. [16] in 2018. Like many bedside swallowing tests, it starts with fluid and the screening process is terminated early when aspiration is suspected. The GUSS consists of 2 stages, indirect assessment and direct assessment, and is a 20-point test in total. The first part consists of the ability to maintain wakefulness for 15 minutes, to cough and/or clear the throat voluntarily at least twice, and to swallow saliva successfully without change in voice or drooling. Patients who pass this first part of the GUSS with 5 full points pass to the second stage, which is a 15-point direct swallowing test to be evaluated with semi-solid, liquid and solid foods, respectively. Patients who score less than 20 full points as a result of the test are referred to instrumental swallowing evaluation for further clinical evaluation [17].

Turkish Swallowing Quality of Life Questionnaire (T-SWAL-QOL)

The T-SWAL-QOL was used to assess patients' swallowing-related quality of life. The T-SWAL-QOL assesses the impact of swallowing disorder on quality of life from the patient's perspective. It consists of 44 questions assessing different dimensions of quality of life. The questions are scored between 1 and 5 (1=completely true, 5=not true at all). A higher score indicates a higher quality of life. The questionnaire has 11 headings including general complaints, desire to eat, time of eating, social, food choice, fear of eating, sleep, fatigue, communication, mental health, and symptom frequency. Turkish validity and reliability study was conducted [18].

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) Version 26.0 (IBM SPSS Inc., Chicago, IL, USA). The "Shapiro Wilk Test" was used to determine whether the data conformed to normal distribution. Parametric tests were used to analyze the data conforming to normal distribution and nonparametric tests were used to analyze the data not conforming to normal distribution. In the statistical analysis of the study, continuous variables were defined as mean (Mean), standard deviation (SD), median, minimum and maximum values and categorical

Table 1. Demographic and clinical characteristics of patients (n=38)

| Characteristics | Data |
|--------------------------------|-------------|
| Age (years) | 64.61±12.6 |
| Sexuality, man, n (%) | 24 (63.2%) |
| Disease duration (year), n (%) | 8.38±5.38 |
| 1 year | 1 (2.63%) |
| <5 year | 7 (18.41%) |
| 5-10 year | 19 (49.97%) |
| <10 year | 23 (60.49%) |
| 10-30 year | 14 (36.82%) |
| >30 year | 1 (2.63%) |
| Education status, n (%) | |
| Primary education | 20 (52.6%) |
| Middle school | 3 (7.8%) |
| High school | 8 (21.1%) |
| University | 7 (18.4%) |
| EAT-10 | 4.05±7.6 |
| DHI | 11.89±17.7 |
| GUSS | 19.76±0.7 |
| T-SWAL-QOL | 82.14±16.4 |

Data are shown as mean±standard deviation or n (%). EAT-10=Eating Assessment Tool-10, DHI=Dysphagia Handicap Index, GUSS=Gugging Swallowing Screen, T-SWAL-QOL=Turkish Swallowing Quality of Life Questionnaire, SD=Standard Deviation

variables were defined as number (n) and percentage (%). The correlation analysis of the non-normally distributed data was performed using Spearman Correlation Analysis. The direction of the relationship level was determined according to whether the Spearman correlation coefficient "r" value was positive or negative, while the strength was determined according to the magnitude of the "r" value. All statistical analyses were performed at 95% confidence interval and significance was evaluated at P<0.05 level.

RESULTS

The study included 38 participants. Of the participants, 24 (63.2%) were male and 14 (36.8%) were female. The mean age of the participants was 64.61±12.6 years and the mean duration of illness was 8.38±5.38 years. The duration of the disease was less than 10 years for 60.52% of the participants, between 10-30 years for 36.84% and more than 30 years for 2.63%. The mean scores of the participants from the scales

Table 2. Results of the relationship between GUSS total score and EAT-10 and DHI total scores

| | | EAT-10 total score | DHI total score |
|------------------|---------|--------------------|-----------------|
| GUSS total score | r | 548 | 490 |
| | P value | 0.0004** | 0.002** |
| | n | 38 | 38 |

EAT-10=Eating Assessment Tool-10, GUSS=Gugging Swallowing Screen, DHI=Dysphagia Handicap Index **P<0.01 were considered significant

Eur Res J. 2025;11(4):697-704 Bingöl et al

Table 3. Results of the relationship between T-SWAL-QOL total scores and EAT-10, DHI and GUSS total scores.

| | | EAT-10 total score | DHI total score | GUSS total score |
|------------------------|---------|--------------------|-----------------|------------------|
| T-SWAL-QOL total score | r | 583 | 751 | 0.393 |
| | P value | 0.0001** | 0.0001** | 0.015* |
| | n | 38 | 38 | 38 |

EAT-10=Eating Assessment Tool-10, DHI=Dysphagia Handicap Index, GUSS=Gugging Swallowing Screen, T-SWAL-QOL=Turkish Swallowing Quality of Life Questionnaire

used were EAT-10: 4.05±7.6, DHI: 11.89±17.7, GUSS: 19.8±0.7, and T-SWAL-QOL: 82.14±16.4, respectively. Demographic and clinical characteristics of the patients are presented in Table 1.

The results of the correlation between the screening test in which the clinician evaluates the patient's swallowing and the scales in which the patient evaluates his/her own swallowing are shown in Table 2.

There was a statistically significant, negative, moderate, statistically significant, negative, moderate correlation between the GUSS total scores and EAT-10 scores (r:-0.548; P=0.0004) and a statistically significant, negative, low correlation between the DHI scores (r:-0.490; P=0.002) (Table 2.). All three methods indicating the severity of swallowing disorder are correlated with each other.

The results of Parkinson's disease patients' swal-

lowing disorder scores obtained by clinical evaluation and scales and swallowing-related quality of life scores are presented in Table 3.

There was a statistically significant, negative, medium level (r:-0.583; P=0.0001), statistically significant, negative, high level (r:-0.751; P:0.0001) and statistically significant, positive, low level (r:0.393; P=0.015) correlation between T-SWAL-QOL total scores and EAT-10 score, DHI score and GUSS score (Table 3.). As a result, it was observed that quality of life deteriorated more as the severity of swallowing disorder increased.

The sub-fields of the quality of life questionnaire were examined to determine how the quality of life of Parkinson's patients was affected by the swallowing disorder they experienced, and it was observed that all areas were negatively affected, the most in the areas

Table 4. T-SWAL-QOL subscores and total scores (n=38).

| | Median | Min-Max | Mean±SD |
|--------------------|--------|---------------|------------------|
| Fatigue | 58.30 | 0-100 | 56.77±31.6 |
| Sleep | 68.75 | 0-100 | 61.51±39.6 |
| Communication | 75 | 0-100 | 70.39 ± 34.4 |
| Eating time | 100 | 12.5-100 | 82.57±28.1 |
| Symptom frequency | 92.31 | 34.62-100 | 86.34 ± 14.8 |
| Fear of eating | 100 | 25-100 | 86.68±25 |
| Desire to Eat | 100 | 25-100 88.58± | |
| Mental health | 100 | 0-100 91.28± | |
| Food choices | 100 | 50-100 | 92.11±17.3 |
| General complaints | 100 | 0-100 | 92.43±23.5 |
| Social life | 100 | 25-100 | 94.87 ± 18 |
| T-SWAL-QOL total | 86.25 | 3.6-100 | 82.14±16.4 |

T-SWAL-QOL=Turkish Swallowing Quality of Life Questionnaire, Min=minimum, Max=maximum, SD=standard deviation

^{*}P<0.05, **P<0.01 were considered significant.

of fatigue, sleep and communication, and the least in the areas of social and food selection (Table 4).

DISCUSSION

Motor and non-motor findings are observed in patients with Idiopathic Parkinson's disease and may negatively affect the quality of life [6]. Dysphagia, which is frequently observed in the course of the disease, also has a negative effect on quality of life and may lead to social and psychological problems for the individual [4].

Various studies in the literature have examined the effect of swallowing disorder on quality of life in individuals with swallowing disorder and found that swallowing-related quality of life decreased with increasing severity of swallowing disorder [19-21]. This study examines the effect of severity of swallowing disorder on swallowing-related quality of life in patients with idiopathic Parkinson's disease. As a result of our study, a statistically significant, negative correlation was found between EAT-10 total scores and DHI total scores and T-SWAL-QOL total scores of patients with idiopathic Parkinson's disease in accordance with the literature. The presence of a statistically significant, negative correlation between these two values indicates that patients with less severity of swallowing disorder have a higher quality of life, and as the severity of swallowing disorder increases, the quality of life is negatively affected.

Similar studies in the literature have evaluated the swallowing-related quality of life of patients with idiopathic Parkinson's disease using scales in which the patients evaluated their swallowing disorder themselves [7-10]. However, studies in which the swallowing disorder of Parkinson's patients was also evaluated by a clinician are limited. Therefore, the GUSS scale, which allows the clinician to evaluate the severity of the patient's swallowing disorder, was included in this study. At the end of the study, a statistically significant negative correlation was found between the GUSS scale and the EAT-10 and DHI scales, and a statistically significant positive correlation was found between the GUSS scale and the T-SWAL-QOL scale. The relationship between the GUSS scale and other scales shows that scales in which the therapist evaluated the patient's swallowing yield similar results and scales in which the patient evaluated his/her own swallowing. In this study, similar to other studies examining the relationship between the GUSS scale and swallowing evaluation scales, significant results were obtained, consistent with the literature [22]. This result shows that including scales in which the patient evaluated himself/herself in the evaluation may be consistent with the clinician's evaluation. It is important for clinicians to have scales that they can use in the clinic to determine whether a patient is at risk for swallowing disorders so that they can evaluate the patient correctly.

Although similar studies are very limited in the literature, Bengisu et al. used the EAT-10 scale, which includes self-assessment of swallowing disorders, and the Videofluoroscopic Swallowing Study (VFSS), which is an instrumental swallowing assessment method, but observed inconsistency between the results of the two methods [23]. In our study, scales including the clinician's assessment and scales including the patient's self-assessment gave consistent results. This may Dysphagia may accompany IPD in varying degrees of severity from the early stages of its course. This study shows that screening for swallowing disorders using self-assessment scales or clinical measurement tools yields correlated results and negatively affects quality of life in many ways in proportion to its severity. This suggests that the use of self-assessment scales may also be useful in situations where rapid assessment is required, such as in outpatient clinic settings. However, using this assessment together with a subjective or objective assessment by the clinician will increase the reliability of the result.

A study comparing the results of the self-assessment scales used in this study with the results of an instrumental assessment method may provide more reliable information to the literature about the reliability of self-assessment scales.

Ethical Statement

This study was approved by the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (Date: 26.10.2021, Decision No: 1060) and informed written consent was obtained from all participants.

Authors' Contribution

Study Conception: ST, SB, DB; Study Design: ST, SB, DB; Supervision: ST, SB, ZT; Funding: ZT, ENB, HAH; Materials: ZT, ENB, HAH; Data Collection

and/or Processing: DB, END; Statistical Analysis and/or Data Interpretation: ZT, HAH; Literature Review: ST, SB, DB; Manuscript Preparation: ST, SB, DB and Critical Review: ST, SB, DB.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Psychiatry

The correlation between anxiety and depression levels with bulimic symptomatology and body mass index during COVID-19 quarantine measures: A 2-month follow-up study

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ABSTRACT

Objectives: This study aims to investigate the relationship between anxiety and depression levels with bulimia symptoms and body mass index (BMI) during the quarantine measures.

Methods: Voluntary individuals were included, and individuals were evaluated before and after 2-month quarantine period, and self-report questionnaires were administered. In addition to the sociodemographic data form, Hospital Anxiety and Depression Scale (HADS) and Bulimic Investigatory Test, Edinburgh (BITE) were applied twice to the participants and their BMI were recorded.

Results: An increase in HADS-A scores was observed after quarantine (z=-6.456, P<0.001). Upon comparing the scale scores, and BMI values recorded at the onset of the quarantine period and two months later, a negative correlation was observed between the BITE-2 (after 2-month follow-up) score and both the BMI-2 value and the HADS-A1 (baseline measurement) score, with correlation coefficients of r =-0.493, P<0.001, and r =-0.267, P=0.041, respectively. Additionally, BMI-1 values were positively correlated with HADS-D1 (r=0.186, P=0.028) and negatively correlated with BITE-1 score (r=-0.323, P<0.001).

Conclusions: The finding of higher BMI in individuals with high depressive symptom severity, the negative correlation of bulimic symptoms with BMI, and higher anxiety levels after quarantine period reveal the impact of mental health on eating behavior and effect of pandemic on psychiatric symptoms. Our study can provide a unique perspective on eating behaviors and psychiatric symptomatology due to quarantine measures.

Keywords: Eating disorder, anxiety, depression, COVID-19, bulimia nervosa

he novel human coronavirus disease has been defined as a life-threatening global pandemic, starting in late 2019 and known to affect millions of individuals worldwide [1]. Originating from China, COVID-19 quickly spread to Asia, Eu-

rope, and America, becoming a prevalent issue globally [1]. As scientists have endeavored to tackle the COVID-19 outbreak, they have also attempted to address its various dimensions, discovering that this global epidemic has led to significant changes in

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human life. Among these changes are the quarantine process and secondary psychiatric problems resulting from the quarantine measures [2]. It has been supported by numerous studies that the pandemic and quarantine measures lead to no change in some individuals, while causing anxiety, depressive symptoms, and sleep problems in others [3-5]. Although it is generally accepted that quarantine and the pandemic process act as predisposing factors for psychiatric conditions, the impact on eating attitudes remains unclear due to the cross-sectional nature of clinical studies and conflicting findings [6].

Eating behaviors can be characterized as the choices individuals make regarding their food consumption, influenced by trends, personal preferences, specific diets, and calorie monitoring [7]. Clinical research to date supports that individuals' eating behaviors are influenced by sociocultural factors, economic factors, nutritional awareness, physiological needs, general health status, and psychological factors [7]. Psychological factors such as stress, emotional states, depression, etc., are among the primary influences on eating behaviors. For instance, while some people may eat more under stress, others might lose their appetite [8]. In some cases, exposure to environmental and psychological stressors can lead to the diagnosis of eating disorders [8]. Eating disorders are known as psychopathologies involving abnormal behaviors and thoughts regarding food intake, which can impair an individual's physical health, emotional well-being, and social functioning [9]. The most common disorders among eating disorders include anorexia nervosa, characterized by excessive weight loss and low body weight aimed at controlling and limiting body weight; bulimia nervosa, characterized by compensatory behaviors after bouts of uncontrolled eating; binge eating disorder, involving individuals regularly consuming excessive amounts of food and experiencing a loss of control over this issue; and avoidant/restrictive food intake disorder, characterized by a limitation/excessive selectivity in food intake [9].

The social isolation caused by COVID-19 pandemic, changes in daily routines, decreased appetite due to loss of taste and smell, and emotional eating behaviors due to stress appear to be the main reasons underlying the pandemic's triggering effect on eating disorders [10]. However, the lack of clinical research and inconsistent evidence on this subject makes it

challenging for mental health professionals to provide clear evidence. This research aims to reveal the effect of COVID-19 quarantine measures on psychiatric symptoms and eating behaviors.

METHODS

Study Design and Sample Selection

This research was designed as a prospective clinical study, including a sample of 140 volunteers aged between 18-65 from Sakarya/Türkiye. Volunteers who were literate, without an active mental/cognitive illness diagnosis, and consented to participate were included in the study. Under COVID-19 measures, local quarantine protocols were enacted, and volunteers were evaluated twice: at the start and at the end of the 2-month quarantine period. During the initial assessment, volunteers' comorbid diseases, medical history, body mass indexes (BMI), and sociodemographic data were recorded. Scores from the Hospital Anxiety and Depression Scale (HADS) and the Bulimic Investigatory Test Edinburgh (BITE) were documented at both the beginning and 2 months following the start of the local quarantine.

Ethics committee approval was received from Sakarya University Faculty of Medicine non-invasive research ethics committee with date and decision number 2020/316. The study was conducted in compliance with the Declaration of Helsinki.

Sociodemographic Data Form

The gender, age, marital status, place of residence, educational status, monthly income, active employment status, and occupation of the volunteers included in the study were recorded with the sociodemographic data form and the data of the participants were obtained.

Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) comprises two subscales: Anxiety (HADS-A) and Depression (HADS-D), each with seven items scored from 0-3 based on the individual's feelings over the past week. Cut-off scores categorize cases as mild (8-10), moderate (11-15), or severe (16+). The Turkish form's validity and reliability were first assessed by Ömer Aydemir *et al.* in 1997 [11].

Bulimic Investigatory Test, Edinburgh (BITE)

The Bulimic Investigatory Test, Edinburgh (BITE) is a diagnostic tool conducted by Kiran SG. *et al*. [12] in 2000, the Turkish validity and reliability study of the BITE scale measures eating habits and concerns related to eating, shape, and weight. The symptom subscale scores are categorized into low (0-9), medium (10-20), and high (20-30) levels of symptomatology.

Statistical Analysis

The obtained results were analyzed using the IBM SPSS (Statistical Package for the Social Sciences) Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY), utilizing descriptive statistics, the Kolmogorov-Smirnov test for normal distribution, Student's T-test, Wilcoxon test, Mann-Whitney U test, ANOVA, Kruskal-Wallis test, one-way analysis of variance, Levene's test, Tukey's HSD, and Spearman's correlation analysis. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 140 individuals aged between 18-65 participated in the research. 59.3% of the participants were female (n=83) and 40.7% were male. The ages of the participants ranged from a minimum of 18 to a maximum of 65 years, with a mean age of 29.84 ± 9.30 years. Detailed information on sociodemographic characteristics of participants is presented in Table 1. The body mass indexes (BMIs) of the participants were evaluated. The smallest BMI was 17.16, and the largest BMI was 39.06. The mean BMI of all participants was $23.64 \pm 3.91 \text{ kg/m2}$.

Psychiatric History of Participants

Ten (7.1%) participants reported that they had at least one psychiatric diagnosis during childhood and/or adolescence and received treatment for this reason. When the participants were asked whether they had been diagnosed with bulimia nervosa at any time,

Table 1. Sociodemographic characteristics of participants

| | n | % | | n | % |
|---------------------------|-----|------|----------------------|-----|------|
| Gender | | | Place of Residence | | |
| Female | 83 | 59.3 | Rural | 13 | 9.3 |
| Men | 57 | 40.7 | Urban | 127 | 90.7 |
| Marital status | | | Income Level | | |
| Married | 47 | 33.6 | TRY 0-2000 | 40 | 28.6 |
| Single | 91 | 65 | TRY 2001-5000 | 38 | 27.1 |
| Divorced | 2 | 1.4 | TRY 5001-10.000 | 54 | 38.6 |
| Education level | | | TRY 10.001 and above | 8 | 5.7 |
| Primary school | - | - | Occupation | | |
| Middle School | 1 | 0.7 | Student | 48 | 34.3 |
| High school | 14 | 10 | Public officer | 55 | 39.3 |
| University | 96 | 68.6 | Worker | 8 | 5.7 |
| Master's Degree and above | 29 | 20.7 | Shopkeeper | 5 | 3.6 |
| Comorbidity | | | Self-employed | 1 | 0.7 |
| Yes | 26 | 18.6 | Other | 23 | 16.4 |
| No | 114 | 81.4 | Working Status | | |
| | | | Regular employee | 79 | 56.4 |
| | | | Working irregularly | 10 | 7.1 |
| | | | Unemployed | 51 | 36.4 |
| Total | 140 | 100% | Total | 140 | 100% |

it was found that none of them had been diagnosed with bulimia nervosa. When asked whether they had been diagnosed with anorexia nervosa at any time, 0.7% (n=1) reported that they had been diagnosed with anorexia nervosa.

One (0.7%) participant reported that their family members had been diagnosed with anorexia nervosa or bulimia nervosa.

The rate of those who reported receiving any psychiatric diagnosis in adulthood was 19.3% (n=27), and the rate of those who reported receiving psychiatric treatment for any reason in adulthood was 17.9% (n=25).

Non-Psychiatric Comorbidities

Twenty-six (18.6%) participants reported that they had at least one chronic disease, while others reported that they did not have any chronic disease. Comorbid conditions are shown in Table 2.

When participants were asked whether they had a positive or suspected COVID infection detected by tests and/or imaging examinations, 5.7% (n=8) re-

ported having a positive or suspected COVID infection, while the remaining participants reported not having such a condition.

Comparison of Participants' Scale Scores at the Beginning of the Quarantine Period

The comparison of sociodemographic data, BITE-1, HADS-A-1 and HADS-D-1 scores and BMI-1 values are shown in Table 3. Based on the statistical data in Table 3, it was determined that the mean values of HADS-A-1 [U=1822,0; z=-2,329; P=0.020] and BMI-1 [U=1368,0; z=-4,231; P<0.001] showed significant differentiation according to the gender variable. Accordingly, the mean value of HADS-A1 was higher in female individuals (X=9.002; SD=2.42) than in male individuals (X=8.09; SD=2.03).

According to Table 4, when the participants were evaluated in terms of HADS-A-1, HADS-D-1 and BITE-1 scores, it was determined that there was a statistically significant correlation between the scale scores. BITE-1 score was negatively correlated with BMI-1, HADS-A-1, HADS-D-1 scores (P<0.001;

Table 2. Non-Psychiatric Comorbidities of Participants

| Comorbid Conditions | | Percentage of Responses |
|------------------------------|-----|-------------------------|
| | n | % |
| Allergy | 2 | 6.90% |
| Asthma | 5 | 17.20% |
| Chronic bronchitis | 2 | 6.90% |
| Diabetus mellitus | 3 | 10.30% |
| Familial Mediterranean fever | 2 | 6.90% |
| Hypothyroidism | 4 | 13.80% |
| HIV | 1 | 3.40% |
| Hepatitis B | 1 | 3.40% |
| Migraine | 1 | 3.40% |
| Meniere's disease | 1 | 3.40% |
| Peptic ulcer | 4 | 13.80% |
| Osteoarthritis | 1 | 3.40% |
| Irritable bowel syndrome: | 1 | 3.40% |
| Hypertension | 1 | 3.40% |
| Total | 29* | 100.00% |

HIV=Human immunodeficiency virus

^{*}Due to the presence of multiple comorbid conditions, n is calculated as 29 instead of 26

Eur Res J. 2025;11(4):705-713 Erdoğan Kaya *et al*

Table 3. Comparison of sociodemographic characteristics and HADS-A-1, HADS-D-1, BITE-1, and BMI-1 scores at the Initial Assessment

| | HADS-A-1 | HADS-D-1 | BITE-1 | BMI-1 |
|-----------------------------|---------------|---------------|---------------|----------|
| Gender | U=1822.0 | U=2241.0 | U=2320.0 | U=1368,0 |
| | z=-2.329 | z=531 | z=193 | z=-4.231 |
| | P=0.020 | P=0,595 | P=0.847 | P<0.001 |
| Marital status ^a | U=1873.5 | U=2153.5 | U=1598.5 | F=4.662 |
| | z=-1.391 | z=-1.142 | z=-2.595 | t=3.797 |
| | P=0.164 | P=0.887 | P=0.009 | P<0.001 |
| Psychiatric diagnosis | U=913.00 | U=1477.0 | U=1468.5 | F=.099 |
| | z=-3.268 | z=258 | z=302 | t=937 |
| | P=0.001 | P=0.797 | P=0.763 | P=0.350 |
| Weight status ^c | U=2049.5 | U=1586.0 | U=1437.0 | U=.000 |
| | z=164 | z=-2.270 | z=-2.935 | z=-9.421 |
| | P=0.869 | P=0.023 | P=0.003 | P<0.001 |
| Income level ^b | U=1809.0 | U=1832.0 | U=2226.0 | U=2184.5 |
| | z=-2.581 | z=-2.473 | z=807 | z=980 |
| | P=0.001 | P=0.013 | P=0.420 | P=0.327 |
| Comorbidity | U=1410,5 | U=1440.5 | U=1479.0 | U=1401,5 |
| | z=387 | z=224 | z=016 | z=431 |
| | P=0.699 | P=0.823 | P=0.987 | P=0.666 |
| Employment status | $x^2=12.561$ | $x^2 = 7.879$ | $x^2 = 5.298$ | F=.832 |
| | P=0.002 | P=0.019 | P=0.071 | P=0.437 |
| Education level | $x^2 = 3.810$ | $x^2=1.300$ | $x^2 = 0.666$ | F=2.899 |
| | P=0.149 | P=0.522 | P=0.717 | P=0.058 |

HADS=Hospital Anxiety and Depression Scale, HADS-A=Anxiety, HADS-D=Depression, BITE=Bulimic Investigatory Test, Edinburgh, BMI=Body Mass Index

Mann Whitney U, Kruskall Wallis, Student's T Test, ANOVA Tests were applied.

P=0.024 and P=0.007, respectively) and positively correlated with age (P=0.009). There was a statistically significant positive correlation between HADS-A-1 and HADS-D-1 scores (P<0.001).

Assessment of Participants Accessible Two Months Later

At the end of two months, 42.1% (n=59) of the participants could be reached. 66.1% (n=39) of the patients who could be reached were female and the others were male.

Since the p values of BITE, HADS-D and BMI were P<0.005 according to the Kolmogorov-Smirnov test, it was determined that they did not show a normal distribution and non-parametric tests were applied. No statistically significant difference was detected between the HADS-D, BITE scores and BMI values of the participants who could be reached two months later, before and after quarantine. (z=-1.011, P=0.312; z=-1.314, P=0.189; z=-.111, P=0.912, respectively). There was a statistically significant difference between the HADS-A scores of participants who could be

^aMarital status; Married single

^bIncome Level; TRY 5000 and below – TRY 5000 and above

^cWeight Status: Normal or Underweight - Recategorized as Overweight or Obese.

| | , , | , 0 | | | | |
|----------|--------|--------------|----------|----------|-------|-----|
| n=140 | | BITE-1 score | HADS-D-1 | HADS-A-1 | BMI-1 | Age |
| BITE-1 | r | 1 | | | | |
| | Pvalue | | | | | |
| HADS-D-1 | r | 226 | 1 | | | |
| | Pvalue | 0.007 | | | | |
| HADS-A-1 | r | 190 | .386 | 1 | | |
| | Pvalue | 0.024 | 0.001 | | | |
| BMI-1 | r | 323 | .186 | -0.075 | 1 | |
| | Pvalue | 0.001 | 0.028 | 0.378 | | |
| Age | r | .247 | -0.032 | 230 | .368 | 1 |
| | Pvalue | 0.003 | 0.708 | 0.006 | 0.001 | |

Table 4. HADS-A1, HADS-D1, BITE-1, age and BMI evaluation at the initial assessment

HADS=Hospital Anxiety and Depression Scale, HADS-A=Anxiety, HADS-D=Depression, BITE=Bulimic Investigatory Test, Edinburgh, BMI=Body Mass Index

Spearman Correlation Analysis was applied

reached two months later, before and after quarantine (z=-6.456, P<0.001). Accordingly, HADS-A scores increased significantly after quarantine.

HADS-A, HADS-D, BITE scale scores applied at the beginning and after the quarantine period and BMI values of the participants who could be reached after two months were compared, it was found that the BITE-2 score was negatively correlated with BMI-2 value and HADS-A1 score (r=-.493, P<0.001 and r=-.267, P=0.041, respectively).

In this sample, BMI-1 values were positively correlated with HADS-D1 (r=.186, P=0.028) and negatively correlated with BITE-1 score (r=-.323, P<0.001).

DISCUSSION

The COVID-19 pandemic is a global event that seriously affects public health and social life around the world [13]. It has been understood that this pandemic affects human health through many different mechanisms and triggers mental/physical pathologies [13]. In the post-pandemic period, the long-term effects of the virus are still being discussed. This study tried to draw attention to the effects of the quarantine period during the pandemic on the psychological health of individuals between the ages of 18-65 and some related eating behaviors. The study is noteworthy in that it

provides a comprehensive analysis by taking into account various factors such as sociodemographic characteristics, BMI, psychiatric background, comorbid conditions and traumatic experiences of the participants. The participants included in our study were distributed across a wide age range (18-65), genders (59.3% female, 40.7% male) and socioeconomic groups. The average age is 29.84 years and they generally live in urban areas. Socioeconomic profiles varied; working people, university graduates and individuals from different income levels were included in the study. Similarly, individuals' Body mass indexes have a wide distribution (average 23.64±3.91 kg/m2). When the psychiatric background of the participants was analyzed, the rate of psychiatric diagnosis in childhood was 7.1%. This rate was particularly low for bulimia nervosa and anorexia nervosa. Additionally, 28.6% of the participants experienced a traumatic event in their childhood. Participants' anxiety and depression levels were evaluated with HADS scores during the quarantine period. The findings showed that women, married individuals, those with low income groups and those who had previously received a psychiatric diagnosis had higher anxiety levels. In the evaluation made after the two-month quarantine period, the anxiety, depression and bulumic symptomatology scores of the participants were examined regarding their psychological states. A significant increase was detected in anxiety levels, but no significant change was detected in depression and bulimia scores.

The participant profile of the study is examined sociodemographically, it is seen that it was conducted on a population aged 29.84±9.30. It is important to evaluate this demographic structure in terms of responses to pandemic conditions and stress because this age range covers a period when both working life and family life continue actively. This is important in terms of the individual's coping mechanisms and the potential to be affected by the isolation experienced during the pandemic. Participants included in similar studies focusing on the relationship between the pandemic and eating disorders were found to consist mainly of young individuals [14, 15].

In terms of psychiatric background and comorbidity, it is noteworthy that the study participants had psychiatric diagnosis and treatment both in childhood and adolescence and in adulthood. These findings suggest that during the pandemic, psychologically more vulnerable groups may be more affected. Gender differences have also been an important parameter in terms of psychological effects during the pandemic period. The fact that HADS-A scores in female participants were significantly higher than in males may indicate that women may be more affected by the pandemic. This differentiation may be attributed to the additional stress that women often face due to societal role expectations and the responsibility of managing multiple tasks within the household. Also, the finding of a significant difference in BMI values by gender indicates that there are differences between genders in healthy nutrition and body weight management during the pandemic. A similar study has found that women were at a higher risk for eating disorders and vulnerable for psychiatric symptoms during the pandemic period [16].

Findings regarding marital status and place of residence indicate that higher BMI and BITE scores are encountered, especially in married individuals and those living in urban areas. These findings suggest that married individuals and people in densely populated cities may have to struggle more with the psychological and physiological pressures that may occur during the pandemic, suggesting that these may be related to the complexity of urban life and the stresses of home life. These risk factors, which caused changes in eating behavior, have similarly been emphasized in previous research [6, 17, 18].

Although no significant correlation was found between the presence of comorbid diseases and psychological stress, this may create a significant health management burden during the pandemic and indirectly affect quality of life, mental health and general well-being. Individuals with chronic diseases may need to apply to healthcare systems more frequently, which may lead to increased risk perception and health concerns during the pandemic. In a similar follow-up study on eating disorders and the pandemic, it was observed that individuals with early trauma or insecure attachment were particularly vulnerable [19].

In the follow-up evaluation two months later, it was observed that HADS-Anxiety scores increased significantly compared to the early stages of the pandemic, but there was no significant change in HADS-Depression, BITE scores and BMI values. This supports the hypothesis that prolonged quarantine and pandemic conditions continue to affect people's anxiety levels, but that symptoms of depression and eating habits may stabilize over time. This may suggest that in the later stages of the pandemic, people are to some extent able to adapt to uncertain environments and ever-changing conditions, or that the associated emotional responses may change over time. However, these findings are important in that the increase in anxiety levels over time indicates the persistence of economic, social and health-related concerns that the pandemic is likely to bring. The literature on research conducted on the pandemic and eating disorders shows variable evidence regarding the association with symptoms of depression and anxiety [20-22].

The pandemic and quarantine measures have had multidimensional and complex effects on human psychology [18]. Although this study reflects the effects over a specific time period, the long-term psychosocial consequences of the pandemic are not yet fully known. It highlights the need to design interventions and support services that aim to promote well-being during and after the pandemic, with a focus on groups at risk for mental health. Also, how health habits and lifestyle choices will be affected under pandemic conditions and their impact on overall health should be carefully monitored.

The generalizability of the findings should be evaluated depending on the methodological limitations of the study and the participant profile. However, this study can be seen as a first step based on important data that contributes to the understanding of the psychosocial effects associated with the pandemic. In future studies, it is important to further deepen these findings, to examine their relationship with various individual and social variables in more detail and to understand their long-term effects. The data presented in this study provide reference points that can be used to make sense of the impact of the pandemic on human behavior and mental health.

Strengthening psychosocial support systems is vital for the development of strategies and services to help individuals cope with the challenges they face during and after global crises such as the pandemic. Such research also provides valuable information to improve the effectiveness of public health policies and intervention programs.

Limitations

As for study limitations, the limited sample size and demographic diversity require caution regarding the adaptability of the findings to the general population. Additionally, due to the cross-sectional design of the study, definitive conclusions cannot be drawn about cause-effect relationships. Also, the fact that mental symptoms were assessed with self-report scales and that other factors that may affect mental status, such as genetic factors or family environment, were not addressed can be considered as other main limitations. However, comprehensive and long-term prospective studies are needed to understand the effects of the pandemic on the psychosocial status of individuals.

CONCLUSION

The findings of this study show that COVID-19 quarantine measures have profound effects on people's psychology and eating habits. In particular, the observed correlation between increased depressive symptoms and anxiety levels and disruptions in eating patterns highlights the need to assess the pandemic in terms of psychological stressors and their possible long-term effects on behavior. Such information can be vital in developing strategies to respond to future health crises and strengthen mental health support systems.

Ethical Statement

Ethics committee approval was received from Sakarya University Faculty of Medicine non-invasive research ethics committee with date and decision number: 22.05.2020/316. The study was conducted in compliance with the Declaration of Helsinki. Informed consent was obtained from all subjects involved in the study.

Authors' Contribution

Study Conception: AEK, ÇT, AE; Study Design: AEK, ÇT, YSO, NY, AE; Supervision: AE; Funding: N/A; Materials: N/A; Data Collection and/or Processing: ÇT, NY; Statistical Analysis and/or Data Interpretation: AEK, ÇT; Literature Review: AEK, ÇT, YSO; Manuscript Preparation: AEK, ÇT, YSO, NY, AE; and Critical Review: AE.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Anesthesiology and Reanimation

Are systemic and topical tranexamic acid superior to each other in bleeding control in coronary bypass surgery?

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ABSTRACT

Objectives: Tranexamic acid significantly reduces postoperative bleeding and transfusion requirements in cardiac surgery. Intravenous administration has been associated with thromboembolism and seizures. The complex protocols and serious side effects associated with this administration increase interest in intrapericardial administration, and its preferability is being reviewed. The purpose of this prospective, randomized, double-blind study was to compare the effects of intrapericardial tranexamic acid administered following cardiac surgery with those of intravenous administration on postoperative bleeding and possible complications.

Methods: The study included 60 patients over the age of 18 who were undergoing elective coronary artery bypass grafting for the first time. The patients were randomized into intravenous and intrapericardial groups. Primary postoperative bleeding and transfusion requirements, and secondarily complications, reoperation and discharge times were evaluated.

Results: The 60 coronary artery bypass grafting patients included in the study, consisting of 30 patients in intravenous and intrapericardial groups, were not different from each other in terms of demographic data and Euroscore parameters. Postoperative 24-hour chest tube drainage was measured as 890±551 mL in the intrapericardial group and 708±504 mL in the intravenous group. The similar drainage amounts detected in the two groups did not create a statistically significant difference (P=0.190). Transfusion requirements were similar in both groups. No complications developed in any patient and no reoperation was required due to bleeding. Conclusions: In conclusion; intrapericardial tranexamic acid application in coronary artery bypass grafting surgery reduces postoperative bleeding and transfusion requirement at an equivalent rate to intravenous. Intrapericardial application, which can provide the same effect without creating extra risk, may be a simpler and more practical method than systemic application, which includes complex protocols regarding dose and timing. Keywords: Transfusion, antifibrinolytic, intrapericardial, postoperative bleeding, tranexamic acid, anesthesia, coronary artery bypass grafting

pen heart surgeries are major surgeries that frequently use cardiopulmonary bypass (CPB) pumps, have a high risk of bleeding [1]. Blood

transfusion rates are 30-70%, and reoperation rates due to bleeding are 2-7%. 50-80% of bleeding is due to nonsurgical causes [2, 3]. The pump is held respon-

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sible for bleeding caused by fibrinolysis. Fibrinolysis accounts for 25-45% of serious bleeding and continues for 24 hours after the pump [4, 5]. Tranexamic acid (TXA), a synthetic lysine analog, prevents fibrin destruction and bleeding by inhibiting the conversion of plasminogen to plasmin on the fibrin surface [6]. Its effectiveness in controlling bleeding has also been shown in surgeries other than cardiac surgery [7, 8]. It is known that TXA reduces bleeding, transfusion requirements and reoperation rates after CPB. Its use is recommended with a high level of evidence by the American Society of Thoracic Surgeons, Transfusion Management Guidelines, and the Society of Cardiovascular Anesthesiologists. However, no consensus has been established on the optimum dose and method of use [6, 9-11]. Adverse effects such as thromboembolism and seizures seen with intravenous use have increased interest in topical application. Seizures associated with high intravenous (IV) doses are due to the antagonistic effect of TXA due to its similarity to β-aminobutyric acid (GABA) [12]. While previous literature focused on placebo-controlled efficacy studies, current literature focuses on comparisons of systemic and topical effects [10, 13-16]. The hypothesis of this

study is that the effect of topical TXA on postoperative bleeding control is no different from systemic administration. For this purpose, we investigated the effect of IV and intrapericadial (IP) TXA on postoperative bleeding and transfusion requirement in coranary arteriy bypass grafting (CABG) surgery.

METHODS

A prospective randomized, double-blind study was conducted after receiving approval from the local Ethics Committee (2008/11-17), and included 60 patients aged >18 years who were undergoing CABG on pump for the first time. Patients with chronic renal failure (plasma creatinine level >2 mg/dL), hepatic dysfunction (active hepatitis, cirrhosis), history of pulmonary embolism, deep vein thrombosis, cerebrovascular disease, allergy, history of hematological disorders, use of fibrinolytics or antiplatelets within the last week, those who needed an intraaortic balloon pump at the end of the operation, and those who did not give consent for participation were excluded from the study. The 60 patients who were found suitable for

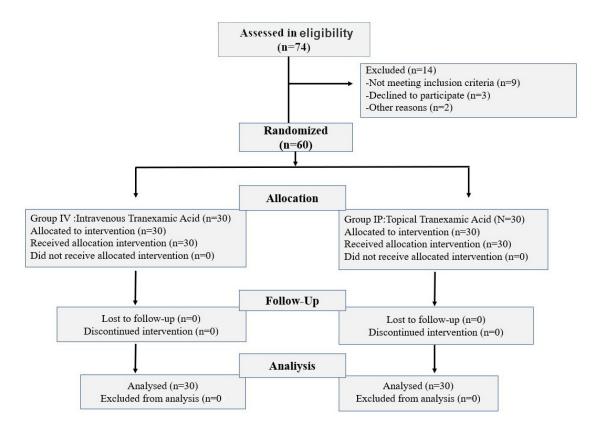


Fig. 1. Study protocol and intervention. IP=intrapericardial, IV=intravenous, TXA=tranexamic acid

the study were randomized into 2 groups using the sealed envelope method. The anesthesiologists and surgeons participating in the study were blind to the content of the 100 mL mixture administered and the patient groups. The determination of the patient groups and the preparation of the mixture were the responsibility of an anesthesiologist not involved in the study. Group IV: 100 ml of a mixture containing 40 mg kg-1 TA+ saline was administered IV (15 min), the pericardial cavity and mediastinal tissues were washed with 100 mL of physiological serum.

Group IP: 100 mL of physiological serum was administered IV (15 min). The pericardial cavity and mediastinal tissues were washed with 100 mL of the mixture (2 g TA+saline). (Fig.1.)

Procedure in Coronary Artery Bypass Grafting

Patients underwent routine anesthesia, perioperative care, and surgical procedures. Before CPB, 300 units/kg heparin was administered IV to ensure ACT>400 sec. Additional doses of heparin (100 units/kg) were administered if necessary. After CPB, antagonization was performed with protamine sulfate. Mediastinal and thoracic drains were clamped before sternum closure. IP and IV mixtures were applied after clamping. After sternum closure, clamped drains were opened. IV application was not continued in the intensive care unit.

Outcome Measures

Primary outcome

Postoperative bleeding amount was determined as the total bleeding amount between 0-3, 312, 12-24 hours in the intensive care unit and the first 24 hours.

Secondary outcomes

Transfusion amounts, Hematological data; Hemoglobine (Hb), Hematocrit (Htc), Platelets, coagulation parameters; Prothrombin time (PZ), Partial Tromboplastin time (PTZ), International normalized ratio (INR), ACT, demographic data, EuroScore, Complications (myocardial Infarction, thromboembolism, cerebrovascular ischemic attack, bleeding, seizure), intraoperative data (CPB and Cross Clamp time, heparin dose, protamine dose, number of bypassed vessels, Internal Mammarian Artery (IMA) use, time from protamine administration to sternum closure), reoperation rate, hospital stay and discharge time were determined.

According to the common transfusion protocol applied to the patients, erythrocyte suspension (Es) was given to patients with Hb<9 mg/dL as a result of arterial blood gas taken after the aortic cannula was removed or hemogram in the intensive care unit During intensive care follow-up, it was planned to give platelet suspension to patients with leakage type bleeding and platelet count <100,000 despite normal ACT values, and fresh frozen plasma (FFP) to patients with prolonged PT values (1.2 times the control value). Chest tubes were removed from patients with serous drainage of less than 100 mL for 8 hours.

Statistical Analysis

SPSS 15.0 program was used for statistical analysis of the data. In comparisons between two groups, Student t test was used for parametric data and chisquare test was used for nonparametric data. A P value of <0.05 was accepted as significant. Data were given as mean±standard deviation (Mean±SD).

RESULTS

The study was completed with 60 patients. The patients' Euroscore values were calculated. Demographic data and Euroscore scores were similar in both groups (Table 1).

There was no statistical significance between the groups in terms of operative data (number of bypass vessels, cross-clamp, CPB, sternum closure times, IMA usage status, amounts of heparin and protamine used) and postoperative data (reoperation, intubation, intensive care, discharge times). No complications developed throughout the study. No patients underwent reoperation (Table 2).

When preoperative and postoperative blood values (Hb, Htc, and Platelet), coagulation parameters (PZ, PTZ, INR) and ACT times were compared, no difference was found between the groups (Table 3). Postoperative Hb, Htc, ACT values of the 3rd, 12th, 24th days were similar in both groups. (Tablo 4).

When the amount of bleeding was examined between the 0-3, 3-12, 12-24th hours postoperatively, no significant difference was found between the groups (P=0.72, P=0.322, and P=0.975; respectively). The total amount of postoperative 24-hour bleeding was similar in both groups, and no statistical difference

Table 1. Demographic data and preoperative follow-up parameters of the groups

| | Group IV (n=30) | Group IP (n=30) | P value |
|-----------------------|--------------------|--------------------|---------|
| Age (years) | 61±9.2 | 63.3±7.5 | 0.303 |
| Gender (M/F) | 27/3 | 27/3 | |
| Body mass index (BMI) | 26.1±2.52 | 25.8±2.66 | 0.206 |
| EF (%) | 43.3±9.5 | 47.5±11.7 | 0.135 |
| EuroScore | 2.7±1.8 | 2.9± 1.5 | 0.136 |

Data are shown as mean±standard deviation or number (n). IV=intravenous, IP=intrapericardial, M/F=Male/Female, EF=ejection fraction

was found between them. (P=0.190) (Table 5).

The amounts of ES and FFP used in the postoperative period were similar in both groups (P=0.220, P=0.388, respectively). Platelet suspension was not used in any of the patients included in the study.

DISCUSSION

This double-blind randomized clinical study has shown that the use of IP TXA in CABG surgery is

equivalent to IV in terms of postoperative bleeding, transfusion requirement, complication and reoperation rates. The tissue plasminogen activator in the pericardial area is higher than that in the systemic circulation. The purpose of this is to prevent adhesion by increasing fluidity [17]. Surgical intervention increases fibrinolytic activity in this area [18]. Pericardium reduces the transfer of drugs applied to this area to the systemic circulation. The fact that IP-applied TXA remains below the detection level in blood is due to minimal systemic transfer [19, 20]. All these reasons

Table 2. Intraoperative and postoperative follow-up parameters for the groups

| | Group IV (n=30) | Group IP (n=30) | P value |
|----------------------------|--------------------|--------------------|---------|
| Number of bypassed vessels | 3.1±1.1 | 3.1±0.8 | 0.847 |
| Cross Clamp time (min) | 69±25 | 62±27 | 0.397 |
| CPB time (min) | 80.4±32 | 77.3±19.2 | 0.289 |
| Closure time (min) | 38.1±5.1 | 39.5±4.3 | 0.062 |
| Amount of heparin (mg) | 232±25 | 238±35 | 0.262 |
| Amount of protamine (mg) | 305±60 | 312±53 | 0.088 |
| IMA use | 30/30 | 30/30 | |
| Complication | 0 | 0 | |
| Number of reoperations | 0 | 0 | |
| Intubated stay (h) | 12.6±3.4 | 13.1±4.1 | 0.246 |
| ICU stay (h) | 26.9 ± 3.8 | 28.8±2.2 | 0.323 |
| Discharge time (days) | 7.3±2.8 | 8.1±1.9 | 0.412 |

Data are shown as mean±standard deviation or number (n). IV=intravenous, IP=intrapericardial, CPB=Cardiopulmonary bypass time, IMA=Internal Mammarian Artery, MI=Myocardial Infarction, CVA=Cerebrovascular ischemic attack, VTE=Venous thromboembolism, ICU=Intensive care unit.

Eur Res J. 2025;11(4):714-721 Gözen and Maltepe

Table 3. Blood values, coagulation parameters, ACT of the groups in the preoperative and postoperative periods

| | Group IV (n=30) | Group IP (n=30) | P value |
|---------------------------------|--------------------|------------------|---------|
| Preoperative | | | |
| Hemoglobin (gr/dL) | 13±1.8 | 13.6±4.3 | 0.468 |
| Hemotocrit (%) | 37.7±5 | 36.6±6.4 | 0.493 |
| Platelet (×10 ³ /mL) | 256±179 | 204±81 | 0.158 |
| PTT (sec) | 38.03 ± 16.1 | 33.57±7.9 | 0.179 |
| PT (sec) | 13.6±8.8 | 13±4.2 | 0.744 |
| INR | 1.01 ± 0.9 | 1.01±0.11 | 0.710 |
| ACT (sec) | 146.7±17.5 | 141.8±11.9 | 0.214 |
| Postoperative | | | |
| Hemoglobin (gr/dL) | 10.3±0.8 | 10.4±1.2 | 0.586 |
| Hemotocrit (%) | 29.9±2.3 | 30.3±3.9 | 0.637 |
| Platelet (×10 ³ /mL) | 152±57 | 134±46 | 0.178 |
| PTZ (sec) | 39.4±17.75 | 38.6 ± 18.05 | 0.853 |
| PZ (sec) | 13.4±1.25 | 13.5±1.28 | 0.706 |
| INR | 1.14±0.1 | 1.12 ± 0.09 | 0.906 |
| ACT (sec) | 145.4±12.8 | 138.8±25.9 | 0.598 |

Data are shown as mean±standard deviation. IV=intravenous, IP=intrapericardial, ACT=Activated clotting time, PT=Prothrombin time, PTT=Partial thromboplastin time, INR=International normalized ratio, Hb=Hemoglobin, Htc=Hematocrit

support the use of IP TXA in terms of side effects. Although it is generally reported that topical TXA reduces bleeding and transfusion rates independently of the dose, it has been shown that low doses (10 mg/mL) are ineffective in cardiac surgery and the effect is dose-dependent [10, 21]. It is stated in the sources that topical TXA doses above 25-50 mg/mL may prevent re-epithelialization and cause bleeding [6]. It has also been reported that IV doses above 50 mg/kg are not superior to low doses in bleeding control and increase the risk of seizures [6, 22]. It has been shown that 2 g of TXA administered IP in CABG surgeries significantly reduces bleeding and blood product use [23]. The TXA doses we used in our study were determined using this information. It has been reported that 24hour values are used in determining the amount of bleeding in cardiac surgeries and that Hb monitoring is not reliable due to hemodilution [24]. It has been shown in different placebo-controlled studies that

IPapplied TXA reduces postoperative bleeding in the 24 hours without increasing the risk of thromboembolism and seizures [16]. In the literature, the effectiveness of topical TXA application in controlling bleeding in patients using oral anticoagulants or with a disturbed bleeding profile has been reported [25-28].

In our study, the amount of postoperative 24-hour bleeding was measured as 890±551 mL in the IP group. This amount is consistent with similar sources (791±483, 733±930) in IP applications [3, 25]. Our results show that the amount of bleeding is higher in the first 3 hours postoperatively. In fact, it has been reported that bleeding is higher in the first 3 hours after CPB and that antifibrinolytics used in this period reduce the transfusion requirement by 1-2 U [25, 29]. In a source similar to our study, it was reported that IP T·A was equivalent to IV in terms of postoperative 24-hour bleeding amounts, transfusion rates, complications and discharge time. This source, which is

Table 4. Postoperative Hb, Htc, ACT values at 3rd, 12th, 24th hours

| | | Group IV (n=30) | Group IP (n=30) | P value |
|-----------|------------|--------------------|--------------------|---------|
| Hb(gr/dL) | 3rd hours | 10.3±1.06 | 10±0.8 | 0.204 |
| | 12th hours | 10.6±1.05 | 11±4.21 | 0.649 |
| | 24th hours | 11±1.16 | 11.4±4.3 | 0.614 |
| Htc (%) | 3rd hours | 30.5±3.1 | 29.3±2.3 | 0.107 |
| | 12th hours | 31.9±2.7 | 30±2.1 | 0.212 |
| | 24th hours | 32.1±2.8 | 30.4 ± 2.6 | 0.303 |
| ACT (sec) | 3rd hours | 146.5±13.6 | 138.3 ± 13.6 | 0.598 |
| | 12th hours | 134.5±11.18 | 138.4±10.7 | 0.707 |
| | 24th hours | 131.6±8.4 | 133.9 ± 7 | 0.729 |

Data are shown as mean±standard deviation. IV=intravenous, IP=intrapericardial, Hb=Hemoglobin, Htc=Hematocrit, ACT=Activated clotting time

consistent with our results, differs from our study in that surgeries other than CABG were also included, patients using anticoagulants were included, higher TXA doses (5 g) were used and different application protocols were followed [16]. Variable results in the literature regarding the amount of bleeding and transfusion need may be due to the type of cardiac surgery performed, TXA doses, application times, differences in case numbers, use of antithrombotics and application of different transfusion policies [16]. In studies reporting higher postoperative bleeding, it was reported that the bleeding-reducing effect of IP TXA was more pronounced [3, 25]. Survival rate with CABG

surgery can be calculated with the Euroscore scoring system to get an idea about patient-specific mortality, morbidity, and hospital stay. In our study; similar results were recorded in both groups in terms of Euroscore values, characteristic features, and hemostatic parameters. For this reason, we think that we have fully ensured the reliability of the comparison by eliminating patient and surgical causes.

Limitations

Our study has some limitations. The first of these is the lack of a placebo group. This is because $T \cdot A$ is routinely applied for bleeding prophylaxis in our

Table 5. Postoperative bleeding amount, total transfusion values

| | Group IV (n=30) | Group IP (n=30) | P value |
|--------------------------------|--------------------|--------------------|---------|
| Postoperative first 3 hrs (mL) | 366±146 | 468±266 | 0.72 |
| Postoperative 3-12.hrs (mL) | 242±258 | 317±318 | 0.322 |
| Postoperative 12-24.hrs (mL) | 93±173 | 94±108 | 0.975 |
| Postoperative first 24 hrs | 708 ± 504 | 890±551 | 0.190 |
| Total (mL) | | | |
| ES (U) | 1.3±1.3 | 1.8±1.5 | 0.220 |
| FFP (U) | 3.9±1.6 | 3.6±1.2 | 0.388 |
| Platelet(U) | 0 | 0 | 0 |

Data are shown as mean±standard deviation. IV=intravenous, IP=intrapericardial, FFP=Fresh frozen plasma, ES=Erythrocyte suspension

clinic. Our study may be insufficient to evaluate side effects. Because no complications were observed in any patient. Another limitation is that IP application inhibits fibrinolysis, causes adhesions, and may create a safety problem for reoperation. Although it is suggested that this situation can be balanced with a simultaneous anti-inflammatory effect, it is not clear how long patients should be followed for this purpose [30, 31]. The follow-up period limited to discharge in our study is weak in evaluating adhesions in IP applications. We believe that our study contributes to the literature due to the limited number of prospective studies comparing the effectiveness of IP and IV TXA with a single type of cardiovascular surgery and a similar patient profile (Euroscore).

CONCLUSION

As a result; IP TXA application in CABG surgery reduces postoperative bleeding and transfusion requirements at an equivalent rate to IV application. IP application, which can provide the same effect without creating additional risks, may be a simpler and more practical method than systemic application with complex protocols. Large randomized double-blind clinical studies are needed to confirm these findings.

Ethical Statement

This study was approved by the Dokuz Eylül University Medical Faculty Drug Research Local Ethics Committee (Decision no. 08/18-20, Date: 17.11.2008).

Authors' Contribution

Study Conception: FG, FM; Study Design: FG, FM; Supervision: FG, FM; Funding: FG, FM; Materials: FG, FM; Data Collection and/or Processing: FG, FM; Statistical Analysis and/or Data Interpretation: FG, FM; Literature Review: FG, FM; Manuscript Preparation: FG, FM and Critical Review: FG, FM.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Anesthesiology and Reanimation

Factors influencing difficult and failed intubation in patients undergoing gynecologic oncology surgery: a retrospective cohort study

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ABSTRACT

Objectives: Difficult and unsuccessful intubation is a leading cause of anesthesia-related morbidity and mortality. This study aimed to investigate the incidence and contributing factors of difficult and unsuccessful intubation in patients undergoing gynecologic oncology surgery, particularly those with significant comorbidities and obesity.

Methods: The study included 653 patients over 18 years of age who underwent gynecologic oncology surgery with planned intubation under general anesthesia between January 1 and July 1, 2024. Data collected included demographic information, number of intubation attempts, personnel involved in intubation, auxiliary methods employed, intubation duration, complications, mouth opening, sternomental distance, thyromental distance, neck mobility, upper lip bite test results, presence of retrognathia or micrognathia, obstructive sleep apnea, and mobile dentures.

Results: The incidence of difficult intubation in our cohort was 7.5%, with no cases of failed intubation. Significant factors associated with increased risk of difficult intubation included body mass index (P=0.008), obstructive sleep apnea (P<0.001), Mallampati score (P<0.001), and mouth opening <4 cm (P<0.001). Among patients with difficult intubation, statistically significant differences were observed for age (P=0.001), ASA score (P=0.002), presence of comorbid conditions(P=0.004), Cormack-Lehane score(P<0.001), sternomental distance <12 cm (P<0.001), thyromental distance <6 cm (P<0.001), limited neck mobility (P<0.001), upper lip bite test results (P<0.001), retrognathia/micrognathia (P<0.001), and presence of dentures (P<0.001).

Conclusions: This study demonstrated that preoperative assessments of body mass index, obstructive sleep apnea, Mallampati score, and mouth opening are significant risk factors for difficult intubation. To reduce the risk of airway-related complications, patients undergoing gynecologic oncology surgery should undergo thorough and careful preoperative evaluation.

Keywords: Gynecologic oncology, airway management, difficult intubation, predictive, general anesthesia

nesthesiologists are equipped with basic airway management tools and adhere to globally accepted guidelines. According to the 2022

guidelines from the American Society of Anesthesiologists (ASA), a situation requiring multiple attempts or in which tracheal intubation fails despite attempts

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is defined as 'difficult or unsuccessful intubation' [1]. With updated guidelines, advances in technology, and auxiliary devices, airway management has become safer, helping to prevent severe complications, including life-threatening events [2].

While managing expected or unexpected difficult intubation is a fundamental skill for all anesthesiologists, a thorough preoperative evaluation of patients remains essential. However, no test offers high sensitivity and specificity for predicting difficult intubation during preoperative assessment [3]. Standard preoperative evaluations alone are insufficient in accurately predicting difficult intubation [4, 5]. The incidence of difficult intubation in general anesthesia ranges from 1% to 13%, with unsuccessful intubation occurring in up to 0.1%-0.2% of cases [4, 6].

The patient population undergoing gynecologic oncology surgery is considered high-risk due to the presence of serious comorbidities, as well as prior exposure to radiotherapy and chemotherapy [7]. While obesity and a high body mass index (BMI) are commonly observed in this population, low BMI can also occur [8]. The combination of obesity and comorbidities may lead to both anticipated and unanticipated airway-related complications. A thorough understanding of the demographic characteristics of this population is essential for managing difficult or unsuccessful intubation, as well as minimizing morbidity and mortality [9]. It is crucial for patient safety that any challenges encountered in airway management are addressed according to current guidelines, with proper preparation and equipment.

This study aimed to determine the incidence of difficult and unsuccessful intubation and the factors influencing these outcomes in patients undergoing gynecologic oncology surgery with significant comorbidities.

METHODS

This retrospective study was conducted at a tertiary education and research hospital and was approved by the Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (AEŞH-BADEK-2024-528). The study adhered to the principles outlined in the Declaration of Helsinki. Patients over the age of 18 who underwent gynecologic oncology sur-

gery with general anesthesia and planned intubation between January 1, 2024, and July 1, 2024, were included. Patients with missing data were excluded from the analysis. Data were collected from the hospital information system, preoperative anesthesia evaluation forms, and operating room observation records. The study examined patients' demographic data, preoperative anesthesia evaluations, previous airway history, first successful oxygenation method, intubation attempts, the number of personnel involved, use of the Back-Up Rightward Pressure (BURP) maneuver, application of assistive methods, Cormack-Lehane score, intubation duration, and complications. Additionally, following routine quality standards in the operating room, we evaluated mouth opening (<4 cm), sternomental distance (<12 cm), thyromental distance (<6 cm), neck mobility, upper lip bite test (-:unable to bite/+:able to bite), presence of retrognathia/micrognathia, obstructive sleep apnea, and mobile dentures. The tertiary health center where the study was conducted is staffed by specialist physicians and anesthesiology residents. The residents have between 1 and 5 years of training and work under the supervision of at least one attending physician as part of a rotational program. In cases of difficult or failed intubation, various adjunct techniques and devices are used following ASA guidelines, depending on the provider's skill and experience. These include a stylet, bougie, video laryngoscope, laryngeal mask airway, fiberoptic bronchoscope, and invasive airway devices (e.g., various tracheostomy sets).

Statistical Analysis

Statistical data were analyzed using SPSS 22.0 (Statistical Package for the Social Sciences) software. The normality of continuous variables was assessed using both visual and analytical methods. Categorical variables are presented as counts and percentages, while continuous variables are expressed as mean±standard deviation or median (range). For comparisons between two groups, the Student's t-test was used for normally distributed continuous variables, and the Mann-Whitney U test was used for non-normally distributed continuous variables. Categorical variables were compared between groups using the Chi-square test or Fisher's exact test. Variables showing statistical significance (P<0.05) in pairwise comparisons were further evaluated with confidence

intervals using univariate logistic regression analysis. Statistically significant variables (P<0.05) from univariate analysis, which were identified as potential independent risk factors for difficult and unsuccessful intubation, were assessed using a multivariate logistic regression model. Subjective evaluations, which may vary depending on the clinician, and variables with high correlations that could disrupt model compatibility, were excluded from the model. Adjusted odds ratios (adjusted OR) and 95% confidence intervals were calculated. A significance level of P<0.05 was considered statistically significant for this study. Other statistical methods were applied as necessary.

RESULTS

A total of 680 patients met the study criteria between January 1, 2024, and July 1, 2024. Twenty-seven patients were excluded due to missing data, and the data

from 653 patients were included in the analysis. Of these, 7.5% (49 patients) experienced difficult intubation, and no patients had unsuccessful intubation (Fig. 1).

The mean age of patients in the difficult intubation group was 57.9±11.5 years, compared to 51.6±13.8 years in the non-difficult intubation group (Table 1). A statistically significant difference in mean age was observed between the groups (P=0.001); however, no significant association was found between age and difficult intubation in the multivariate logistic regression analysis (OR: 0.997, 95% CI: 0.965–1.030, P=0.859) (Table 2). The mean BMI in the difficult intubation group was 38.7±5.8, compared to 29.7±6.5 in the nondifficult intubation group, with a statistically significant difference between the groups (P<0.000) (Table 1). Furthermore, the multivariate logistic regression analysis revealed that a 1-unit increase in BMI was associated with a 1.094-fold increased risk of difficult intubation (OR: 1.094, 95% CI: 1.023-1.169, P=0.008)

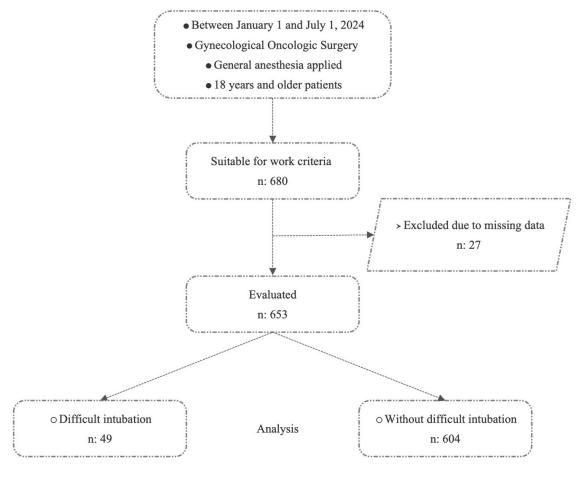


Fig.1. Flowchart.

Table 1. Demographic data

| | Without difficult intubation | Difficult intubation | P value |
|--------------------------|------------------------------|----------------------|-------------|
| | (n=604) | (n=49) | |
| Age (years) | 51.6±13.8 | 57.9±11.5 | 0.001^{1} |
| BMI (kg/m ²) | 29.7±6.5 | 38.7±5.8 | 0.008^{1} |
| ASA Score | | | |
| I | 61 (10.1) | 0 | 0.002 |
| II | 331 (54.8) | 21 (42.9) | |
| III | 212 (35.1) | 28 (57.1) | |
| Comorbidities | 375 (62.1) | 41 (83.7) | 0.004 |
| Hypertension (mmHg) | 207 (34.3) | 23 (46.9) | 0.103 |
| Diabetes | 114 (18.9) | 16 (32.7) | 0.033 |
| COPD | 59 (9.8) | 9 (18.9) | 0.098 |
| Hypothyroidism | 78 (12.9) | 9 (18.4) | 0.389 |
| CAD | 53 (8.8) | 7 (14.3) | 0.198 |
| Obstructive sleep apnea | 19 (3.1) | 13 (26.5) | <0.001 |

Data are shown as mean±standard deviation or n (%) n %).

ASA=ASA Physical status score, BMI=Body mass index, CAD=Coronary artery disease, COPD=Chronic obstructive pulmonary disease

(Table 2). When comparing ASA classifications, no patients in the difficult intubation group were classified as ASA I, and a statistically significant difference was found between the groups (P=0.002) (Table 1).

When patients were compared based on the presence of additional diseases, a statistically significant difference was found (P=0.004) (Table 1). A significant difference was observed in the presence of diabetes and sleep apnea between patients with and without difficult intubation (P=0.033, P<0.001, respectively), whereas no significant difference was

found for hypertension, chronic obstructive pulmonary disease (COPD), hypothyroidism, or coronary artery disease (CAD) (Table 1). When examining the relationship between the presence of diabetes and sleep apnea and difficult intubation, the presence of diabetes was not associated with difficult intubation in the multivariate logistic regression analysis (OR: 0.754, 95% CI: 0.333-1.709, P=0.498). However, the presence of sleep apnea was associated with an 8.8-fold increased risk of difficult intubation (OR: 8.826, 95% CI: 3.184-24.465, P<0.001) (Table 2).

Table 2. Multilogistic regression analysis of predictive parameters for difficult intubation.

| | OR | 95%CI | P value |
|-------------------------|-------|--------------|---------|
| Age | 0.997 | 0.965-1.030 | 0.859 |
| BMI | 1.094 | 1.023-1.169 | 0.008 |
| Diabetes | 0.754 | 0.333-1.709 | 0.498 |
| Obstructive sleep apnea | 8.826 | 3.184-24.465 | <0.001 |
| Mallampati | 6.943 | 2.650-18.191 | <0.001 |
| <4 cm Mouth Opening | 8.327 | 2.956-23.458 | <0.001 |

OR=Odd's Ratio, BMI=Body mass index.

¹Independent sample t-test

Eur Res J. 2025;11(4):722-731 Kına et al

Table 3. Some parameters evaluated

| | Without difficult intubation (n=604) | Difficult intubation (n=49) | P value |
|------------------------------|--------------------------------------|-----------------------------|---------|
| Mallampati | (II-004 <i>)</i> | (II—4 <i>9)</i> | |
| 1 | 228 (37.7) | 0 | <0.001 |
| 2 | 279 (46.2) | 11 (22.4) | 10.001 |
| 3 | 96 (15.9) | 25 (51.0) | |
| 4 | 1 (0.2) | 13 (26.5) | |
| Cormack Lehane | 1 (0.2) | 13 (20.3) | |
| 1 | 416 (68.9) | 2 (4.2) | <0.001 |
| 2 | 147 (24.3) | 9 (18.8) | 0,001 |
| 3 | 41 (6.8) | 28 (58.3) | |
| 4 | 0 | 9 (18.8) | |
| <4 cm mouth opening | 35 (5.8) | 16 (32.7) | <0.001 |
| <12 cm sternomental distance | 25 (4.1) | 38 (77.6) | < 0.001 |
| <6 cm thyromental distance | 26 (4.3) | 37 (75.5) | <0.001 |
| Limited neck joint Mmvements | 30 (5.0) | 16 (32.7) | <0.001 |
| Upper lip bite test* | 12 (2.0) | 31 (63.3) | < 0.001 |
| Retro/micrognathy | 14 (2.3) | 23 (46.9) | < 0.001 |
| Mobile dental prosthesis | 96 (15.9) | 29 (59.2) | < 0.001 |

Data are shown as n %).

There were no patients with a Mallampati score of 1 in the difficult intubation group, and a statistically significant difference was observed in Mallampati scores between the groups (P<0.001) (Table 3). A Mallampati score of 3-4 was associated with a 6.9-fold increased risk of difficult intubation compared to scores of 1-2 (OR: 6.943, 95% CI: 2.650-18.191, P<0.001) (Table 2). In the difficult intubation group, 32.7% of patients had a mouth opening of less than 4 cm, with a statistically significant difference between the groups (P<0.001) (Table 3). Mouth opening <4 cm was associated with an 8.3-fold increased risk of difficult intubation (OR: 8.327, 95% CI: 2.956–23.458, P<0.001) (Table 2). Significant differences were also found between the groups for Cormack-Lehane score, sternomental distance (<12 cm), thyromental distance (<6 cm), limited neck mobility, upper lip bite test, retrognathia/micrognathia, and presence of mobile dentures (P<0.001) (Table 3).

Only 8.2% of patients with difficult intubation had a history of difficult intubation (Table 4). While 40.8%

of patients required 3 or 4 intubation attempts, 79.6% were intubated by a single individual (Table 4). The Back-Up Rightward Pressure (BURP) maneuver was applied in 83.7% of cases, and at least one auxiliary method was used in 91.8% of patients (Table 4). The most commonly used auxiliary methods included stylet (35.6%), videolaryngoscope (VL) with stylet (26.7%), and bougie (20%) (Table 4). The first successful oxygenation method for patients with difficult intubation was mask ventilation, and no cases of unsuccessful intubation were reported. Complications, such as soft tissue injury, were observed in only 3 patients. The mean intubation time for patients with difficult intubation was 5.1±1.73 minutes.

DISCUSSION

This study investigated the incidence and contributing factors of difficult and unsuccessful intubation in a high-comorbidity population undergoing gynecologic

^{*}Patients who cannot bite their upper lip

Table 4. Parameters of patients with difficult intubation*

| | Difficult intubation (n=49) |
|--|-----------------------------|
| History of difficult intubation, n (%) | 4 (8.2) |
| Number of intubation attempts, n (%) | |
| 2 | 29 (59.2) |
| 3 | 15 (30.6) |
| 4 | 5 (10.2) |
| Number of People who attempted intubation, n (%) | |
| 1 | 39 (79.6) |
| 2 | 9 (18.4) |
| 3 | 1 (2.0) |
| BURP maneuver, n (%) | 41 (83.7) |
| Use of assisted methods, n (%) | 45 (91.8) |
| Auxiliary method used, n (%) | |
| Style | 16 (35.6) |
| VL+ Style | 12 (26.7) |
| Bougie | 9 (20) |
| SAD+ Bougie | 3 (6.7) |
| SAD+ Style | 2 (4.4) |
| VL+ Bougie | 1 (2.2) |
| VL+SAD | 1 (2.2) |
| VL | 1 (2.2) |
| Complication, n (%) | 3 (6.1) |
| Intubation time (min) | 5.1±1.73 (2.3-10.5) |

Data are shown as mean±standard deviation or minimum-maximum or n (%) n %).

BURP=Back UP Rightward Pressure, VL=Videolaryngoscope, SAD=Supraglottic airway device.

oncologic surgery. The incidence of difficult intubation was 7.2%, with no cases of unsuccessful intubation observed in our cohort. In this high BMI population, factors associated with difficult intubation included BMI, obstructive sleep apnea, Mallampati score, and limited mouth opening.

The incidence of difficult and unsuccessful intubation in patients undergoing general anesthesia ranges from 1.5% to 8.5% [6, 10], while difficult laryngoscopy and intubation rates are reported to be higher among obese patients, ranging from 8.2% to 16.2% [9]. In obese patients, primary concerns for

anesthesiologists include intubation difficulty, apnea, hypoxia, and compromised respiratory mechanics. Literature indicates that standard tests used to predict difficult or unsuccessful intubation are insufficient in detecting these major complications [3, 5, 11]. Various airway management societies have established guidelines with predictive tests, measurements, and specialized devices to reduce morbidity and mortality in difficult airway cases, underscoring the vital importance of effective airway management in anesthesia [1, 12, 13]. In our study, the incidence of difficult intubation in a specific high comorbidity population in-

^{*}The first successful oxygenation method was Mask ventilation 49 (100%), Intubation success: 100% successful, Complication type: Soft tissue damage in 3 people.

dependent of gender was 7.2%, lower than most reported rates in the literature. Previous studies have identified age 40-59 as a risk factor for difficult intubation and noted fewer surgical cases in patients aged 60 and above [3, 14]. In our cohort, mean ages for the two groups were 51.6 and 57.9, and while there was a statistically significant age difference between groups, age was not associated with a higher risk of difficult intubation. This may be due to a lower frequency of surgeries, and thus difficult intubation cases, among patients over 60, potentially resulting in an insufficient sample size. Age, comorbidities, and ASA scores are closely correlated. Schnittker et al. also reported that a high ASA score was associated with increased risk for difficult intubation [15]. Consistently, we observed a statistically significant difference between our groups regarding ASA scores and comorbidity presence. We suggest that while age, comorbidities, and high ASA scores may indeed be risk factors for difficult intubation, they are interrelated.

Obesity has been linked to difficult intubation due to increased fat tissue in the oropharyngeal region, altered anatomical planes, and increased neck circumference [8, 10, 15-17]. Although studies report varying degrees of increased risk, with rates ranging from 1.06 to 2.48-fold, some research has suggested that obesity is not a significant risk factor for difficult intubation [15-17]. Obesity is, however, commonly observed in patients undergoing gynecologic oncologic surgery [20]. In our study, the mean BMI in the difficult intubation group was 38.7±5.8 kg/m², with a statistically significant association between BMI and intubation difficulty; a 1 unit increase in BMI corresponded to a 1.094-fold increase in risk. In this female-only population, obesity was prevalent and likely contributed to an elevated risk of difficult intubation, especially given associated conditions like diabetes and obstructive sleep apnea. While both diabetes and obstructive sleep apnea were significantly different between groups, obstructive sleep apnea, in particular, was associated with an 8.8-fold increased risk of difficult intubation. Our findings suggest that obesity is a risk factor for difficult intubation, with undiagnosed obstructive sleep apnea potentially further elevating this risk in obese patients [20].

The Mallampati score, upper lip bite test, mouth opening, sternomental distance, thyromental distance, limitation of neck joint movements, retro/microg-

nathia, and presence of dentures are among the predictive tests for difficult intubation [11, 21]. However, no single test has shown sufficient sensitivity and specificity to reliably predict difficult intubation [1, 10, 12, 22]. While the reported sensitivity of the Mallampati score varies widely in the literature, from 10% to 90%, our study found that a high Mallampati score (3-4) was associated with a 6.94-fold increased risk of difficult intubation [23]. Our findings are consistent with studies that combine the Mallampati score, thyromental distance, and upper lip bite test as predictive tools [10, 24]. Nonetheless, it is essential to consider potential challenges, such as clinicians' variability in accurately assessing the Mallampati score.

Sternomental and thyromental distances are critical measurements for achieving optimal head and neck alignment in the intubation position, contributing to improved glottic visibility [25]. In our study, these distances showed statistically significant differences between groups. Another key predictor, mouth opening, is a practical bedside anatomical measurement. We found that a mouth opening of less than 4 cm was associated with an 8.32-fold increased risk for difficult intubation, likely due to reduced visibility of glottic structures and increased difficulty in guiding the endotracheal tube. Based on these findings, we recommend incorporating multiple predictive tests in the preoperative evaluation for gynecologic oncologic surgery to improve assessment accuracy.

Although a history of difficult intubation is a strong predictor, as shown in our study, difficult intubation can still occur in patients without such a history [26]. Only 8.2% of our patients had a prior history of difficult intubation, with most cases being unpredictable. This underscores the importance of a thorevaluation ough preoperative to mitigate airway-related complications. Masashi et al. [27] reported that the BURP maneuver can enhance glottic visibility in difficult intubation cases. In our study, the BURP maneuver was applied to 83.7% of patients with difficult intubation, supporting this finding. We believe that the BURP maneuver improves glottic visibility and intubation success, particularly in high BMI patient populations.

In patients with difficult intubation, using auxiliary methods such as stylet, bougie, videolaryngoscope (VL), and supraglottic airway device (SAD) has been shown to increase intubation success [1, 3, 28].

The choice of auxiliary method often depends on the operator's clinical experience and expertise [1, 13]. Current airway guidelines recommend equipment such as VL as the primary choice in anticipated difficult intubation cases, including maxillofacial trauma, conhead and neck malformations, orthognathic surgery. A study by Jaber et al. reported that using a stylet reduced intubation time by 30% and decreased unsuccessful intubation rates [29]. Other studies indicate that VL improves field of vision, enhances glottic visibility, and shortens intubation time, particularly when used with the BURP maneuver [22, 30]. In our study, auxiliary methods were used in 91.8% of patients with difficult intubation. Of these patients, 35.6% received a stylet, and 26.7% received both a stylet and VL (Table 3). Consistent with the findings of the literature, we recommend using and combining auxiliary equipment in this high-risk population with elevated BMI and significant comorbidities. Among patients with difficult intubation, 79.6% were intubated by a single operator, and 59.2% required only two attempts, with no failed intubations. Major complications such as hypoxia, arrest, or death were absent in this group, and only three patients experienced soft tissue injury. We attribute our low complication rate to the availability and combined use of auxiliary equipment. In patients with high comorbidities undergoing gynecologic oncologic surgery, auxiliary equipment may help reduce airway-related complications and decrease mortality and morbidity.

Limitations

Our study has several limitations. Firstly, as a retrospective analysis, it relies on data recorded in medical files, which may lead to incomplete or inconsistent entries. Additionally, patients with missing data were excluded, potentially introducing selection bias. Certain values, such as specific measurements, were sometimes recorded only as 'small' or 'large' without precise quantification, which may affect the accuracy and granularity of our findings. These limitations should be taken into account when interpreting our results and their applicability to broader patient populations. It should also be considered that among the practitioners are anesthesiology residents with varying levels of training (1-5 years) who work as part of a rotational program.

CONCLUSION

In conclusion, patients undergoing gynecologic oncologic surgery represent a high-risk group with considerable comorbidities, high BMI, and histories of chemotherapy and radiotherapy. To minimize complications related to difficult or unsuccessful intubation, we recommend comprehensive preoperative evaluation, thorough preparation of auxiliary airway equipment, and vigilant anesthetic monitoring in this population. While our study, like most in this field, is retrospective, we believe that prospective, controlled clinical studies are needed to further validate these findings and improve airway management strategies in gynecologic oncology patients.

Ethical Statement

This study was approved by the Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (Decision no. AEŞH-BADEK-2024-528, date: 05.06.2024).

Authors' Contribution

Study Conception: SFK, ZK, DU, AS, SA, JE; Study Design: EK, AG; Supervision: EK, IY; Funding: EK, IY; Materials: EK, AG; Data Collection and/or Processing: EK, BT; Statistical Analysis and/or Data Interpretation: EK, BT; Literature Review: EK, AG; Manuscript Preparation: EK, IY and Critical Review: EK, CA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Medical Biochemistry

The utilization of the large unstained cell (LUC) parameter in lymphoid, haematopoietic and related tissue's malignant neoplasms

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ABSTRACT

Objectives: Large unstained cells (LUCs) are a differential count parameter reported by routine hematology analysis, and LUC percentages (LUC%) reflect active lymphocytes and peroxidase-negative cells. We aimed the evaluate the LUC% parameter in routine practice towards malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic, and related tissue.

Methods: LUC analysis was performed with Siemens ADVIA® 2120 Hematology System. Data were obtained from Ankara Bilkent City Hospital's laboratory information system.

Results: A statistical difference in the LUC % data in the case of LUC % <4.5 and LUC % ≥4.5 among preliminary diagnoses was observed (P<0.001). According to the Kruskal-Wallis test, a statistical difference was observed between preliminary diagnosis and LUC % values (P<0.001). The One-way ANOVA test with Bonferroni correction was performed for post hoc multiple comparisons of the preliminary diagnosis among LUC%. LUC% was higher in Hodgkin Lymphoma patients than Myeloid leukaemia patients (P=0.002). LUC % was higher in the Lymphoid leukaemia patients than in the patients with Hodgkin lymphoma (P<0.001), Other and unspecified types of non-Hodgkin lymphoma (P<0.001), Multiple myeloma and malignant plasma cell neoplasms (P<0.001), Follicular lymphoma (P<0.001), Non-follicular lymphoma (P<0.001), Mature T-Cell and Natural Killer Cell lymphomas (P<0.001), Other and unspecified types of non-Hodgkin lymphoma (P<0.001), Malignant immunoproliferative diseases (P<0.001), Multiple myeloma and malignant plasma cell neoplasms (P<0.001), Lymphoid leukaemia (P<0.001), Myeloid leukaemia (P<0.001), Other leukaemias of specified cell type patients (P<0.001).

Conclusions: The present study underscores the importance of LUC% in line with ICD-10 and may provide ideas for new research. Prospective studies including patient and control groups may be useful in assessing LUC%.

Keywords: Large unstained cells (LUCs), Siemens ADVIA 2120, complete blood cell count, ICD-10, neoplasms

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aboratory tests, along with anamnesis and physical examination, are included in the diagnosis of hematological diseases. Complete blood cell count (CBC) is a commonly performed blood test. It presents hemoglobin, the count of platelets, the indices of the red blood cell, the count of white blood cells (WBC), and its differential, which provides information about the different subset percentages of WBC and their absolute numbers [1]. The assessment of hemoglobin, the indices of red blood cells, and hematocrit maintain knowledge concerning the patient's oxygen-carrying capacity while evaluating the WBC count ensures that information about the immune system is available. CBC has a role in diagnosing anemia, immune deficiencies, infection, acute hemorrhagic conditions, and some types of cancer [2]. Hematological malignancies represent a heterogeneous group of tumors and constitute 6.5% of whole cancer types and 7.2% of cancer-related deceases according to the World Health Organization [3].

Large unstained cells (LUCs), and LUC percentages (LUC%) are displayed on some automatic cell counters [4]. In a letter to the editor, it was stated that of the twenty-two doctors in the study, nineteen had no idea about the LUC abbreviation meaning, and seventeen did not know how to interpret high LUC results [5]. LUC is one of the differential count parameters reported during routine hematology analyses, and LUC % externalizes and peroxidase-negative cells and active lymphocytes [4]. LUC presents virocytes, hematopoietic stem cells, large lymphocytes, abnormal cells, and blasts [6]. An increment of LUC% may be observed in some infectious and hematological diseases [7].

Nosology is systematically sorting diseases. International Classification of Diseases (ICD) is among the most preferred nosologies [8]. The ICD system was created to track diseases in the population accurately (2). International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) Version:2019 contains 22 chapters. The neoplasms take place in Chapter II. The diseases under the title of malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic, and related tissue are as follows: Hodgkin lymphoma, Follicular lymphoma, Non-follicular lymphoma, Mature T-cell and NK- cell lymphomas (Mature T/NK-cell lymphomas), Other and unspecified types of non-Hodgkin lymphoma, Other specified types of T/NK-cell lymphoma,

Malignant immunoproliferative diseases, Multiple myeloma and malignant plasma cell neoplasms, Lymphoid leukaemia, Myeloid leukaemia, Monocytic leukaemia, Other leukemias of specified cell type, Leukaemia of unspecified cell type, Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue [9].

The diagnoses placed in the laboratory information system of the Ankara Bilkent City Hospital are in line with ICD-10. The purpose of the present study was the assessment of the LUC% parameter in routine practice towards the codes of malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic, and related tissue to provide new data on LUC% in the literature.

METHODS

In Ankara Bilkent City Hospital, CBC tests and WBC differentials are performed on the Siemens ADVIA® 2120 Hematology System (Siemens Healthineers, Erlangen, Germany) devices. Calibration and internal quality controls are performed daily on the device. After being deemed appropriate by biochemistry experts, analysis begins on the device. External quality controls are performed once a month.

The ADVIA® 2120 autoanalyzer analyzes whole blood samples which are obtained in Ethylenediaminetetraacetic acid tubes. The device uses flow cytometry as its basis for measurements. The device uses light scattering to ensure CBC, WBC differentials, reticulocyte counts, WBC lysis, myeloperoxidase, and oxazine 750 staining. It does not require cyanide to measure hemoglobin colorimetrically. WBCs are sorted into neutrophils, eosinophils, basophils, granulocyte monocytes, lymphocytes, and LUC [10].

The codes of ICD-10 consisting of the malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic, and related tissue between 01/02/2019 and 29/02/2020, were acquired from the laboratory information system of the hospital. In this retrospective study, only each patient's first result and preliminary diagnosis were included.

The LUC% data were evaluated according to gender and age intervals: pediatric group (0-18 years), adult group (19-64 years), and geriatric group (65 years and over).

Statistical Analysis

Categorical numerical variables were stated as percentages, and the descriptive statistics data were stated as median and interquartile ranges (IQR). Kruskall Wallis, chi-square tests, and Post Hoc ANOVA tests were carried out to compare data among the groups. A P-value <0.05 was accepted as statistically expressive. All the statistical analyses were performed with IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 1710 LUC% data were rolled in the present study. Quantitative variables distribution is presented

in Table 1. Quantitative data among genders is presented in Table 2. Quantitative data among age intervals is presented in Table 3. LUC% data among preliminary diagnoses is presented in Table 4.

Fig. 1 presents LUC% values among preliminary diagnoses with error bars. The Median and IQR levels of LUC% among preliminary diagnoses are presented in Table 5.

A flag occurs in Siemens ADVIA 2120 device when LUC% data LUC% ≥4.5. In the present study, a statistical difference in the LUC% data in the case of LUC% <4.5 and LUC% ≥4.5 among preliminary diagnoses was observed (P<0.001).

According to the Kruskal-Wallis test, a statistical difference was observed between preliminary diagnosis and LUC % values (P<0.001). The one-way

Table 1. Quantitative variables distribution

| | n | % |
|--|------|------|
| Gender | | |
| Female | 853 | 49.9 |
| Male | 857 | 50.1 |
| Age (years) | | |
| 0-18 | 238 | 13.9 |
| 19-64 | 854 | 49.9 |
| 65 and over | 618 | 36.1 |
| LUC% | | |
| LUC% <4.5 | 1459 | 85.3 |
| LUC% ≥4.5 | 251 | 14.7 |
| Preliminary diagnosis | | |
| Hodgkin lymphoma | 201 | 11.8 |
| Follicular lymphoma | 46 | 2.7 |
| Non-follicular lymphoma | 116 | 6.8 |
| Mature T/NK-cell lymphomas | 36 | 2.1 |
| Other and unspecified types of non-Hodgkin lymphoma | 251 | 14.7 |
| Malignant immunoproliferative diseases | 9 | 0.5 |
| Multiple myeloma and malignant plasma cell neoplasms | 226 | 13.2 |
| Lymphoid leukaemia | 507 | 29.6 |
| Myeloid leukaemia | 279 | 16.3 |
| Other leukaemias of specified cell type | 19 | 1.1 |
| Leukaemia of unspecified cell type | 17 | 1 |
| Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue | 3 | 0.2 |

LUC=Large Unstained Cell

Table 2. Quantitative data among genders

| | Fe | male | M | ale | P value |
|--|-----|-------|-----|------|---------|
| | n | % | n | % | |
| ge (years) | | | | | |
| 0-18 | 105 | 12.3 | 133 | 15.5 | < 0.001 |
| 18-64 | 400 | 46.9 | 454 | 53.0 | |
| 65 and over | 348 | 40.8 | 270 | 31.5 | |
| LUC% | | | | | |
| LUC % <4.5 | 712 | 83.47 | 747 | 87.2 | 0.031 |
| LUC % ≥4.5 | 141 | 16.53 | 110 | 12.8 | |
| reliminary diagnosis | | | | | |
| Hodgkin lymphoma | 84 | 9.8 | 117 | 13.7 | <0.001 |
| Follicular lymphoma | 28 | 3.3 | 18 | 2.1 | |
| Non-follicular lymphoma | 63 | 7.4 | 53 | 6.2 | |
| Mature T/NK-cell lymphomas | 25 | 2.9 | 11 | 1.3 | |
| Other and unspecified types of non-Hodgkin lymphoma | 107 | 12.5 | 144 | 16.8 | |
| Malignant immunoproliferative diseases | 3 | 0.4 | 6 | 0.7 | |
| Multiple myeloma and malignant plasma cell neoplasms | 117 | 13.7 | 109 | 12.7 | |
| Lymphoid leukaemia | 253 | 29.7 | 254 | 29.6 | |
| Myeloid leukaemia | 152 | 17.8 | 127 | 14.8 | |
| Other leukaemias of specified cell type | 15 | 1.8 | 4 | 0.5 | |
| Leukaemia of unspecified cell type | 4 | 0.5 | 13 | 1.5 | |
| Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue | 2 | 0.2 | 1 | 0.1 | |

LUC= Large Unstained Cell.

ANOVA test was performed with Bonferroni correction for post hoc multiple comparisons of the preliminary diagnosis among LUC%. A statistical difference in LUC% was observed between Hodgkin lymphoma and Myeloid leukaemia (P=0.002).

Statistical differences of LUC % between Lymphoid leukaemia and the other diagnoses were as follows: Hodgkin lymphoma (P<0.001), Other and unspecified types of non-Hodgkin lymphoma (P<0.001), Multiple myeloma and malignant plasma cell neoplasms (P<0.001). Statistical differences of LUC% between leukemia unspecified cell type and the other diagnoses were as follows: Hodgkin lymphoma (P<0.001), Follicular lymphoma (P<0.001), Non-follicular lymphoma (P<0.001), Other and unspecified

types of non-Hodgkin lymphoma (P<0.001), Malignant immunoproliferative diseases (P<0.001), Multiple myeloma and malignant plasma cell neoplasms (P<0.001), Lymphoid leukaemia (P<0.001), Myeloid leukaemia (P<0.001), Other leukaemias of specified cell type (P<0.001).

DISCUSSION

As far as the authors know, the LUC% among malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic, and related tissue was evaluated retrospectively for the first time with a biochemistry laboratory perspective.

LUC parameters were evaluated in various hema-

^{*}Chi-squared test.

Table 3. The Quantitative data among age intervals

| | | Age intervals | | | | | |
|--|------|---------------|-----|----------|-------|---------|----------|
| | 0-18 | 8 | 18 | -64 | 65 ar | nd over | P value* |
| | n | % | n | % | n | % | |
| LUC% | | | | | | | |
| LUC % <4.5 | 205 | 86.1 | 766 | 89.7 | 488 | 79.0 | < 0.001 |
| LUC % ≥4.5 | 33 | 13.9 | 88 | 10.3 | 130 | 21.0 | |
| Preliminary diagnosis | | | | | | | |
| Hodgkin lymphoma | 24 | 10.1 | 151 | 17.7 | 26 | 4.2 | < 0.001 |
| Follicular lymphoma | 4 | 1.7 | 21 | 2.5 | 21 | 3.4 | |
| Non-follicular lymphoma | 13 | 5.5 | 56 | 6.6 | 47 | 7.6 | |
| Mature T/NK-cell lymphomas | 1 | 0.4 | 24 | 2.8 | 11 | 1.8 | |
| Other and unspecified types of non-Hodgkin lymphoma | 10 | 4.2 | 128 | 15.0 | 113 | 18.3 | |
| Malignant immunoproliferative diseases | 0 | 0 | 4 | 0.5 | 5 | 0.8 | |
| Multiple myeloma and malignant plasma cell neoplasms | 0 | 0 | 84 | 9.8 | 142 | 23.0 | |
| Lymphoid leukaemia | 175 | 73.5 | 200 | 23.4 | 132 | 21.4 | |
| Myeloid leukaemia | 7 | 2.9 | 175 | 20.5 | 97 | 15.7 | |
| Other leukaemias of specified cell type | 0 | 0 | 6 | 0.7 | 13 | 2.1 | |
| Leukaemia of unspecified cell type | 3 | 1.3 | 5 | 0.6 | 9 | 1.5 | |
| Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue | 1 | 0.4 | 0 | 0 | 2 | 0.3 | |

LUC=Large Unstained Cells

tological conditions. According to Merter *et al.*, LUC may play a role in the timing of CD34 counting by flow cytometry in peripheral blood and also LUC may be used to predict the mobilization success [6].

In a study involving 118 acute leukemia patients, LUC values were found as follows; M1 leukemias had high proportions of LUC, M2 and M3 leukemias had low LUC values, M4 leukemias had large and M5 leukemias had very large numbers of LUC [11]. It has been suggested that LUC % could be useful for improving chronic B-cell leukemia diagnostic reproducibility [12].

It has been stated that adding the LUC parameter to the reflex review parameters in acute leukemia patients concluded in all acute leukemia patients' detection [13].

A LUC % value above 10 % may indicate an ac-

celerated stage of chronic granulocytic leukemia [14]. In a study, that included 148 chronic B-lymphocytic leukemia patients with no treatment before, an association among LUC values and survival was found. It was stated that the increase in LUC numbers coincided with the worsening of the clinical condition [15].

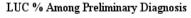
In a study including 48 untreated and 30 treated patients whose diseases directly or indirectly affected hematopoiesis, the LUC value was found to be high in patients with refractory anemia with excess blasts or in transformation, and dys-myelopoietic syndrome while the LUCvalue was found to be low in patients with lymphoma [16]. The LUC rate is increased in myelodysplastic syndrome [17]. Investigating the cell suspensions stated that the LUC value was higher in non-Hodgkin's lymphoma patients and lower in patients with non-neoplastic lymphadenopathies [18].

^{*}Chi-squared test (Likelihood Ratio).

Table 4. The LUC% data among preliminary diagnosis

| | | LU | C% | | |
|--|-----|--------|-----|--------|----------|
| | LUC | % <4.5 | LUC | % ≥4.5 | P value* |
| | N | % | N | % | |
| eliminary diagnosis | | | | | |
| Hodgkin lymphoma | 198 | 13.6 | 3 | 1.2 | < 0.001 |
| Follicular lymphoma | 45 | 3.1 | 1 | 0.4 | |
| Non-follicular lymphoma | 105 | 7.2 | 11 | 4.4 | |
| Mature T/NK-cell lymphomas | 36 | 2.5 | 0 | 0.0 | |
| Other and unspecified types of non-Hodgkin lymphoma | 230 | 15.8 | 21 | 8.4 | |
| Malignant immunoproliferative diseases | 9 | 0.6 | 0 | 0.0 | |
| Multiple myeloma and malignant plasma cell neoplasms | 210 | 14.4 | 16 | 6.4 | |
| Lymphoid leukaemia | 366 | 25.1 | 141 | 56.2 | |
| Myeloid leukaemia | 241 | 16.5 | 38 | 15.1 | |
| Other leukaemias of specified cell type | 10 | 0.7 | 9 | 3.6 | |
| Leukaemia of unspecified cell type | 7 | 0.5 | 10 | 4.0 | |
| Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue | 2 | 0.1 | 1 | 0.4 | |

LUC=Large Unstained Cell.



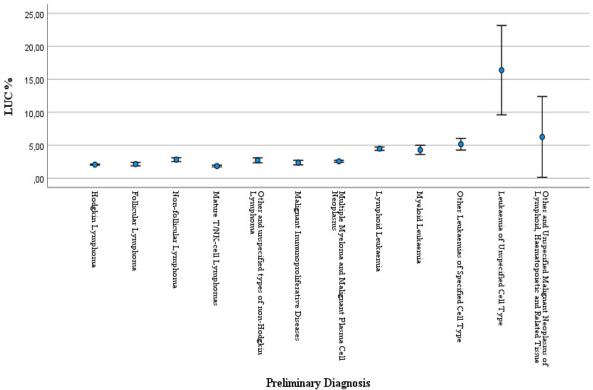


Fig. 1. LUC% among preliminary diagnosis.

^{*}Chi-squared test,

Table 5. Median and interquartile values of LUC% among preliminary diagnosis

| | LU | С% |
|--|--------|------------|
| Preliminary D, diagnosis | Median | IQR |
| Hodgkin lymphoma | 2 | [1.5-2.5] |
| Follicular lymphoma | 2.1 | [1.3-2.6] |
| Non-follicular lymphoma | 2.2 | [1.7-2.9] |
| Mature T/NK-cell lymphomas | 1.7 | [1.4-2.1] |
| Other and unspecified types of non-Hodgkin lymphoma | 1.9 | [1.5-2.6] |
| Malignant immunoproliferative diseases | 2.1 | [1.9-2.75] |
| Multiple myeloma and malignant plasma cell neoplasms | 2.2 | [1.6-3.1] |
| Lymphoid leukaemia | 2.7 | [1.8-5] |
| Myeloid leukaemia | 1.9 | [1.5-2.8] |
| Other leukaemias of specified cell type | 4.3 | [2.6-6.4] |
| Leukaemia of unspecified cell type | 7.5 | [2.2-16.7] |

LUC=Large Unstained Cell, IQR=Interquartile Ranges

In the present study, a statistical difference in the LUC % data in the case of LUC% <4.5 and LUC% \geq 4.5 among preliminary diagnoses was observed (P<0.001). LUC% was higher in patients with Hodgkin Lymphoma than in Myeloid leukaemia patients (P=0.002).

LUC% was higher in the Lymphoid leukaemia patients than in the patients with Hodgkin lymphoma (P<0.001), Other and unspecified types of non-Hodgkin lymphoma (P<0.001), Multiple myeloma and malignant plasma cell neoplasms (P<0.001).

LUC% was higher in patients with leukemia unspecified cell type than Hodgkin lymphoma (P<0.001), Follicular lymphoma (P<0.001), Non-follicular lymphoma (P<0.001), Mature T/NK-cell lymphomas (P<0.001), Other and unspecified types of non-Hodgkin lymphoma (P<0.001), Malignant immunoproliferative diseases (P<0.001), Multiple myeloma and malignant plasma cell neoplasms (P<0.001), Lymphoid leukaemia (P<0.001), Myeloid leukaemia (P<0.001), Other leukaemias of specified cell type patients (P<0.001).

Not only in hematologic diseases but also changes in LUC were observed in some different diseases. LUC is a valuable parameter that can help assess immune activation levels in HIV infection [19]. It has been noted that the LUC% value changes significantly in HIV-infected individuals and correlates with mark-

ers of immune activation and disease progression [20]. Shin et al. [21] suggested that the LUC% parameter could be used to differentiate varicella caused by varicella zoster from Kaposi's varicelliform eruption and disseminated herpes zoster. It has been stated that WBC, LUC, neutrophils, lymphocytes, and platelets bind to dengue virus-infected endothelial cells more than control group endothelial cells, and this increase in binding may be the cause of the neutropenia and thrombocytopenia that occur in dengue hemorrhagic fever [22]. In Nixon et al.'s study [23], as a result of 9000 whole blood analyses, 62 patients had high LUC values and were followed up for signs of viral infection. It was stated that 40 patients had viral infections, 26 of which were caused by the Epstein-Barr virus. Changes in LUC may be due to medication. In a study conducted by Bononi et al. [24], it was stated that the LUC value could be one of the biological indicators of leukocyte recovery after chemotherapy in the hematological response to the rHu-G-CSF medication.

Strengths and Limitations

The strengths of the present study were as follows: Our study contains 13 months of data from one of the largest hospitals in Türkiye. Only the first result and preliminary diagnosis of each patient were included. LUC% values were analyzed according to gender, age, and preliminary diagnosis, and the results were presented.

In light of the literature, our study's limitation is that it did not include information about the patient's medication and additional diseases.

CONCLUSION

In our study that evaluated the LUC% value retrospectively from a laboratory perspective some differences were observed in LUC% in lymphoid, haematopoietic, and related tissue's malignant neoplasms. Prospective studies including patient and control groups may be useful in assessing LUC%. The present study underscores the importance of LUC% in line with ICD-10 and may provide ideas for new research.

Ethical Statement

This study was approved by the Ankara City Hospital Clinical Research Ethics Committee No. 1 (Decision no. E1-20-481, date: 30.04.2020).

Authors' Contribution

Study Conception: GG, SE, EA, GY, ÖE, FMY; Study Design: GG, SE, EA, GY, ÖE, FMY; Supervision: GG, SE, EA, GY, ÖE, FMY; Funding: N/A; Materials: N/A; Data Collection and/or Processing: GG, SE, EA, GY, ÖE, FMY; Statistical Analysis and/or Data Interpretation: GG, SE, GY, ÖE; Literature Review: GG, SE, GY, ÖE, FMY; Manuscript Preparation: GG, SE, EA, GY, ÖE, FMY and Critical Review: GG, SE, EA, GY, ÖE, FMY.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Primary Health Care

Analysis of validity and reliability of the risk assessment form for children

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ABSTRACT

Objectives: This study aimed to evaluate the psychometric parameters of an assessment tool developed by Turkish Ministry of Family and Social Services in 2024 to identify risks faced by children under vulnerable conditions.

Methods: In the research, the scientific validity and reliability of the "Risk Assessment Form for Children" were examined. The study was designed as a cross-sectional survey employing a quantitative approach. The sample was obtained by the simple random sampling method. Data were obtained from 418 children through the developed form.

Results: Data analysis was performed to assess the construct validity of the risk items, utilizing the Cronbach's alpha (α) value for reliability analysis. Factor analysis was used in the validity assessment. The form reveals an adequate distribution as determined by the explanatory factor analysis of the Kaiser-Meyer-Olkin test. Cronbach's alpha (α) was calculated to be 0.9. Six sub-dimensions have been identified. A robust consistency has been seen among the sub-dimensions of the shape.

Conclusions: The findings indicate that the Risk Assessment Form for Children comprises 46 components in total. The findings demonstrate that the form is a reliable measurement tool for assessing risks to children. **Keywords:** Vulnerable child, risk factors, validity, reliability, measurement

ulnerable groups generally need more social protection and assistance to improve their physical, psychological, social, cultural, economic, and political conditions [1]. Children are consistently overrepresented in vulnerable population, involving adverse conditions and risky environment affect their development and increase their need for

protection. The children under vulnerable conditions generally refer to children who experience neglect and abuse, are raised by a single parent, are refugees or asylum seekers, suffer from substance dependence, are in child labor, engage in criminal activities, have emotional and behavioral disorders, face health challenges, possess special needs, live on the streets, or have on-

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Available at https://dergipark.org.tr/en/pub/eurj



line addiction [2]. Due to a wide range of risks, these children's need for protection is higher than the general child population.

In fact, the challenging life situations encountered by children represent a global concern. It is estimated that over one billion children between the ages of 2-17 suffer from maltreatment, such as neglect or physical, sexual, or emotional abuse [3]. According to, one billion children globally are living in multifaceted poverty, which affects their access to basic necessities like food, water, housing, healthcare, and education [4]. In addition to poverty, many children around the world are severely impacted by conflict and the climate disaster [5]. Once more, it has been estimated that 300 million children between the ages of 2-4 are exposed to physical and/or psychological abuse by their parents or other caregivers [6]. It is estimated that at least 140 million children globally lack parental care when a variety of factors are taken into consideration; however, the true number is likely higher than official figures [7]. In Turkish context, around 350,000 children have lost one or both of their parents, 720,000 children aged 5 to 17 work in economic activities, 4.1% of children aged 5 to 14 have a disability in at least one bodily function, and seven million children live in poverty, according to official data [8, 9, 10, 11]. On the other hand, due to Turkey's substantial children population, which includes a significant non-resident migrant demographic, the child protection system must prioritize severe risks impacting children. Furthermore, in a changing society, the number of vulnerable children will probably increase considerably, necessitating the implementation of effective child protection and preventative measures [12].

To protect children under vulnerable conditions, immediate assessment and prioritize of the risks are essential [13]. The evaluation of risk factors aims to ensure the child's best interests by reducing and eliminating elements that harm the child through protective and preventive measures [14]. Assessing risk factors that adversely impact children's life and development is essential for identifying their vulnerability and represents a fundamental element of an efficient child protection system [15]. Risk assessment helps determine the nature and extent of the risk by considering potential dangers that could harm children and families, as well as the current conditions of vulnerability [16, 17]. Consequently, it is necessary to effectively

use risk assessment tools by integrating them into protective and preventive services as well as case management processes [18].

These processes require a multidimensional perspective, an interdisciplinary approach, interinstitutional collaboration, and a holistic strategy [19]. The expertise, knowledge, skill level, and value awareness of professionals are important for the success of professional methods in identifying, analyzing, and interpreting risks [20].

The risk identification process involves assessing risks in different dimensions (cultural, environmental, social) an categorizing the level of detected risks (low, medium, or high). This is crucial for developing appropriate service models and intervention programs for children [21]. Public institutions and non-governmental organizations serving at-risk youth must undertake risk assessment processes in a comprehensive and holistic manner [20]. Structured measurement and evaluation tools employed in particular countries enable practitioners to perform assessments with enhanced clarity, specificity, and transparency; concurrently, they significantly reduce adverse effects such as bias and exclusion in the proposed services [22].

This study aimed to evaluate the scientific validity and reliability of the "Risk Assessment Form for Children," developed by the Ministry of Family and Social Services in 2024, which is based on scale design, in order to identify the risks affecting children under vulnerable conditions within the specified framework.

METHODS

The research was designed using a cross-sectional survey model based on quantitative methods. In this section, the methodological steps undertaken to determine the psychometric properties of the scale developed within the scope of the research are presented.

Ethics committee approval for the research was obtained from Giresun University Social Sciences, Science and Engineering Sciences Research Ethics Committee with the decision dated 04.04.2024 and numbered 5704, and the study was carried out between May and August 2024.

Population and Sample Selection

The research sample consists children in vulnera-

ble conditions who represent the target group for the services offered by the Ministry of Family and Social Services (MFSS). In this context, children who received services based on measures under the Child Protection Law No. 5395 (care, health, education, or counseling), obtained assistance from the Provincial Directorates of Family and Social Services, including Social and Economic Support (SED) service, and were identified in the field by the Children Are Safe Mobile Team were included in the study sample.

The sample size was determined by simple random sampling, a type of probability sampling. According to the 2022 Bulletin on Children Statistics from the Turkiye Statistics Institute, with a total children population of 22,578,378, the sample size was calculated as follows. Minimum numbers have been determined for the number of children to be included in the study (Min.≅384).

$$n_0 = \frac{Nt^2pq}{d^2(N-1) + t^2pq} = \frac{22578378(1,96)^20,5*0,5}{(0,05)^2(22578378 - 1) + (1,96)^2*0,5*0,5} \cong 384$$

The t-table value is 1.96 with a 95% probability. Due to the presence of both high-risk and low-risk youngsters, P=0.5, q=0.5

N=Total population size

P=The frequency of the occurrence under examination

q=The frequency of the occurrence not being observed

t=the theoretical value obtained from the t-table at a specific degree of freedom and defined error level.

d=the deviation intended based on the frequency of the event's occurrence.

Layer weight =
$$\frac{384}{22578378}$$
 = 0.000017007 (whoel sample)

The study retrieved data on 418 children. The pilot study provided a statistically representative sample of children from the population. It is aimed to reflect the information obtained from the participating children, their parents, teachers, healthcare workers, and security personnel about the risks the sampled children are exposed to in the data collection tool.

Data Collection Tools

Data were collected using the Short Information

Form to obtain the socio-demographic details of the children in the sample, and the Draft Risk Assessment Form, developed by the researchers and validated for content validity based on professionals' reviews, to identify risks related to the children.

The Draft Risk Assessment Form, intended for validity and reliability studies in the research, contains items aimed at identifying risks related to children. Each item includes a response scale to determine the presence and level of the risk it describes. The response scale is of the 5-point Likert type and includes the categories "Very low risk (-2)", "Low risk (-1)", "Uncertain risk (0)", "High risk (+1)", and "Very high risk (+2)".

During the data collection for content validity, an online version of the form was developed for effective implementation. Researchers gave comprehensive training to professionals on utilizing the Risk Assessment Form for data gathering. Thus, structure of the form incorporates a data gathering methodology grounded in professional assessments and observations, as instead of participants' self-reporting.

Statistical Analysis

In this section, results from validity and reliability analyses of the Draft Risk Assessment Form are presented.

Descriptive Anaysis

The demographic information includes numerical and percentage values as descriptive statistics. Demographic data includes information such as gender, nationality, family status, school enrollment, protective measures, unaccompanied status, and risk to personal safety.

Analyses of Validity and Reliability

The exploratory factor analysis of the acquired data set was conducted using the IBM SPSS Statistics Standard Concurrent User v.27 statistical software package. In exploratory factor analysis, dimensions representing the linear combination of observed variables serve as factors.

Factors are hypothetical variables formed by the observed variables. In the statistical testing of the correlation between variables in the data matrix, the Bartlett test of sphericity is used. The Bartlett test of sphericity determines whether the matrix generated by

the items is an identity matrix. Additionally, the Kaiser-Meyer-Olkin (KMO) measure, obtained by utilizing correlation and partial correlation coefficients, is also an important criterion for evaluating the suitability of the data for factor analysis.

In the study, the principal component method was used to obtain the factors. In determining the appropriate number of factors, the criterion of selecting as many factors as the number of eigenvalues greater than one has been taken into account. Furthermore, factor rotation was conducted to clarify the variables that contribute to the development of each common factor. The varimax approach was utilized for the specified procedure. Since the data did not follow a normal distribution in the analysis of correlations between factors, the Spearman rho coefficient was used. Confirmatory factor analysis was also applied to test the suitability of the factors obtained through exploratory factor analysis to hypothetical or theoretical factor structures. Confirmatory factor analysis is used to validate the structure obtained from exploratory factor analysis or the theoretical factor structure [20]. In exploratory factor analysis, the appropriate number of factors that will define the underlying structure is determined based on the data matrix, whereas in confirmatory factor analysis, the number of factors is known a priori. In the study, the open-source statistical package Jamovi (Version 2.4.8) was used for confirmatory factor analysis.

RESULTS

This section presents the development process, the descriptive findings of the participants, and the exploratory and confirmatory factor analyses results for the assessment form. The draft tool which was employed in the data collection phase is referred to "Risk Assessment Form for Children" in this section. The results that derived from the form's implementation are detailed below.

Development Process of the Risk Assessment Form for Children

The development process of the Risk Assessment Form for Children has been carried out in three main stages. The stages are explained in detail below.

1. Generating an item pool: A comprehensive pool

of items identifying risks has been established through literature reviews and field studies to identify the items that represent risks impacting the target group. Current assessment tools such as Core Assessment Record, which is provided under Common Assessment Framework in the UK, were useful in generating the item pool. Additional sources referred to include the Guidance Needs Assessment Questionnaire (RİBA), employed by the Turkish Ministry of National Education, along with two others: the Evaluation Guide for Professionals in Child Protection and the Individual Risk Assessment Form (BİRDEF) utilized by the Turkish Ministry of Family and Social Services [9, 23].

In the development process, the perspectives of professionals in the field of social services-such as social workers, psychologists, psychological counselors, educators, law enforcement officers, and municipal officials-who interacted with children in vulnerable situations and delivered various services during field visits across different provinces have been helpful. A detailed list of items, including definitions of potential risks that encountered by children under vulnerable conditions, was gathered for the formation of risk assessment tools. A total of 198 items have been obtained.

- 2. Analyzing scope validity: Examining the relevancy of 198 items in the item pool was performed by the opinions of professionals from various provinces. This phase was carried out with 45 professionals participating online workshops in three different sessions by their convenience. The professionals were requested to express their opinions on the items created into an online format by selecting the options "not appropriate," "requires correction," and "appropriate." Accoring on the collected comments, 98 items with a KVO (Scope Validity Index) score of 50 or higher were included in the pilot study. The scope validity phase has been established, and the first edition of the Risk Assessment Form for Children has been produced.
- 3. Conducting the pilot study: Professionals working for the Ministry of Family and Social Services participated in the real-world implementation of the draft form developed in accordance with the scope of validity. Training sessions on the proper application of the form were conducted for 150 professionals assigned with the implementation process. These professionals filled out the form by interviewing the children and/or their families, utilizing file information, relying on their observations of the children, or

consulting the opinions and information of other related professionals. In the pilot study, data of 418 was children obtained.

Sociodemographic Characteristics

Within the scope of the study, descriptive sociodemographic information about the children from whom data were obtained using the risk assessment form is presented in Table 1.

Table 1 reveals that the vast majority of the children are Turkish citizens, however other ethnicities are also included. 43% of participants live with both parents, 23% have divorced parents, 16% live apart from their parents. 87% of children (326) attend school, while 22% (92) do not. Risk screenings for children are mostly initiated by familial risk (34%, 141). This

is followed by street risks (17%), parental loss (12%), and school risks (10%). For two-thirds of the children (63%), no preventative measures were taken, whereas such measures had been applied to about one-third (37%). No life threats were reported for the vast majority of children (97%), 3% of the sample has been reported as unaccompanied.

Results of Exploratory Factor Analysis

The KMO test assesses the adequacy of a distribution for factor analysis, with a result exceeding 0.60 deemed marginally suitable for this purpose. The KMO value in this study exceeds the threshold level. The Bartlett test yielded a result of 35437.555 (P<0.001). The results indicate that the variable is multivariate within the population parameter. Variance

Table 1. Descriptive characteristics about children included in the research sample

| Sociodemographics | | n | % |
|---|-----------------------------|-----|------|
| Gender | Girl | 222 | 46.9 |
| | Boy | 196 | 53.1 |
| Nationality | Turkiye | 388 | 93.0 |
| | Other | 30 | 7.0 |
| Family status | Parents together | 179 | 43.0 |
| | The parents are divorced. | 98 | 23.0 |
| | The parents live separately | 65 | 16.0 |
| | Mother has passed away | 19 | 5.0 |
| | Dad has passed away | 57 | 11.0 |
| Child's school enrollment | Yes | 326 | 78.0 |
| | No | 92 | 22.0 |
| The starting point of screening | Family risks | 141 | 34.0 |
| | Street-related risks | 74 | 17.3 |
| | Parental loss | 51 | 12.2 |
| | School-related risks | 44 | 10.5 |
| | Other | 108 | 26.0 |
| Precautionary measures undertaken for the child | Yes | 152 | 37.0 |
| | No | 266 | 63.0 |
| The child's unaccompanied status | No | 406 | 97.0 |
| | Yes | 12 | 3.0 |
| Life safety risks | No | 387 | 93.0 |
| | Yes | 31 | 7.0 |
| Total | | 418 | 100 |

Table 2. Variances of scale factors and factor loadings in pretest results

| | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 | Factor 6 |
|-----------------------------|----------|----------|----------|----------------|----------|----------|
| Item 1 | 0.788 | | | | | |
| Item 2 | 0.742 | | | | | |
| Item 3 | 0.738 | | | | | |
| Item 4 | 0.703 | | | | | |
| Item 5 | 0.685 | | | | | |
| Item 6 | 0.671 | | | | | |
| Item 7 | 0.641 | | | | | |
| Item 8 | 0.635 | | | | | |
| Item 9 | 0.623 | | | | | |
| Item 10 | 0.622 | | | | | |
| Item 11 | 0.622 | | | | | |
| Item 12 | 0.600 | | | | | |
| Item 13 | 0.595 | | | | | |
| Item 14 | 0.592 | | | | | |
| Item 15 | 0.575 | | | | | |
| Item 16 | 0.560 | | | | | |
| Item 17 | | 0.789 | | | | |
| Item 18 | | 0.782 | | | | |
| Item 19 | | 0.768 | | | | |
| Item 20 | | 0.748 | | | | |
| Item 21 | | 0.689 | | | | |
| Item 22 | | 0.670 | | | | |
| Item 23 | | 0.653 | | | | |
| Item 24 | | 0.603 | | | | |
| Item 25 | | 0.583 | | | | |
| Item 26 | | | 0.673 | | | |
| Item 27 | | | 0.647 | | | |
| Item 28 | | | 0.627 | | | |
| Item 29 | | | 0.624 | | | |
| Item 30 | | | 0.599 | | | |
| Item 31 | | | 0.583 | | | |
| Item 32 | | | 0.550 | 0.650 | | |
| Item 33 | | | | 0.659 | | |
| Item 34 | | | | 0.633 | | |
| Item 35 | | | | 0.628 0.615 | | |
| Item 36 Item 37 | | | | 0.613 | | |
| Item 38 | | | | 0.541 | 0.724 | |
| Item 39 | | | | | 0.724 | |
| Item 40 | | | | | 0.717 | |
| Item 41 | | | | | 0.623 | |
| Item 42 | | | | | 0.023 | 0.578 |
| Item 43 | | | | | | 0.578 |
| Item 44 | | | | | | 0.548 |
| Item 45 | | | | | | 0.548 |
| Item 46 | | | | | | 0.547 |
| Eigenvalue | 28.569 | 8.609 | 4.902 | 4.290 | 3.350 | 2.859 |
| Variance explanation rate % | 12.111 | 11.081 | 9.074 | 8.483 | 6.224 | 5.606 |
| Croncbach's alpha | 0.934 | 0.922 | 0.877 | 0.855 | 0.865 | 0.774 |
| Стопсоаси в агриа | 0.934 | 0.922 | 0.0// | 0.033 | 0.003 | 0.//4 |

Total explained variance (%)=52.579 Kaiser Meyer Olkin (KMO)=0.924 Bartlett test value =35437.555; P<0.001 Croncbachs' Alpha (α)= 0.945

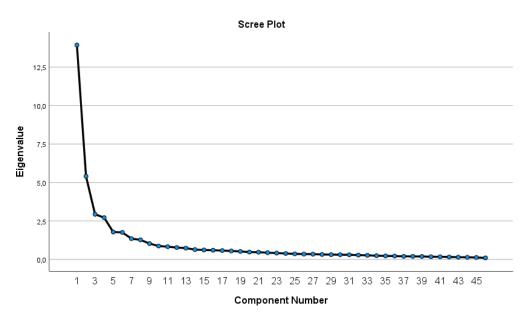


Fig. 1. Scree plot illustrating factor sub-dimensions.

ratios that fluctuate between 40% and 60% are deemed acceptable in factor analysis. (Table 2, Fig. 1).

In factor analysis, variance ratios between 60% and 80% are deemed optimal; so, the variance achieved in this study is at a satisfactory level (52.579).

The factor loadings for the pre-test results are as follows: the first dimension ranges from 0.560 to 0.788, the second dimension from 0.583 to 0.789, the third dimension from 0.550 to 0.673, the fourth dimension from 0.541 to 0.659, and the fifth dimension from 0.623 to 0.724. In the sixth dimension, the factor loadings of the questions vary from 0.547 to 0.578. (Table 2, Fig. 1).

In the reliability analysis conducted for the Risk Assessment Form for Children, the Cronbach's Alpha value was found to be 0.945. This value indicates that the form has a high degree of internal consistency. Generally, a Cronbach's Alpha value of 0.70 and above is considered sufficient for reliability. The value of 0.945 obtained in this study indicates that there is a strong consistency among the sub-dimensions of the

Risk Assessment Form for Children and that the form is a reliable measurement tool for assessing risks to children. Additionally, it shows that there is a strong relationship among the risk factors that all the items in the survey attempt to measure, and that the form can be used appropriately for its intended purpose. Therefore, it can be concluded that the Risk Assessment Form for Children can be safely used in practical applications and will provide a scientific and reliable basis for decision-making processes in the child protection system. (Table 2, Fig. 1).

Results of Confirmatory Factor Analysis

The model derived for the scale (χ 2=1836, df=847) consists of six dimensions. All dimensions are presented in Table 3, and the fit indexes show that the model reveals an acceptable fit.

Factor Correlation Analyses

As can be seen in Table 4, there are statistically significant correlations across all of the examined factors.

The analysis presents a confirmatory factor model

Table 3. Statistical metrics relating to the fit of the structural equation model

| | | | | | | | RMSEA 90% | CI |
|----------|-----|-------------|---------|-------|-------|-------|-----------|-------|
| χ^2 | df | χ^2/df | P value | CFI | TLI | RMSEA | Lower | Upper |
| 1836 | 847 | 2.16 | < 0.001 | 0.925 | 0.909 | 0.052 | 0.049 | 0.056 |

Table 4. Factor correlation analyzes

| | | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 |
|----------|---------|----------|----------|----------|----------|----------|
| Factor 2 | rho | 0.371 | | | | |
| | P value | <0.001 | | | | |
| Factor 3 | rho | 0.457 | 0.524 | | | |
| | P value | <0.001 | <0.001 | | | |
| Factor 4 | rho | 0.523 | 0.324 | 0.435 | | |
| | P value | <0.001 | <0.001 | <0.001 | | |
| Factor 5 | rho | 0.352 | 0.524 | 0.402 | 0.356 | |
| | P value | <0.001 | <0.001 | <0.001 | <0.001 | |
| Factor 6 | rho | 0.502 | 0.330 | 0.284 | 0.456 | 0.357 |
| | P value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

rho=Spearman correlation coefficient

that indicates the interrelations among the sub-dimensions of the Risk Assessment Form for Children. Confirmatory factor analysis was used to validate the structures derived from exploratory factor analysis. Fig. 2 illustrates the contribution of each sub-dimension to the overall framework of the Child Risk Assessment Form and the interrelations among these dimensions. This model illustrates the six sub-dimensions of the Risk Assessment Form for Children (Risky

Behaviors, Basic Needs, Child Labor, Exposure to Violence, Developmental Difficulties, Emotional and Psychological Symptoms) in interaction with one another. Fig. 2 shows the model developed for the confirmatory factor analysis concerning the interaction among the sub-dimensions of the examined scale.

The confirmatory factor analysis model shows that the theoretical sub-dimensions of the Risk Assessment Form for Children work consistently with each other

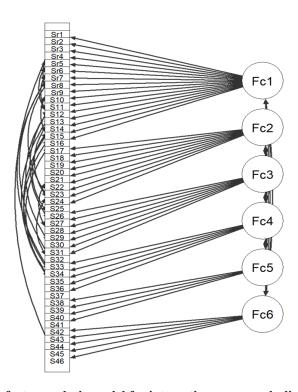


Fig. 2. Confirmatory factor analysis model for interaction among sub-dimensions of the scale.

and are suitable for assessing the risks children are exposed to. This model confirms that there is a strong relationship between the sub-dimensions of the dataset and that each dimension is valid and reliable for measuring the intended risk areas. Additionally, the results of the fit indexes presented in the model (CFI, TLI, RMSEA) indicate that the model is well-aligned with the data set (Table 3). This result supports the notion that the Risk Assessment Form for Children is a consistent and scientifically valid measurement tool for identifying risks to children.

DISCUSSION

This study examines the psychometric features of the Risk Assessment Scale for Children, a pioneering tool in Turkiye designed to assess the main risks encountered by children under vulnerable conditions.

Validity and reliability analyses ensure the scale reliably and consistently measures the phenomenon at issue [24, 25]. Validity requires a measurement tool to accurately assess the intended phenomena and assess it without ambiguity across several domains. In this instance, the scale must have goal-oriented content and undergo comprehensive construct validity evaluation [24, 26]. In comparison to scales previously established in the literature, this scale demonstrates notable differences in both comprehensiveness and originality. The Child Behavior Assessment Scale [27], the Risky Behaviors Scale [28], the Social Exclusion Scale for Children [29], the Attitude Scale towards Bullying for Children [30], the Online Child Exploitation Risk Scale [31], the Nutrition Screening Tool for Preschool Children [32], and the Research and Assessment Form for Children and Adolescents in Conflict with the Law [33] are instruments that primarily focus on specific risks encountered by children, rather than integrating various risk dimensions tied with a single case.

The current study aims to establish a framework for a combined assessment of such risks to address this issue. The six dimensions outlined by the scale (risky behaviors, unmet basic needs, child labor, exposure to violence, developmental difficulties, emotional and psychological symptoms) underscore the significance of integrating risk factors that represent the character-

istics of cases observed in the practical setting.

Several internationally developed comprehensive evaluation inventories, such as the Child and Adolescent Needs and Strengths (CANS), Structured Decision Making (SDM), and Common Assessment Framework (CAF), which included various iterations for risk assessments targeting children and families, particularly in developed nations, provided valuable insights for comparison. Using comprehensive risk assessment inventories in practice might have some disadvantages. The long and complex structure of such tools is often seen as a disadvantage from the practitioners' perspective. The fact that practitioners have to spend a long-time completing evaluation can be challenging in practice environments with a high case turnover.

On the other hand, applying and interpreting these tools effectively requires a certain level of expertise or training [34, 35, 36]. The requirements for a certain competency level and extensive training to utilize these instruments may raises challenges for institutions and organizations with constrained resources regarding personnel and infrastructure. Consequently, the current tool was designed to be both multidimensional and user-friendly while fulfilling few professional requirements.

The Individual Risk Assessment Scale (BİRDEF), developed in Turkiye, provided a primary reference for the scale examined in this study. BİRDEF has been developed as a tool to assess the risks and needs of children in institutional care [22]. In this regard, BİRDEF emphasizes on a specific category of at-risk youth. The tool addresses the present risks to children, including economic status, abuse, behavioral problems, individual characteristics, living conditions, and familial characteristics, as outlined in the assessment tool examined in this study. The Child Risk Assessment Form, on the other hand, is considered a distinguishing feature of the scale as it is designed to be applied to a broader population of children at risk. Risk assessments must incorporate contextual and cultural diversity of the risks faced by children. In this perspective, cultural sensitivity was prioritized in the scale development process, and ongoing engagement with field professionals was emphasized along the development process [37].

To figure out the structural validity of the scale, a factor analysis model was employed, and upon

analysing the statistical values related to the fit of the structural equation model, it can be concluded that the model's fit indexes are at an acceptable level. The KMO value obtained prior to factor analysis should exceed 0.50 to ensure sample size sufficiency [37]. The KMO test result in our study is 0.924. The KMO value in the study is at a borderline acceptable level. To determine the adequacy of the sample size, the outcome of the Bartlett test of sphericity must be statistically significant. The Bartlett test result in our study was 35437.555 (P<0.001). This result indicates that the measurement variable is multivariate in the population parameter. This study considered variance ratios in factor analysis acceptable between the 40% to 60% range.

In factor analysis, given that variance ratios between 60% and 80% are ideally accepted, it can be asserted that the variance acquired in this research is also at an adequate level (52.579). The KMO test returned a value of 0.924, and the findings of the Bartlett test for sphericity analysis were also examined. The Cronbach α analysis performed to evaluate the reliability coefficients of the scale indicates that the coefficients are adequate. The Cronbach α method is particularly recommended to evaluate the reliability of Likert-type scales and serves as a methodology for calculating the internal consistency of the items within the measurement tool [38]. To define a measurement tool appropriate, the reliability coefficient should approach [39]. The Cronbach α coefficient indicates measurement instrument reliability as follows: less than 0.40 signifies unreliability; 0.40-0.59 indicates moderate reliability; 0.60-0.79 reflects considerable dependability; and 0.80-1.00 represents great reliability [37]. The study calculated Cronbach's α to assess internal consistency dependability. The Cronbach's a reliability coefficient was determined to be 0.945. The internal consistency of the scale is significantly reliable.

The Risk Assessment Form for Children presented in the study indicates adequate distribution as indicated by the Kaiser-Meyer-Olkin test and exploratory factor analysis. The confirmatory factor analysis model demonstrates that the theoretical sub-dimensions of the form are consistently aligned and appropriate for assessing the dangers faced by children. The confirmatory factor analysis model demonstrates strong connections among the sub-dimensions of the scale, affirming the validity and reliability of each dimension in assessing the designated risk areas.

CONCLUSION

The Child Risk Assessment Form, developed to identify risks affecting children under vulnerable conditions, functions as a comprehensive and reliable tool for assessing such risks in Turkiye. To improve the efficacy of the child protection system, it is crucial to precisely and consistently identify risks, particularly for early interventions. These sub-dimensions systematically address the risks encountered by children, facilitating the establishment of protective and preventative measures. The form influences practitioners' decision-making processes, establishing a scientifically grounded basis for policies and actions focused on child protection.

Evaluation tools based on systematic and scientific foundations play a critical role in the development of child protection policies. Therefore, sharing the results of risk assessments with policymakers will contribute to decisions regarding children's rights being based on more solid foundations. At the national level, it is recommended that these results be incorporated into policy development processes. Additionally, addressing risk assessment processes with a multidisciplinary approach that includes experts from various sectors such as health, education, and security, not just social service professionals, will ensure a more comprehensive evaluation of risks. Therefore, it is recommended to strengthen the cooperation mechanisms with all relevant stakeholders during the implementation process of the Risk Assessment Forum for Children. Additionally, considering the diversity of risks faced by children in different regions, it is important to conduct risk analyses that take regional differences into account. In this context, it is recommended to develop unique service models for each region based on the data from the Risk Assessment Form for Children and to create intervention strategies tailored to regional needs.

It is recommended that the training of practitioners utilizing the Risk Assessment Form for Children be constantly updated, and that training programs focused on the proper effective use of the form should be developed. Additionally, the proficiency of practitioners in risk identification can be improved, and additional qualitative data can be acquired. Furthermore, to guarantee that the risk assessment outcomes are not limited to temporary detections, continuous monitoring of

children should be implemented. The data obtained through the Risk Assessment Form for Children can be utilized to monitor changes in children's risk situations over time and to assess the efficacy of intervention efforts. Ultimately, providing the Risk Assessment Form for children on digital platforms would facilitate more rapid and more effective data processing.

Furthermore, it is recommended to implement a national data tracking system to continuously evaluate risks to children and enhance service delivery with current data. This method facilitates the creation of risk maps at both regional and national levels. The national implementation of the Risk Assessment Form for Children will improve the quality of child protection programs and assist in the effective mitigation of risks faced by children.

In conclusion, subsequent research informed by these recommendations will enhance the fficacy of child protection programs by broadening comparative analyses and supporting them with additional data.

Ethical Statement

Ethics committee approval for the research was obtained from Giresun University Social Sciences, Science and Engineering Sciences Research Ethics Committee with the decision dated 04.04.2024 and numbered 5704, and the study was carried out between May and August 2024.

Authors' Contribution

Study Conception: MT, NÇ, AS, TT, İKE; Study Design: MT, NÇ, AS, TT, İKE; Supervision: MT, NÇ, AS; Funding: TT, İKE; Materials: MT, NÇ, AS, TT, İKE; Data Collection and/or Processing: MT, NÇ, AS, TT, MAT; Statistical Analysis and/or Data Interpretation: MAT; Literature Review: MT, NÇ, AS; Manuscript Preparation: MT, NÇ, AS, TT, MAT and Critical Review: MT, NÇ, AS, TT, İKE, MAT.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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The authors disclosed that they did not receive any grant during the conduction or writing of this study.

Annotation

This study was carried out as a task within the project titled as "Technical Assistance for the Support for Children's Rights in Turkiye" which implemented under the EU Instrument for Pre- accession Assistance (IPA-2). In the scope of Project Activity 4.1 "Development of methods for identifying children under vulnerable conditions", the authors committed to develop tools for identifying children at-risk for the Main Beneficiary of the project, the Turkish Ministry of Family and Social Services.

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Editor's note

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Gastroenterological Surgery

Comparison of preoperative and postoperative frailty in elderly following gastrointestinal cancer surgery

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ABSTRACT

Objectives: This study aimed to compare preoperative and postoperative frailty status in patients undergoing elective gastrointestinal cancer surgery using the FRAIL (Fatigue, Resistance, Ambulation, Illness, and Loss of weigh) and Clinical Frailty Scale (CFS) indices and to determine the relationship between frailty and early postoperative complications as well as surgical outcomes.

Methods: This prospective study included patients aged 65 years and older who underwent elective gastrointestinal cancer surgery. Preoperative and early postoperative frailty assessments were conducted using the FRAIL and CFS scores. Statistical analyses were conducted to investigate the association between frailty scores and surgical/clinical outcomes.

Results: Of the 91 patients included in the studythe mean age was 70.9 ± 6.1 years (range: 65-75). The mean FRAIL score increased postoperatively (1.9±1.2 preoperatively to 2.3±1.5 postoperatively, Δ post-pre: 0.4±0.9, P<0.001). A similar trend was observed in the CFS scale, the mean CFS score increased postoperatively (4.8±1.2 preoperatively to 5.1±1.6, postoperatively, Δ post-pre: 0.3±0.8, P<0.001). Patients with higher baseline frailty levels exhibited longer hospital stays (P=0.015), higher mortality rates (P=0.030), and increased rates of discharge with an ostomy or drain (P=0.003).

Conclusions: Our findings suggest that while frailty scores may increase postoperatively, higher baseline frailty score is associated with several adverse outcomes, including prolonged hospital stays, increased mortality, and a higher likelihood of requiring ostomies or drains upon discharge.

Keywords: Elderly patient, frailty, gastrointestinal cancer surgery, mortality, FRAIL, CFS scale

ancer is an important health problem that increases in frequency with age. The number of cancer cases, which was determined to be 1.6 million in 2010, is expected to increase to 2.3 million in 2030. The most important reason for the increase in cancer cases is the aging population. It is expected that 67% of total cancer cases will be elderly individuals [1]. Gastrointestinal (GI) system cancers are very

common cancers, accounting for 1 in 4 cancer cases and 1 in 3 cancer deaths worldwide [2]. Surgical treatment is the gold standard for GI system cancers; however, the physiological limitations of older individuals, including their physical condition and comorbidities, can significantly impact their ability to tolerate surgical interventions. Another factor affecting the success of GI system cancer surgeries is frailty [3].

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Frailty, a physiological decline associated with a marked sensitivity to stress factors, is a complex syndrome with diverse clinical consequences [4]. It is common in older patients. Frailty in the elderly is a complex condition that often results from diminished physiological reserves and a weakened ability to maintain homeostatic balance. These factors, combined with age-related physiological changes, increase an individual's susceptibility to environmental stressors. The risk of morbidity and mortality increases in frail elderly individuals, especially after major medical interventions such as surgery. Therefore, when performing clinical evaluations of elderly patients, not only tumor characteristics and existing comorbidities but also the level of frailty should be taken into account [5]. However, if frailty assessment is inadequate, elderly patients may either be inadequately treated or, conversely, may be at risk of serious weakening after treatment. In this context, better understanding and managing frailty is critical to improving health outcomes of the older population. Therefore, this study aimed to compare preoperative and postoperative frailty status in patients undergoing elective gastrointestinal (GI) cancer surgery using the FRAIL (Fatigue, Resistance, Ambulation, Illness, and Loss of weigh) and Clinical Frailty Scale (CFS) indices and to determine the relationship between frailty and early postoperative complications as well as surgical outcomes.

METHODS

Study Design and Setting

This is a prospective cohort study conducted on patients aged 65 years and older who underwent elective GI cancer surgery at the Department of Gastroenterological Surgery, Adana City Training and Research Hospital, Adana, Turkey, between February and December 2024. The study protocol was approved by the Institutional Ethics Committee (decision number 3178, dated 15.02.2024). Written informed consent was obtained from all participating patients.

Patients scheduled to undergo elective GI cancer surgery were prospectively enrolled in the study. Exclusion criteria included: age younger than 65 years, emergency surgery, and refusal to participate in the study.

Patients presented with the following diagnoses: rectal cancer (n=25), colon cancer (n=33), gastric can-

cer (n=19), pancreatic tumor (n=11), and hepatic tumor (n=3). All patients with gastric cancer (n=19) received neoadjuvant chemotherapy. Patients with rectal cancer received either total neoadjuvant chemoradiotherapy (n=22) or neoadjuvant chemoradiotherapy (n=3).

Preoperatively and postoperatively, all patients underwent systematic assessment using the FRAIL index and CFS. Early postoperative local and systemic complications were recorded. Data collected included; surgery type (open/laparoscopic/open after laparoscopy), length of hospital stay, need for intensive care unit (ICU), time to oral feeding resumption, mortality status, and FRAIL index and CFS scores. The patients' biochemical laboratory data were also recorded. Mortality was defined as death occurring within 30 days of discharge or during the postoperative hospital stay. Demographic characteristics incuding; gender, marital and educational status, smoking habits, alcohol consumption, body mass index (BMI) were also noted. Statistical analyses were performed to compare preoperative and postoperative frailty scores and to investigate the association between frailty and surgical outcomes.

Frailty Assessment

Two distinct frailty assessment tools were employed: the Clinical Frailty Scale (CFS) and the FRAIL Scale. Both scales were administered to each patient twice: preoperatively and 48 hours postoperatively. Patients were evaluated preoperatively either during their outpatient clinic visit for preoperative preparation prior to elective surgery or upon hospital admission.

The CFS, a clinician-rated scale, assesses frailty based on overall clinical judgment. It utilizes a 9-point scale (1-9), where 1 represents "very healthy" and 9 represents "end-stage patient." Individuals were categorized as "non-frail" (CFS score 1-3), "pre-frail" (CFS score 4), and "frail" (CFS score ≥5) [6].

The FRAIL Scale is a self-reported instrument comprising five questions: 1) Fatigue; 2) Stair climbing ability; 3) Walking distance; 4) Multimorbidity (≥5 diseases); and 5) Unintentional weight loss (≥5% in 6 months). Caregivers were interviewed when patients lacked adequate cognitive function. Scores range from 0 to 5, with each component contributing one point. Individuals were classified as "non-frail" (score 0), "pre-frail" (score 1-2), and "frail" (score 3-5) [7].

Eur Res J. 2025;11(4):753-761

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY). Continuous variables were summarized as mean±standard deviation or median with interquartile range (IQR). Categorical variables were presented as frequencies and percentages. Chi-square test or Fisher's exact test (where appropriate) was used to compare categorical variables. For paired ordinal data (FRAIL Scale Categories), McNemar-Bowker test was employed. The normality of the numerical variables was assessed using the Shapiro-Wilk test. Continuous data with a normal distribution were compared using Student's t test, while Mann-Whitney U test was employed when the data were not normally distributed. For comparison of 3 or more independent discrete variables Kruskal Wallis test was used. For paired samples of the continuous variables, paired samples t test or Wilcoxon signed rank test was used according to the distribution of the data. Comparison of Multiple Groups: Kruskal-Wallis test was used for comparing three or more independent groups. A P-value of less than 0.05 was considered statistically significant.

RESULTS

Study Population

Of the 91 patients included in the study, 60 (65.9%) were male and 31 (34.1%) were female. The mean age of these patients was 70.9±6.1 (65-75) years. Demographic characteristics of the patients, including educational status, marital status, clinical findings, drug usage, operation type, postoperative conditions, use of formula, colostomy status, and other relevant factors, are presented in Table 1. The median BMI value was 25.0 (Q1:22-Q3:28).

Clinical Assessments and Outcomes

Biochemical parameters, along with pre-operative and post-operative CFS and FRAIL scale values, were obtained and the results are presented in Table 2. The median hospitalization duration was 6 days (Q1:5-Q3:8), and the median ICU stay was 1 day (range 0-23). The median time to feeding initiation was 2 days (range 0-10). An evaluation of the FRAIL index revealed a significant increase in frailty post-operatively. The mean FRAIL scale score was 1.9±1.2 pre-opera-

Table 1. Demographic characteristics and clinical findings

| | | n (%) |
|-------------------------|------------------------|-----------|
| Gender | Male | 60 (65.9) |
| | Female | 31 (34.1) |
| Marital status | Married | 55 (60.4) |
| | Single | 18 (19.8) |
| | Divorced | 18 (19.8) |
| Education status | Illiterate | 6 (6.6) |
| | Literate | 10 (11.0) |
| | Primary School | 29 (31.9) |
| | Middle School | 26 (28.6) |
| | High School | 7 (7.7) |
| | University | 13 (14.3) |
| Smoking | Smoker | 33 (36.3) |
| | Nonsmoker | 46 (50.5) |
| | Ex-smoker | 12 (13.2) |
| Alcohol consumption | Yes | 7 (7.7) |
| | No | 84 (92.3) |
| Polypharmacy | Yes | 30 (33.0) |
| | No | 61 (67.0) |
| Operation type | Open | 69 (75.8) |
| | Laparoscopy | 19 (20.9) |
| | Open after laparoscopy | 3 (3.3) |
| Local complication | Yes | 27 (29.7) |
| | No | 64 (70.3) |
| Systemic complications | Yes | 13 (14.3) |
| | No | 78 (85.7) |
| Ostomy status | Yes | 23 (25.3) |
| | No | 68 (74.7) |
| Use of formula | Yes | 59 (64.8) |
| | No | 32 (35.2) |
| Discharge with drain | Yes | 9 (9.9) |
| | No | 82 (90.1) |
| Mortality | Yes | 9 (9.9) |
| | No | 82 (90.1) |

tively and 2.3 ± 1.5 post-operatively. The mean change (Δ post-pre) was calculated as 0.4 ± 0.9 (P<0.001).

Table 2. Biochemical findings and Frailty scores (CFS and FRAIL scale)

| | Mean±SD | Median (Q1-Q3) |
|-----------------------------|-------------|-----------------|
| TSH (mIU/L | 1.6±1.4 | 1.2 (0.7-1.8) |
| Vitamin D (ng/mL) | 18.4±10.6 | 15.8 (9.9-24) |
| Vitamin B12 (pg/mL) | 313.9±202.4 | 253.5 (172-398) |
| Hemoglobin (g/dL) | 11.6±2.2 | 11.7(9.8-13.4) |
| Albumin (g/dL) | 36.6±6 | 38 (32-41) |
| FRAIL scale – preoperative | 1.9±1.2 | 2 (1-3) |
| FRAIL scale – postoperative | 2.3±1.5 | 2 (1-3) |
| CFS –preoperative | 4.8±1.2 | 5 (4-6) |
| CFS -postoperative | 5.1±1.6 | 5 (4-6) |

CFS=Clinical Frailty Scale, TSH=Thyroid Stimulating Hormone, FRAIL=Fatigue, Resistance, Ambulation, Illness, and Loss of weigh, SD=standard deviation, Q1=25th percentile, Q3=75th percentile

A similar trend was observed in the CFS scale, with a higher mean score post-operatively (P=0.001). The mean change (Δ post-pre) was calculated as 0.3±0.8, with pre-operative measurements indicating a mean score of 4.8±1.2 and post-operative measurements showing a mean score of 5.1±1.6.

Frailty Status Transition

Preoperatively, 11 patients were categorized as robust, 49 as pre-frail, and 31 as frail based on the FRAIL scale (Fig. 1). Postoperatively, the distribution

shifted: 9 patients were robust, 45 were pre-frail, and 37 were frail. A detailed analysis revealed that 9 of the 11 initially robust patients transitioned to the pre-frail category postoperatively. Moreover, 8 of the 49 pre-frail patients progressed to the frail category, indicating an increase in frailty. Conversely, 11 patients demonstrated a decrease in their frailty level. Although a higher number of patients experienced an increase in frailty compared to those with a decrease, this difference did not reach statistical significance according to the McNemar-Bowker test (P=0.146).

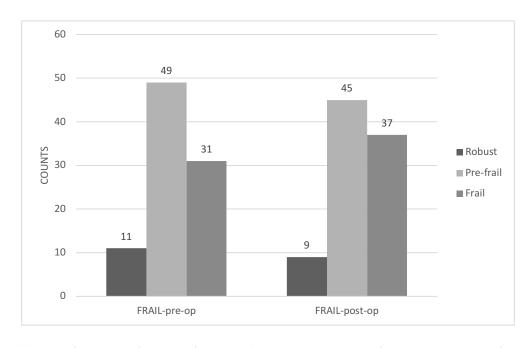


Fig. 1. Frailty categories according to FRAIL scale at pre-operatively and post-operatively

Table 3. Investigation of factors in patients with and without increased frailty according to the FRAIL scale

| | | Change i | in frailty | |
|-----------------------------|------------------------|------------------|--------------------|---------|
| | | Did not | Increased | P value |
| | | change/decreased | | |
| TSH (mIU/L | | 1.21 (0.75-1.65) | 1.26 (0.685-1.845) | 0.847 |
| Vitamin D (ng/mL) | | 15.9 (9.1-23.7) | 15.1 (11.8-24.4) | 0.934 |
| Vitamin B12 (pg/mL) | | 273 (184-398) | 224 (162-399) | 0.330 |
| Hemoglobin (g/dL) | | 12.2 (10.1-13.5) | 11.1 (9.7-12.9) | 0.151 |
| Albumin (g/dL) | | 38 (37-43) | 35 (30-39) | 0.001 |
| Operation duration (minu | utes) | 197 (140-244) | 230 (165-263) | 0.189 |
| Duration of hospitalization | on (days) | 6 (5-7) | 7 (5-12) | 0.015 |
| Time to feeding (hours) | | 2 (1-3) | 3 (1.5-3) | 0.132 |
| Intensive care duration (d | lays) | 1 (1-1) | 1 (1-2) | 0.143 |
| Age (years) | | 71.3±6.5 | 70.6 ± 5.8 | 0.599 |
| Mortality | Yes | 1 (2.2) | 8 (17.4) | 0.030 |
| | No | 44 (97.8) | 38 (82.6) | |
| Operation type | Open | 33 (73.3) | 36 (78.3) | 0.640 |
| | Laparoscopy | 11 (24.4) | 8 (17.4) | |
| | Open after Laparoscopy | 1 (2.2) | 2 (4.3) | |
| Local complication | Yes | 10(22.2) | 17 (37) | 0.169 |
| | No | 35 (77.8) | 29 (63) | |
| Systemic complications | Yes | 1 (2.2) | 12 (26.1) | 0.002 |
| | No | 44 (97.8) | 34 (73.9) | |
| | No | 43 (97.7) | 42 (91.3) | |
| Ostomy status | Yes | 5 (11.1) | 18 (39.1) | 0.003 |
| | No | 40 (88.9) | 28 (60.9) | |
| Use of formula | Yes | 26 (57.8) | 33 (71.7) | 0.192 |
| | No | 19 (42.2) | 13 (28.3) | |
| Discharge with drain | Yes | 0 (0) | 9 (19.6) | 0.003 |
| | No | 45 (100) | 37 (80.4) | |
| Gender | Male | 30 (66.7) | 30 (65.2) | 0.999 |
| | Female | 15 (33.3) | 16 (34.8) | |
| Marital status | Married | 31 (68.9) | 24 (52.2) | 0.301 |
| | Single | 7 (15.6) | 11 (23.9) | |
| | Divorced | 7 (15.6) | 11 (23.9) | |
| Education status | Illiterate | 4 (8.9) | 2 (4.3) | 0.923 |
| | Literate | 5 (11.1) | 5(10.9) | |
| | Primary School | 14 (31.1) | 15 (32.6) | |
| | Middle School | 13 (28.9) | 13 (28.3) | |
| | High School | 4 (8.9) | 3 (6.5) | |
| | University | 5 (11.1) | 8 (17.4) | |
| Smoking | Smoker | 15 (33.3) | 18 (39.1) | 0.878 |
| | Non smoker | 24 (53.3) | 22 (47.8) | |
| | Ex-smoker | 6 (13.3) | 6 (13) | |
| Alcohol consumption | Yes | 4 (8.9) | 3 (6.5) | 0.714 |
| 1 | No | 41 (91.1) | 43 (93.5) | |
| Polypharmacy | Yes | 13 (28.9) | 17 (37) | 0.505 |
| | No | 32 (71.1) | 29 (63) | |

Data are shown as mean±standard deviation or median (Q1-Q3) or n (%). FRAIL=Fatigue, Resistance, Ambulation, Illness, and Loss of weigh

Table 4. CFS scores according to patient characteristics

| | | Median (Q1-Q3) | P value |
|-------------------------|------------------------|----------------|---------|
| Mortality | Yes | 8 (8-9) | 0.001 |
| | No | 5 (4-5) | |
| Operation type | Open | 5 (4-6) | 0.334 |
| | Laparoscopy | 5 (4-7) | |
| | Open after Laparoscopy | 4 (4-4) | |
| Local complication | Yes | 5 (4-6) | 0.117 |
| | No | 5 (4-7) | |
| Systemic complications | Yes | 5 (4-5) | < 0.001 |
| | No | 8 (7-8) | |
| Ostomy status | Yes | 7 (5-7) | < 0.001 |
| | No | 5 (4-5) | |
| Use of formula | Yes | 4 (4-5,5) | 0.008 |
| | No | 5 (4-7) | |
| Discharge with drain | Yes | 5 (4-6) | 0.875 |
| | No | 5 (4-6) | |
| Gender | Male | 5 (4-6) | 0.699 |
| | Female | 5 (4-6) | |
| Marital Status | Married | 5 (4-6) | 0.333 |
| | Single | 4 (3-7) | |
| | Divorced | 5 (4-7) | |
| Education Status | Illiterate | 5 (4-5) | 0.755 |
| | Literate | 5 (4-5) | |
| | Primary School | 5 (4-6) | |
| | Middle School | 4 (4-6) | |
| | High School | 5 (4-7) | |
| | University | 6 (4-7) | |
| Smoking | Smoker | 6 (4-7) | 0.029 |
| | Non smoker | 5 (4-5) | |
| | Ex-smoker | 4 (4-5) | |
| Alcohol consumption | Yes | 7 (4-8) | 0.084 |
| | No | 5 (4-6) | |
| Polypharmacy | Yes | 5 (4-6) | 0.215 |
| - | No | 5 (4-7) | |

CFS=Clinical Frailty Scale

Clinical Outcomes and Associations

Patients with increased frailty exhibited significantly lower serum albumin levels (P=0.001). These patients also demonstrated: prolonged hospitalization (P=0.015), higher mortality rates (P=0.030), increased rates of systemic complications (P=0.002), higher rates of ostomy and discharge with drain (P=0.003). These findings are summarized in Table 3.

CFS Scale Associations

Analysis of the CF) revealed weak but statistically significant positive correlations with: duration of ICU stay (r=0.317, P=0.002), duration of hospitalization (r=0.314, P=0.002). A significant difference in CFS scores was observed between survivors and non-survivors. The mortality group exhibited a significantly higher median CFS score (8 [8-9]) compared to the survival group (5 [4-5]) (P=0.001). Furthermore, a higher CFS score was associated with: development of systemic complications, presence of ostomy, use of formula feeding. These associations are detailed in Table 4.

DISCUSSION

This study analyzed preoperative and postoperative frailty status in elderly patients who underwent elective GI system cancer surgery. Both CFS and FRAIL scale results showed a statistically significant increase postoperatively. Also, the prevalence of frailty increased from 34.1% preoperatively to 40.7% postoperatively. Furthermore, significant associations were observed between high frailty scores and: low serum albumin levels, prolonged hospital stay, increased mortality. These findings underscore the negative impact of surgical procedures on frailty levels in elderly patients. Frailty, a condition of decreased physiological reserve and increased vulnerability, is crucial for risk assessment in aging and oncology, especially in cancer patients where it's more prevalent. Identifying frail older cancer patients is vital due to the stress of aggressive treatments [8, 9]. In the general population, frailty prevalence increases significantly with age. While approximately 10% of individuals aged 65 and over exhibit frailty, this rate rises substantially to 25-50% in those aged 85 and over. Among cancer patients, Handforth et al. [8] reported a median frailty

prevalence of approximately 43% in individuals aged 72 or older.

Frailty in elderly colorectal cancer surgery patients ranges from 25-46% [10]. Meta-analysis shows 31% prevalence [11], with a study reporting 34% [12]. Frailty prevalence in gastric surgery patients increased from 34.1% preoperatively to 40.7% postoperatively, as shown in our study. This aligns with reported frailty rates in similar populations (29% [3]). Both FRAIL and CFS scores significantly increased postoperatively.

GI surgery in elderly patients increases frailty risk, likely due to cancer-related stress and post-operative complications like delayed feeding, drains, and ostomies. Our study confirms this, showing increased frailty scores with ostomy or drain placement.

Serum albumin levels, reflecting nutrition and inflammation, are key health indicators, especially in surgical and elderly patients. Lower serum albumin levels correlate with higher frailty scores, indicating hypoalbuminemia as a frailty marker. Combining albumin measurements with frailty assessments improves prediction of surgical outcomes, including complications, mortality, and hospital stay [13, 14]. Prior research has underscored the significant association between frailty and hypoalbuminemia. A study involving patients undergoing free tissue flap reconstruction demonstrated that a combined assessment of frailty and hypoalbuminemia served as a strong predictor of postoperative outcomes, emphasizing their interdependent relationship [15]. Further supporting this, a study examining the relationship between frailty and outcomes following laparoscopic gastrectomy in elderly patients (≥80 years) with gastric cancer revealed significantly lower preoperative albumin levels in frail individuals [16]. Consistent with these findings, our study observed lower albumin levels in patients with increased frailty. Moreover, these patients exhibited prolonged hospital stays. These findings collectively emphasize the strong association between serum albumin levels and frailty.

Elderly GI surgery patients with frailty have higher mortality rates. A meta-analysis study further emphasized this association, revealing that frail patients exhibited significantly higher rates of overall mortality and rehospitalization within one year following gastrectomy [17]. Garland *et al.* [18] demonstrated a strong association between higher FRAIL Index scores and increased morbidity in elderly patients with

GI cancer. Chao et al. [19] reported that incorporating frailty scales as continuous variables significantly improved mortality prediction performance in individuals over 50 years of age. Furthermore, a study conducted on individuals over the age of 75 revealed a positive relationship between frailty score and mortality, independent of the underlying hospital admission diagnosis [20]. In the present study, a statistically significant increase in mortality rates was observed among patients with increased postoperative frailty compared to the preoperative period. When analyzing the relationship between frailty and survival status, the median CFS score was significantly higher in non-survivors (median: 8, range: 8-9) compared to survivors (median: 5, range: 4-5). Therefore preoperative frailty assessments are crucial for elderly surgical candidates.

Limitations

Limitations include a small sample size, the inclusion of all patients 65+ potentially obscuring age-related differences, and potential selection bias due to voluntary participation.

CONCLUSION

In conclusion, accurate preoperative frailty assessment holds significant clinical implications for optimizing surgical outcomes in elderly patients. By identifying frail individuals, clinicians can implement targeted interventions to decrease surgical risks and improve postoperative recovery. Conversely, a frailty index can help avoid overtreatment of frail patients who may not benefit from aggressive surgical approaches.

Ethical Statement

This observational prospective, cohort study was approved by the Adana City Training and Research Hospital Clinical Research Ethics Committee (Decision no. 3178, Date: 15.02.2024). Written informed consent was obtained from all participating patients.

Authors' Contribution

Study Conception: GO; Study Design: GO; Supervision: GO, AS; Funding: N/A; Materials: N/A; Data Collection and/or Processing: GO, AS; Statistical Analysis and/or Data Interpretation: GO, AS; Litera-

ture Review: GO; Manuscript Preparation: GO, AS and Critical Review: GO, AS.

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The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Emergency Medicine

The impact of suicide rates on admissions to emergency medical services and the role of education and employment

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ABSTRACT

Objectives: In this research, it was aimed to evaluate the impact of suicide rates on admissions to emergency medical services (EMS) and the role of education and employment.

Methods: In the research, the Ministry of Health of the Republic of Turkey parameter of cases per EMS between 2002 and 2022, deaths due to suicide, education and employment data from the World Bank Turkey Report were used.

Results: Mean cases per EMS in Türkiye for 2002-2022 time period had 1,512.30±560.82 (range: 653-2,428). Mean suicide mortality range was 2.51±0.32 (range: 2.20-3.20). Mean school enrollment rates were 95.45±2.70 ranged from 87.90 to 98.52. Mean employment rate was 44.08±2.12 (range: 41.15-47.37). Cases per EMS was significantly correlated with suicide mortality (r=-0.777; P<0.01), school enrollment (r=-0.832; P<0.01) and employment rate (r=0.704; P<0.01). Year controlled partial correlation analysis results showed that there was a significant correlation between cases per EMS and employment rate (r=0.653; P<0.01). School enrollment and employment on cases per EMS, effect of suicide mortality on cases per EMS was statistically significant (B=-2121.23; P<0.01). Effects of school enrollment and employment on cases per EMS were insignificant (P>0.05).

Conclusions: EMS units are very effective in reducing suicide mortality rates at both the correlation and regression levels. This effectiveness is similar across different education and employment groups. To reduce suicide mortality, it is necessary to focus on EMS access rather than EMS effectiveness.

Keywords: Emergency medical services, suicide, education, employment

mergency services or Emergency Medical Services (EMS) are public units that have very important functions in terms of public health [1]. The fact that patients in emergency departments are in a position that requires acute and urgent intervention shows that the services provided there are not only a public health service, but also a human right to

life [2, 3]. For this reason, the use of EMS has been the subject of both field studies and many scientific research from past to present [4, 5]. The common point of these studies is the increase of EMS effectiveness and at the same time the reduction of the population falling under EMS [6, 7]. For this, it is necessary to focus on diseases and health conditions related to EMS.

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One of the issues related to individuals' right to life within the social structure is suicide cases [8, 9]. Although suicide is seen as an individual ending his life voluntarily, since individuals who commit suicide generally do not have a healthy mental state, suicide is actually a result of an illness, not a decision made by individuals [10, 11]. Suicide events may not always result in death. With early intervention, it may be possible to intervene and protect the lives of individuals who commit suicide Studies on the causes of suicide in the literature mostly examine the reasons for suicide under headings such as adolescence, family and relationship problems, and financial problems [12, 13]. However, regardless of the reason, it can be stated that individuals have an unhealthy mental state in common with all suicides. In terms of the health system, early intervention is an issue that is more emphasized than the causes of suicide cases. Because the causes of suicide vary widely, a multidisciplinary study and evaluation is needed to find the causes and early diagnosis. In today's increasingly multidisciplinary studies, the reflection of the causes of suicide cases on the healthcare system is a subject of interest. The two most important factors in suicide cases in a social sense are education and employment, which are indicators of economic status and also indicators of individual identity [14, 15]. Although studies have been conducted on suicide cases, studies on suicides by EMS are not sufficient. Therefore, this study aimed to analyze multivariately the relationship between the number of cases in emergency departments and suicide-related mortality and the effects of education and employment on this relationship [16, 17].

METHODS

Research Model

The research was designed with a mixed model, including descriptive scanning and relational scanning models. Based on this model, in the first stage, cases per EMS, morale due to suicide, education and employment rates were depicted for Türkiye. Then, the relational screening model was used to investigate the relationships between the variables.

Data Set

In the research, the Ministry of Health of the Re-

public of Turkiye parameter of cases per EMS between 2002 and 2022, deaths due to suicide, education and employment data from the World Bank Turkey Report were used. Parameters used in the research were given as below:

Variables

Dependent variable was sases per emergency service-Ministry of Health statistics. Independent variable was suicide mortality rate (per 100,000 population). Controlling variables were school enrollment, primary (% net) employment to population ratio, 15+, total (%) (modeled ILO estimate).

Statistical Analysis

Research data were described with mean, standard deviation, median and range values. Kolmogorov Smirnov test was used for normality test of research parameters. Pearson's and year-controlled partial correlation analyzes were used for relationships between variables. Due to linearization biases [19, 20], Linear Model with logit transformation to non-normal parameter in the model analysis was used. In this study, Pearson correlation, year controlled partial correlation and the General Linear Model were used. To identify the basic correlations between variables, Pearson correlation was used; however, to determine the actual relationship between the independent variables and EMS admissions, the effect of the year variable was controlled through partial correlation analysis. Furthermore, the General Linear Model (GLM), which is also used in other similar studies, was employed to examine linear relationships among variables. All analyzes were carried out in SPSS 25.0 for windows program, with a 95% confidence interval and a 0.05 significance level.

RESULTS

Mean cases per EMS in Türkiye for 2002-2022 time period had 1,512.30±560.82 (range: 653-2,428). Mean suicide mortality range was 2.51±0.32 (range: 2.20-3.20). Mean school enrollment rates were 95.45±2.70 ranged from 87.90 to 98.52. Mean employment rate was 44.08±2.12 (range: 41.15-47.37). (Table 1). Pearson correlation analysis results showed that cases per EMS was significantly correlated with suicide mortality (r=-0.777; P<0.01), school enrollment (r=-0.832;

Table 1. Cases per EMS, suicide mortality, school enrollment and employment rates for Türkiye for 2002-2022 time period

| | Mean±Standard Deviation | Median (Minimum-Maximum) |
|--|-------------------------|----------------------------|
| Cases per EMS | 1,512.30±560.82 | 1,651.00 (653.00-2,428.00) |
| Suicide mortality, (per 100,000 population) | 2.51±0.32 | 2.40 (2.20-3.20) |
| School enrollment, primary (% net) | 95.45±2.70 | 95.72 (87.90-98.52) |
| Employment rate, 15+, total (%) (modeled ILO estimate) | 44.08±2.12 | 44.71 (41.15-47.37) |

EMS= emergency medical services, ILO=international labour organization

P<0.01) and employment rate (r=0.704; P<0.01). Year controlled partial correlation analysis results showed that there was a significant correlation between cases per EMS and employment rate (r=0.653; P<0.01) (Table 2). According to General Linear Model for effects of suicide mortality, school enrollment and employment on cases per EMS, effect of suicide mortality on cases per EMS was statistically significant (B=-2121.23; P<0.01). Effects of school enrollment and employment on cases per EMS were insignificant (P>0.05) (Table 3).

DISCUSSION

In this study, the relationship between EMS headcount and suicide deaths and the role of education and employment in this relationship were analyzed. In the study, using data from the Turkish Ministry of Health and the World Bank, it was seen that the relationship between people per EMS and suicide-related mortality was statistically significant and negative. It was revealed that the effect of control variables, education

and employment, was significant in the correlation analysis, but statistically insignificant in the regression analysis [18, 19]. EMSs are one of the most socially important units within a healthcare system. The lives of individuals are a constitutional and inherent right, a value above countries and societies [20, 21]. EMS units, on the other hand, are the units with the highest number of positions and positions related to individuals' rights to life within the healthcare system [22, 23]. In this regard, EMS units are of vital importance both in protecting vital health conditions and in reducing the negative effects of advanced health problems in the acute phase. Suicide cases are one of the most important issues in the health services provided by EMS units. Suicide is a behavior in which individuals want to end their lives voluntarily, but usually unconsciously or due to a different illness such as depression [24, 25]. The approach to suicide cases in emergency departments generally varies depending on the type of suicide, its degree, its effects and the patient's current physical examination. Although suicide cases committed by methods such as poisoning, taking drugs, cutting arms and wrists generally have lower mortality in

Table 2. Pearson and year controlled correlation analysis results for relationship between cases per EMS, suicide mortality, school enrollment and employment rate

| | Pearson's correlation | | Year controlled partial | |
|--|-----------------------|---------|-------------------------|---------|
| | r | P value | r | P value |
| Suicide mortality, (per 100,000 population) | -0.777** | 0.000 | 0.164 | 0.559 |
| School enrollment, primary (% net) | -0.832** | 0.000 | -0.282 | 0.309 |
| Employment rate, 15+, total (%) (modeled ILO estimate) | 0.704** | 0.001 | 0.653** | 0.008 |

EMS= emergency medical services, ILO=international labour organization

^{**}P<0.01

Table 3. General linear model for effects of suicide mortality, school enrollment and employment on cases per EMS

| | Unstandardized coefficients | | Standardized coefficients | t | P value | 95.0% confidence | ce Interval for B |
|--------------------------|-----------------------------|------------|---------------------------|-------|---------|------------------|-------------------|
| | В | Std. error | Beta | | | Lower bound | Upper bound |
| (Constant) | 204.62 | 3187.00 | | 0.06 | 0.950 | -6739.25 | 7148.49 |
| Suicide mortality | -2121.23 | 342.46 | -0.532 | -6.19 | 0.000 | -2867.38 | -1375.08 |
| School enrollment | -19.78 | 23.29 | -0.11 | -0.85 | 0.412 | -70.52 | 30.96 |
| Employment | 113.75 | 27.99 | 0.49 | 4.06 | 0.002 | 52.76 | 174.75 |

EMS= emergency medical services

the early period, the time until admission to EMS units is of vital importance in these suicides [26, 27]. In general, the World Bank and the World Health Organization do not separate suicides according to their causes and effects, but rather according to their mortality levels.

Although there are no sufficient studies in the literature on the relationship between suicide and EMS, it can be stated that suicide rates in general will cause lower mortality with EMS intensity, use and effectiveness. In our study, there was a statistically significant and negative relationship between person per EMS and suicide-related mortality in Turkey. This shows that mortality decreases statistically significantly in suicide cases that are referred to EMS units and that EMS units work effectively in suicide cases. On the basis of the findings, it seems that EMS density is negatively correlated with suicide related deaths. However, this study is only cross correlational and does not establish causality. The relationship between the presence of EMS and lower suicide mortality rates may be confounded by other socioeconomic and health policy factors. Therefore, for defining the specific function of EMS in suicide prevention, longitudinal or experimental research is required. Studies are not clear on whether education is a significant factor among the factors affecting suicide cases. Highly educated people may also have high levels of depression and high suicidal tendencies. However, it is possible to state that the relationship between economic income and suicide is negative. In general, suicide rates also increase in individuals with low income and problems making ends meet. In terms of emergency service use, as employment increases, the use of EMS will also increase,

as reasons such as work accidents and similar reasons and getting reports will increase. As education increases, individuals will become more conscious, more sensitive about health, and as a result, EMS applications will decrease. This was also valid in our study, and there was a statistically significant and negative relationship between EMS use and schooling. The relationship between employment and EMS use was statistically significant and positive. It is possible to state that, in general, the findings are compatible with the literature and expectations. Regression analysis results showed that the effect of deaths by suicide on EMS use was statistically significant, but the contribution of education and employment was not significant. Although there may be many reasons for this situation, it is possible to state that if applied to EMS units, a positive and mortality-reducing intervention is made to suicide cases, and this is applied to all education and employment groups.

Limitations

The most important limitation of the study is that the data on suicide rates applying to EMS units is not sufficient and therefore, general population suicide mortalities are used. Although this situation is insufficient to fully reveal the effectiveness of EMS units on suicide, it is a tolerable limitation since the study is a pioneer in the field. This study is based on suicide rates from the general population and does not involve direct collection of data from EMS admitted suicide cases. Therefore, the results of this study do not allow for a definitive conclusion regarding the direct effect of EMS interventions on suicide cases. Future work

should also concentrate on collecting more detailed information about suicide attempts that are admitted to EMS. Another important limitation of the research is the limited data set. Research data has been compiled since 2002, but even in 2024, the latest data for 2021 could be accessed. The last data collected for this study was in 2021. At the time of writing, the latest up to date data was not readily available hence the study might not be up to date with the current situation. This shows that there is a need for better and more timely sharing of data by the relevant public institutions. The Ministry should focus on ensuring more effective, rapid and effective data sharing in this regard. One major limitation of this study is that there is no direct data on suicide cases admitted to EMS. Instead, general suicide mortality rates were used. Future studies should utilize direct EMS records and individual case data to better assess the impact of EMS on suicide cases.

Contributions of the Research to the Field and Literature

The most important contribution of the research to the field is that it shows that the effectiveness of EMS units in suicide cases is sufficient, and that ensuring access to EMS units is important rather than EMS intervention effectiveness. In this regard, research results are important in terms of providing data and resources to the field. The contribution of the research to the literature is that it is among the pioneering studies in this field and provides guidance on issues that are not much mentioned in the literature. Although there are limited studies on EMS density and suicide cases, there are not enough studies examining suicide mortality together with education and employment.

CONCLUSION

According to the results obtained in the study, EMS units are very effective in reducing suicide mortality rates both at the correlation level and at the regression level. This effectiveness is similar across different education and employment groups. To reduce suicide mortality, it is necessary to focus on EMS access rather than EMS effectiveness.

Ethical Statement

The primary reason for not obtaining ethical approval in this study is that the data used were entirely sourced from publicly available and reliable sources. The data used in the study were obtained from the Ministry of Health of the Republic of Turkey and the World Bank Turkey Report. These sources provide publicly accessible statistical data available to everyone. Additionally, the study did not use individual patient data or personal information, nor did it involve experimental applications requiring direct contact or intervention with individuals. All statistical data analyzed in the study are anonymized, and it is impossible to identify any individual's identity. According to national and international ethical guidelines, ethical approval is mandatory only for studies involving the processing of personal data, biomedical interventions, or direct human participants. Since only public databases were used in this study, ethical approval was not required. Furthermore, scientific neutrality and ethical standards were strictly adhered to during the research process, and there were no commercial, financial, or personal conflicts of interest that could influence the outcomes of the research

Authors' Contribution

Study Conception: EB; Study Design: EB; Supervision: EB; Funding: EB; Materials: EB; Data Collection and/or Processing: EB; Statistical Analysis and/or Data Interpretation: EB; Literature Review: EB; Manuscript Preparation: EB and Critical Review: EB.

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Artificial Intelligence and Dermatology

Al as a patient educator: Evaluating ChatGPT's role in disseminating information on herpes zoster ophthalmicus

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ABSTRACT

Objectives: The aim of this study is to evaluate the accuracy and quality of the responses provided by the artificial intelligence model, ChatGPT, to questions about Herpes Zoster Ophthalmicus (HZO). HZO is a condition caused by the involvement of the ophthalmic branch of the trigeminal nerve, which can lead to severe ocular complications. Given the increasing use of artificial intelligence in healthcare, this study explores the capacity of ChatGPT to contribute to patient education on this disease.

Methods: Seven questions selected by a dermatologist and an ophthalmologist from a list of twenty frequently asked questions about HZO were posed to the ChatGPT 4.0 model. The responses were evaluated using a four-point rating scale. Responses were independently rated as "excellent," "satisfactory with minimal explanation required," "satisfactory with moderate explanation required," or "unsatisfactory." The readability of the seven questions was assessed using the Flesch Reading Ease Score (FRES) and Flesch-Kincaid Grade Level (FKGL) criteria.

Results: ChatGPT provided accurate and informative responses to all seven questions. Six responses were rated as "excellent," and one response was rated as "satisfactory with minimal explanation required". Interrater reliability was calculated using Cohen's kappa, which was found to be 0.416 (95% confidence interval, 0.007, 0.825). A subsequent readability analysis using the Flesch Reading Ease Score (FRES) and the Flesch-Kincaid Grade Level (FKGL) revealed that the answers ranged from moderately difficult to challenging. The FRES values ranged from 41.13 to 57.24, while the FKGL scores varied from 9.8 to 13.3, suggesting a reading level corresponding to that of a high school to early college level.

Conclusions: ChatGPT has demonstrated a strong capacity to effectively respond to patient questions about HZO. It was observed that it produced content suitable for readers educated at high school and university level and provided clear and detailed medical information. It can be used as a complementary tool for patient education, especially as a 24/7 resource for patients who have difficulty accessing healthcare services, following prior review by dermatologists and ophthalmologists.

Keywords: Artificial intelligence, ChatGPT, herpes zoster ophthalmicus, patient education

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he term "artificial intelligence" (AI) is defined as a system that is capable of interpreting data received from external sources, acquiring knowledge from this information, and utilising that knowledge in a flexible manner to achieve specific objectives or perform designated tasks [1]. ChatGPT, an AI-supported large language model (LLM) that is capable of producing text in a natural conversational style, is garnering interest in the medical field and its utilisation is becoming increasingly prevalent [2]. It is a computer program that is available to the general public and has a complimentary trial version. This renders it a potent instrument for communication, information propagation and problem solving on a broad range of subjects, including healthcare [3]. With recent advances in AI, ChatGPT is increasingly being utilised in both dermatology and ophthalmology [2, 3-5].

The condition, known as zona zoster, is characterised by the manifestation of a unilateral skin rash, which is limited to one dermatome. The lesions typically evolve from erythematous macules and papules to vesicles and pustules. The lesions crust over after five to seven days [6]. Herpes zoster ophthalmicus (HZO) is defined as involvement of the ophthalmic portion (V1) of the trigeminal nerve (V). Approximately 50-85% of HZO cases result in eye complaints, including conjunctivitis, uveitis, episcleritis, keratitis or retinitis. Rare manifestations include sterile iris abscess, oculomotor nerve palsy, upper orbital fissure syndrome, orbital apex syndrome and isolated non-reactive mydriasis. The condition is categorised as an ophthalmic emergency, as it can result in vision loss. Furthermore, patients diagnosed with HZO have been shown to have a 1.3 to 4-fold increased risk of cerebrovascular events. This increased risk persists even in younger patients after disease onset [7]. The goal of herpes zoster treatment is to relieve pain in the acute phase, limit the spread and duration of the rash, and prevent or alleviate chronic pain and other acute and chronic complications. In order to achieve these goals, it is critical to start treatment as soon as possible, which is only possible if patients seek timely medical attention [6]. This situation creates new opportunities and challenges in the integration of digital health technologies and AI-powered applications into healthcare, and once again highlights the importance of providing accurate and reliable information. It is noteworthy that, akin to all AI tools, the increasing utilisation of ChatGPT in the healthcare sector has led to patients increasingly resorting to these resources prior to consulting a physician regarding their health concerns. In light of this trend, the present study aims to evaluate the responses of ChatGPT to patient inquiries concerning Herpes Zoster Ophthalmicus.

METHODS

A comprehensive search was conducted on Google (www.google.com) for frequently asked questions about shingles, frequently asked questions about shingles in the eye, and information about shingles, as well as information about shingles in the eye. The 'frequently asked questions' sections of numerous clinics and medical associations were analysed. From a comprehensive list of 20 questions, the 7 most common questions were selected by 1 dermatologist (reviewer 1) and 1 ophthalmologist (reviewer 2). The questions were submitted on 21 October 2024 to ChatGPT (version 4.0), the latest premium version with limited free access, with no follow-up questions or repetitions. For grading, we employed a 4-step grading system that has been previously utilised in medical articles to evaluate ChatGPT responses to patient questions.[8] Each response was independently reviewed by the authors (reviewer 1 and reviewer 2) using an evidence-based approach. In this grading system, scores of 1, 2, 3, and 4 corresponded to 'excellent response requiring no explanation', 'satisfactory response requiring minimal explanation', 'satisfactory response requiring moderate explanation', and 'unsatisfactory response requiring substantial explanation', respectively.

Readability Analysis of Questions and Answers

In this study, the readability levels of the seven selected questions and their corresponding answers were evaluated using the Flesch Reading Ease Score (FRES) and the Flesch-Kincaid Grade Level (FKGL) metrics.FRES is a scale ranging from 0 to 100, with higher scores indicating easier readability. FKGL, conversely, estimates the education grade level required to comprehend the text, with higher scores denoting the need for more advanced reading skills [9, 10]

Eur Res J. 2025;11(4):769-775

Yigen İritaş and İritaş

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0; IBM Corp. Inter-rater reliability and confidence interval were then calculated through kappa-analysis. FRES and FKGL scores was analyzed using Pearson correlation coefficients to determine whether higher FRES scores (easier readability) corresponded to lower FKGL scores (less advanced educational requirements). A significance level of P<0.05 was used for all statistical tests.

RESULTS

Please refer to Table 1 for a comprehensive list of the questions and answers provided by ChatGPT 4.0. Reviewer 1 assigned 'excellent' ratings to six responses and 'satisfactory requiring minimal explanation' to one. Reviewer 2 also awarded 'excellent' ratings to six responses and 'satisfactory requiring minimal explanation' to one. Notably, no responses received a 'satisfactory requiring moderate explanation' 'unsatisfactory' rating from either reviewer. The question 'How is shingles in the eye diagnosed?' was rated as 'satisfactory requiring minimal explanation' by reviewer 1 and the answer to the question 'How does shingles in the eye start?' was rated as 'satisfactory requiring minimal explanation' by reviewer 2. In this study, inter-rater reliability was calculated by k analysis. The result was 0.416 (95% confidence interval, 0.007, 0.825).

The readability analysis showed that the questions and answers varied in difficulty. FRES scores ranged from 41.13 (most difficult) to 57.24 (easiest), indicating that the text is moderately challenging overall. FKGL scores ranged from 9.8 to 13.3, showing that the content requires a reading proficiency from late high school to early college level (Table 2).

DISCUSSION

The most significant finding of this study was that ChatGPT 4.0 was capable of producing high-quality responses that can facilitate patient education regarding shingles in the eye. Historically, patient education has been conducted by physicians; however, in recent

years, AI has gained popularity among the general population, leading to an increased reliance on online resources for patient education [11]. Consequently, there has been a surge in publications that evaluate the role of AI tools in patient education. In a study examining ChatGPT answers about acne and atopic dermatitis, 78% of the answers were rated as correct, and in another study, 85% of the answers were rated as perfect [12].

The process of diagnosing ocular shingles is a complex one. The response to this question was characterised by Reviewer 1 as 'satisfactory requiring minimal explanation'. The Tzanck test is a rapid and straightforward procedure with high sensitivity and specificity, and it is frequently utilised in the diagnosis of shingles. Its utilisation is predicated on the absence of any mention of the Tzanck test in the text [13].

The following investigation will explore the manner in which shingles manifests itself within the ocular cavity. The response to this query was deemed to be 'satisfactory requiring minimal explanation' by reviewer 2. The aforementioned reviewer further noted that Herpes zoster was deemed satisfactory as it did not mention the onset of the disease known as herpete, which is primarily characterised by neuralgia [14]. The readability analysis indicates that the questions and answers generated by ChatGPT are moderately challenging to comprehend, rendering them suitable for individuals with high school and university-level education. These findings are consistent with previous research evaluating the role of ChatGPT in patient education and conducting readability analysis. This underscores the potential for ChatGPT to serve as a valuable instrument in the dissemination of medical information. Nevertheless, there is scope for enhancement in the simplification of language to augment accessibility for individuals with low health literacy, thereby ensuring that a more extensive audience can reap the benefits of AI-generated educational content [15, 16].

In the present study, all questions were addressed by ChatGPT-4.0. However, it should be noted that free versions of ChatGPT-4.0 are subject to limitations on the number of questions that can be posed; once this limit is reached, the system will transition to older or simplified versions. This may result in changes in the content and consistency of responses, which may di-

Table 1. Questions asked to ChatGPT, answers and reviewer ratings

| , | ` | |
|-----------------------------------|--|--------------------------|
| Questions | Answers | Answer Accuracy Score |
| Is eye shingles contagious? | • Shingles (herpes) disease in the eye zoster ophthalmicus) is a condition in which the shingles virus spreads to the eye and the surrounding area. Varicella, which causes shingles, chickenpox it is caused by the zoster virus. In people who have had chickenpox, this virus remains inactive in the body and can reactivate as shingles years later when the immune system weakens. | 1-1 |
| | • Shingles in the eye is not contagious, but it can spread the virus to someone who hasn't had chickenpox. That is, a person with shingles in the eye can't spread shingles directly, but they can spread the virus to someone who hasn't had chickenpox, causing chickenpox in that person. People with compromised immune systems, pregnant women, and newborns are more vulnerable to the chickenpox virus. | |
| | It is important not to touch the rash and to pay attention to hygiene rules in order to avoid transmitting the virus. | |
| How is eye shingles diagnosed? | Shingles (herpes) disease in the eye zoster ophthalmicus) diagnosis is usually made based on clinical symptoms. The following steps are followed in the diagnosis process: Medical history and symptoms: The doctor listens to the patient's history and complaints. Symptoms such as rash around the eyes and upper face, severe pain, burning in the eyes, redness, and blurred vision are | 2-1 |
| | questioned. | |
| | Physical exam: The eyes, face, and rash are examined in detail. The shingles virus is usually unilateral, causing a rash and blisters on only one eye and one side of the face. These blisters resemble chickenpox and are usually fluid-filled on a red base. | |
| | • Eye examination: A comprehensive eye examination is performed to evaluate the effects on the eye. Complications such as eye infection, corneal involvement, changes in intraocular pressure, and eyelid inflammation | |
| | Laboratory tests (if necessary): | |
| | Polymerase Chain Reaction (PCR): Can be used to confirm the presence of the shingles virus. This test detects genetic material of the virus in samples from rashes or eye discharge. | |
| | • Viral culture: A sample of the fluid in the rash can be taken and the virus can be cultured in the laboratory. | |
| | Antibody tests: Varicella in the body Detection of antibodies to the zoster virus can aid in the diagnosis of the disease, but is generally not used in the early stages. | |
| | Diagnosis can usually be made quickly based on physical findings, and it is important to begin treatment early. | |
| Does shingles leave scars | • Shingles (herpes) disease in the eye zoster ophthalmicus) can leave scars and lead to serious complications when not treated properly or when it progresses severely. The scarring depends on the severity of the | Ξ |
| on the eyes? | disease, Whether treatment is started early, and the status of the Immunue system. Here are some of the possible seams and complications: Chizacase, Whether real-way as started early, and the status of the Immunue system. Here are some or of the possible seams and complications: | |
| | Solution in the control of the contr | |
| | rosanepue neutaiga. Some peopre wno nave sunges in the eye may develop neive pain that has not a man institute including in the pain can be very unconnotatore and may become chronic. | |
| | Corneal damage: Shingles virus can affect the cornea, which can lead to corneal ulcers and scarring. These scars on the comea can cause vision loss and, in severe cases, can be permanent. | |
| | Vision loss: If the disease seriously affects the inner structure of the eye, long-term vision disorders and even permanent vision loss may develop. The risk is particularly high when there is involvement of the | |
| | comea, retina or optic neive. | |
| | Limited eye movements: Eye muscles may be damaged, resulting in problems such as limited eye movements or double vision (diplopia). In order to prevent shineles from leaving sears in the eve and to prevent complications, early diagnosis of the disease and rapid initiation of antiviral treatment are very important. | |
| Who is more likely to get | Shingles (herpes) disease in the eye zoster ophthalmicus) is usually more common in people with weakened immune systems or those whose immunity decreases with age. Risk factors for the disease are: | 1:1 |
| Shingles in the eye? | Older age: Shingles is more common in people over the age of 50. Because the immune system weakens with age, the risk of both general shingles and shingles in the eye increases in older individuals. | |
| | People with weakened immune systems: Conditions that weaken the immune system increase the risk of shingles in the eye. These conditions include: | |
| | o Immunodeficiency diseases such as HIV/AIDS | |
| | o Those receiving cancer treatment (chemotherapy) or radiotherapy) | |
| | Those who have had an organ transplant and those who use immunosuppressive drugs | |
| | Those receiving steroid treatment (long-term use of corticosteroids) | |
| | o I hose receiving immunosuppressive treatment due to autoimmune diseases | |
| | Stress: Severe physical or emotional stress can weaken the body's immune response, causing shingles to appear. | |
| | People who have had chickenpox before: Shingles in the eye, varicella, which causes chickenpox is at risk of developing shingles and chingles of the eye cenerally if their immune system is weakened or they are older | |
| | • Chronic diseases: People with chronic diseases that affect the immune system, such as diabetes, kidney failure, and chronic lung diseases, are at higher risk of shingles. | |
| | • It is important for people in these risk groups to talk to their doctors about vaccinations and other preventive measures to reduce the effects of shingles. | |
| | | |

Yigen İritaş and İritaş Eur Res J. 2025;11(4):769-775

| Table 1 contunied. | Table 1 contunied. Questions asked to ChatGPT, answers and reviewer ratings | |
|---|---|--------------------------|
| Questions | Answers | Answer Accuracy Score |
| How does shingles in the eye start? | Shingles (herpes) disease in the eye zoster ophthalmicus), usually begins with pain and skin rashes as the first symptoms. This condition is caused by varicella remaining inactive in the body for a long time. It occurs as a result of reactivation of the zoster virus. The initial stages of shingles in the eye are as follows: Prodromal period: Pain and tendemess: The disease may begin with pain, burning, stinging, or tenderness in the skin around the eye. Headden: Some patients may have a headache, which can sometimes indicate shingles around the eyes. Fatigue and vewlences. A general feeling of weakhess or firedness may also be among the prodromal period symptoms. Appearance of rashes: Redness and rashes: Redness and small fluid-filled blisters form over the painful area. These rashes are usually one-sided, affecting one side of the face and the area around the eyes. The blisters eventually burst and curst over. Eye redness: Burning, redness and irritation may occur in the eye. The white part of the eye (sclera) or eyelids may also be affected. Eye pain and sensitivity to light (photophobia): Eye pain and sensitivity to light may develop. Blurred vision. Due to eye involvement, vision disturbances, blurring and focusing problems may occur. Eye discharge: Sometimes watering or discharge may occur in the eye, vision loss, and corneal ulcers can develop. This requires immediate medical attention. Corneal involvement: If the virus affects the cornea, stringing in the eye well in the oye are policed at the beginning of the disease, needers the event complications with early diagnosis and antiviral treatment. If pain, burning and rashes in the eye are policed at the beginning of the disease, medical help should be sought immediately to preven medical attention. | |
| How do eye shingles symptoms spread? | Shingles (therpes) disease in the eye zoster ophthalmicus) typically starts in a specific area and progresses along the nerve time where the virus spreads. The symptoms of the face and even the internal structures of the eye. Below are details about how the disease spreads and the spreading process of the symptoms. One Sided Start. Shingles in the eye usually develops on one side of the face, along the ophthalmic branch of the trigeminal nerve. This nerve controls the upper face, forchead, eyelids, and area around the eyes. The disease is uniformed and different on the skin around the eyes, causing tiching, burning and tingling in this area. Shingles in the eye usually felt in the skin around the eyes, causing tiching, burning and tingling in this area. Spread of Skin Raabes. Rashes and bisters initially appear on the skin around the eyes, especially prominent on the forchead and bisters in similally appear on the skin around the eyes, especially prominent on the forchead and bisters in the eye are sign of more serious complications in the eye. Over time, the rast can spread to the eye-list, eyebrows, forchead, and sometimes the tip of the nose (Hutchinson's sign). This spread indicates that the branches of the trigeminal nerve, intracoular Spread. As shingles progresses, it can affect the internal structures of the eye, leading to more serious symptoms: Intracoular Spread. As shingles progresses, it can affect the internal structures of the eye, leading to more serious southon and optic nerve. The disease can affect the deeper structures of the eye, the retina and optic nerve. The disease can affect the deeper structures of the eye, the retina and optic nerve. Postelopment of Complications. If the disease can appear on the spread of shingles in the eye can cause scarring of the cornea, which can lead to permanent vision loss may occur as a result of inflammation, scarring and nerve damage to the eye.<td>rise is ca).</td> | rise is ca). |
| Can pain continue after shingles in the eye has healed? | • Yes, shingles (herpes zoster) pain may continue in some people after recovery. This condition is called "postherpetic neuralgia". Since the nerves are damaged after shingles, the pain, burning or tingling sensation may continue due to this damage. For some people, this pain can last for months or years. If you are experiencing such a condition, it would be useful to see a doctor. You can get information about treatment options | ation 1-1 |

Table 2. Readability Analysis FRES and FKGL scores

| Question Number | Questions | FRES | FKGL |
|------------------------|---|-------|------|
| 1 | Is eye shingles contagious? | 55.49 | 10.2 |
| 2 | How is eye shingles diagnosed? | 48.72 | 11.6 |
| 3 | Does shingles leave scars on the eyes? | 50.34 | 10.9 |
| 4 | Who is more likely to get shingles in the eye? | 44.91 | 12.4 |
| 5 | How does shingles in the eye start? | 49.87 | 11.2 |
| 6 | How do eye shingles symptoms spread? | 41.13 | 13.3 |
| 7 | Can pain continue after shingles in the eye has healed? | 57.24 | 9.8 |

FRES= Flesch Reading Ease Score, FKGL= Flesch-Kincaid Grade Level.

rectly affect the user experience [17]. In the present study, the questions were posed independently and a clear literary language was employed. It is acknowledged that ChatGPT may generate divergent responses depending on the sequence of prompts received. The quality of the inputs will cause the answers to vary considerably. However, many users are unaware of this situation [18]. The high accuracy rate observed in this study may be attributable to the independent nature of the question-asking process, which was conducted in a literary language.

Even if the latest model of ChatGPT is used, it can make mistakes and provide outdated information [19]. ChatGPT does not disclose its references in many cases, which makes it difficult to control the information. In our study, it also answered the questions asked without specifying the source. This situation can have important consequences for users who do not have sufficient information on the subject.

The findings of this study demonstrated that the latest iteration of the ChatGPT model, namely ChatGPT 4.0, possesses the capacity to respond to queries pertaining to Shingles in the Eye with a high degree of precision. ChatGPT is a promising technology whose use is becoming increasingly widespread. Further research is necessary to ascertain its role in patient education, although it may serve as an adjunctive method in this regard.

CONCLUSION

ChatGPT 4.0 has been demonstrated to provide highly accurate responses to queries posed by patients regard-

ing Shingles in the Eye. ChatGPT, which is distinguished by its perpetual accessibility, can be employed as a complementary educational resource for patients following preliminary evaluation by dermatologists and ophthalmologists.

Ethical Statement

We declare that this study is among the studies that do not require Ethics Committee approval (17.01.2025).

Authors' Contribution

Study Conception: SYİ, İİ; Study Design: SYİ, İİ; Supervision: SYİ, İİ; Funding: SYİ, İİ; Materials: SYİ, İİ; Data Collection and/or Processing: SYİ, İİ; Statistical Analysis and/or Data Interpretation: SYİ, İİ; Literature Review: SYİ, İİ; Manuscript Preparation: SYİ, İİ and Critical Review: SYİ, İİ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Eur Res J. 2025;11(4):769-775

Yigen İritaş and İritaş

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Anesthesiology and Reanimation

Evaluation of the effect of rectus sheath block and transversus abdominis plan block on sevoflurane and fentanyl consumption in laparoscopic cholecystectomy: A randomized controlled study

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ABSTRACT

Objectives: We aimed to compare the total amount of inhalation anesthesia consumed and the amount of fentanyl used as an additional dose in cases where transversus abdominis plane and rectus sheath blocks were applied for postoperative analgesia.

Methods: Eighty patients aged 18-75 years, classified as ASA I-II, who were scheduled for laparoscopic chole-cystectomy, were included. The patients were divided into two groups: those who received a combination of transversus abdominis and rectus sheath blocks under general anesthesia (Group B, n=40), and those who received analgesia with tramadol under general anesthesia (Group C, n=40). Throughout the procedure, both groups were monitored to maintain the entropy target value between 40-60 with a maximum MAC value of 1.3. At the end of the procedure, the total amount of inhalation agent consumed, and the additional need for superficial anesthesia/analgesia, as well as the total amount of fentanyl added as an extra dose, were recorded. **Results:** Comparing the total amount of inhalation agent consumed throughout the case, it was found to be 27.05±7.43 mL in Group C (Control group) and 12.25±4.34 mL in Group B (Block group), with a statistically significant difference between the groups. There was a significant difference in the need for additional intraoperative and the total amount of fentanyl consumed between the groups (P<0.05).

Conclusions: In laparoscopic cholecystectomy cases, we observed that the use of transversus abdominis plane block and rectus sheath block combined with standardized general anesthesia monitored by entropy reduced the amount of inhalation agent consumed, as well as the need for additional intraoperative and total opioid consumption.

Keywords: Transversus abdominis plane block, rectus sheath block, entropy, sevoflurane, fentanyl

Inhalation anesthetics combined with opioid drugs are commonly used to prevent responses to pain but have side effects like prolonged recovery,

nausea, vomiting, bowel dysfunction, respiratory depression, increased postoperative pain, environmental pollution, and higher healthcare costs. Therefore, min-

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imizing intraoperative anesthetic and analgesic use is important for perioperative physicians [1].

Electroencephalography (EEG) is widely recognized as one of the most objective methods for determining the depth of anesthesia [2]. In general anesthesia, changes in the EEG begin with induction, sedation, and maintenance [3-5]. Anesthesia depth neuromonitoring is based on the analysis of EEG changes resulting from the effect of anesthesia on cerebral blood flow and brain metabolism, and monitors that use it include the bispectral index (BIS), Narcotrend index, patient state index (PSI), entropy, SNAP index, and cerebral state index (CSI) [6].

Entropy provides two numerical values: state entropy (SE) and response entropy (RE), measured by using a low-impedance sensor on the frontal cortex EEG [7]. SE ranges from 0 (very deep anesthesia) to 91 (alertness), and RE ranges from 0 to 100, as displayed on the monitör [4]. SE (state entropy) reflects the cortical state more accurately and measures the hypnotic level. Instead of interpreting the RE (response entropy) value alone, it is more accurate to consider the difference between RE and SE, known as ΔRE-SE, which reflects the frontal muscle EMG [8].

Peripheral blocks, aided by ultrasonography, have gained prominence in recent years as a crucial component of multimodal postoperative analgesia. These blocks effectively manage pain in the initial postoperative phase and help diminish the reliance on systemic opioids [9].

In this study, we aimed to compare the amount of inhalation and narcotic (fentanyl) used in anterior abdominal wall blocks applied for analgesia in laparoscopic cholecystectomy patients in whom anesthesia depth monitoring "entropy" monitor (target is in the 40-60 range) was used.

METHODS

The research was started with the approval of the Tekirdağ Namık Kemal University Non-Interventional Clinical Research Ethics Committee on 26.07.2022 with the research protocol number 2022.138.07.05. The research period was planned as one year after ethics committee approval or until the specified number of cases was reached.

Eighty ASA I-II patients, aged between 18-75,

who were planned to undergo elective laparoscopic cholecystectomy, were included in the study by being divided into 2 groups using the randomization (sealed envelope method) method, whose written and verbal consent was obtained after being informed about the research protocol during the preoperative evaluation in the recovery unit. Group C (Control group) (n=40) was determined as Group B (Block group) (n=40), where analgesia was provided with tramadol during general anesthesia and analgesia was provided by adding transversus abdominis plane (TAP)+rectus sheath (RS) block to general anesthesia. The study, planned as randomized and single-blind, was conducted in a single center, in the operating room of Tekirdağ Namık Kemal University Hospital.

Sick sinus syndrome, kidney and liver failure, history of allergy to local anesthetics, intracranial vascular accident, patients with difficulty in establishing cooperation, chronic substance abuse, history of chronic opioid analgesia use, history of intraoperative awareness, pregnant women, morbidly obese patients, patients over 18 years of age. Patients who were younger, older than 75 years of age, diagnosed with a psychiatric disease, or had hemodynamic instability during the intraoperative period were not included in the study.

The same amount of correctly prepared drugs, in accordance with the literature, was administered to the patients in the preoperative, intraoperative and postoperative periods by the same experienced anesthesiologist, who did not monitor the patients during the study. The patients were monitored in the recovery unit for at least 20 minutes by another healthcare personnel who was not involved in the study. Those who were hemodynamically stable were sent to their services.

Demographic data (age, weight, height, body kite index) and ASA scores of the patients in both groups, who were taken to the operating room and monitored on the table in the supine position, were recorded. The patients were standardly monitored (ECG, SpO₂, NBP). Vascular access was established with a 20-gauge intravenous cannula and 0.9% NaCl solution was provided. Entropy (GE Healthcare CARESCAPE Monitor B850, Entropy module) monitoring was added to both groups before induction as anesthesia depth monitoring. Two numerical entropy parameters were obtained on the monitor with the three electrodes of the entropy sensor placed in the frontotemporal region.

- SE-state entropy
- RE-response entropy (Fig. 1)

These values were recorded together with the initial entry hemodynamic parameters as baseline parameters. After 3 minutes of 100% preoxygenation, fentanyl (1-2 μcg/kg), propofol (1-2.5 mg/kg), and rocuronium (0.6 mg/kg) were administered intravenously for standard induction of general anesthesia. After waiting for the neuromuscular blocker effect, all patients were orotracheally intubated with a laryngoscope. Anesthesia maintenance was provided with sevoflurane and an oxygen-air mixture of 50% O₂ and 50% air was used. Sevoflurane in anesthesia maintenance was started with the age-adjusted minimum alveolar concentration (MAC) value and the sevoflurane concentration was increased or decreased by evaluating the depth of anesthesia under the guidance of hemodynamics and entropy. The MAC was allowed to be increased up to a maximum of 1.3. 'Avance CS2 Anesthesia Delivery System' (GE Healthcare) was used as the anesthesia device in the study. For ventilation, the volume control mode (VCV) of the anesthesia device was selected with a tidal volume of 6-7 ml/kg, respiratory frequency 11-14/min, I: E ratio 1:2, and PEEP between 4-6.

For Group C (n=40), selected by randomization, patients were followed up under general anesthesia, and analgesia was administered with 100 mg tramadol intravenously after removal of the gallbladder. Group B (n=40) patients were intubated under general anesthesia and regional analgesia was performed with TAP (20 mL 0.25% bupivacaine) +RS (10 ml of 0.25% bupivacaine to coincide with the right trocar entry site) block under ultrasound guidance.

Sevoflurane concentration was adjusted to keep the entropy target value between 40-60 in both groups throughout the case, with a MAC value of maximum 1.3; starting, before and after induction, 1st minute (min.) after incision, pneumoperitoneum 5-10-15th min., 1st min. after pneumoperitoneum, post extubation, postoperative recovery 1st and 5th min.; The standard monitoring data of the cases, endtidal CO₂ values



Fig. 1. Monitoring screen, E-Entropy module, Entropy electrodes placement.

after orotracheal intubation, SE and RE entropy values, endtidal sevoflurane concentration (%) that kept the entropy value within the target range and simultaneous MAC values were measured and recorded at 5-minute intervals. Throughout the case, the need for analgesia/anesthesia status was monitored through hemodynamic parameters and clinical findings, along with the depth of anesthesia from the entropy monitor, hypertension (increase in the entrance mean arterial pressure by more than 20%), tachycardia (heart rate>120/min.), tears. In cases such as breathing, sweating, etc., or spontaneous breathing effort on the ventilator, an additional dose of fentanyl 1µcg/kg was administered intravenously and the total number of additional doses required was recorded. The maximum

fresh gas flow at the end of surgery was set to 4 l/min. Atropine 0.01 mg/kg and Neostigmine 0.03 mg/kg were administered intravenously to the patients to reverse the neuromuscular blockade effect. Patients whose spontaneous breathing was achieved were extubated. The patient, who remained under observation on the operating room table for another 5 minutes, was delivered to the recovery unit after the postoperative recovery 1st min. and the postoperative recovery 5th min. hemodynamic parameters were recorded.

In all patients included in the study, the total duration of surgery (min.), the pneumoperitoneum pressure applied during the case (mmHg), the total amount of fentanyl used (μ cg), the total amount of inhalation anesthetic consumed at the end of the case (mL) were noted.

Table 1. Comparison of demographic information between groups

| | Group C (n=40) | Group B (n=40) | P value |
|----------------------------------|---------------------|---------------------|---------|
| Age (year) | | | |
| Mean±SD | 46.65±13.99 | 51.75±12.65 | 0.547 |
| Median (min-max) | 47 (22-70) | 53 (27-57) | |
| Height (cm) | | | |
| Mean±SD | 1.64 ± 0.08 | 1.62 ± 0.07 | 0.569 |
| Median (min-max) | 1.67 (1.55-1.85) | 1.64 (1.48-1.80) | |
| Weight (kg) | | | |
| Mean±SD | 77.55±12.38 | 72.25 ± 11.95 | 0.943 |
| Median (min-max) | 77.5 (57-98) | 71.5 (48-95) | |
| BMI (kg/m²) | | | |
| Mean±SD | 28.55±4.22 | 27.30±4.39 | 0.644 |
| Median (min-max) | 28.55 (17.20-36.20) | 28.06 (17.80-36.90) | |
| Gender (M/F), n (%) | | | |
| Female | 25 (62.5%) | 29 (72.5%) | 0.111 |
| Male | 15 (37.5%) | 11 (27.5%) | |
| ASA score, n (%) | | | |
| ASA I | 9 (22.5%) | 14 (35%) | 0.065 |
| ASA II | 31 (77.5%) | 25 (65%) | |
| Presence of Comorbidities, n (%) | | | |
| (+) | 24 (30%) | 20 (25%) | 0.064 |
| (-) | 16 (20%) | 20 (25%) | |

Data are shown as mean±standard deviation or median (minimum-maximum) or n (%) Group C=control group, Group b=Block group, BMI=body mass index, ASA=American Society of Anesthesiologists, M=male, F=female. Mann-Whitney U testi, Pearson Ki-square test, Fisher's Exact Testi

P>0.05 statistically insignificant

Statistical Analysis

SPSS Windows 25.0 (Statistical for social sciences for windows) statistical package program was used for data entry and statistical analysis. The study data were summarized with descriptive statistics (mean, median, standard deviation, minimum-maximum value, percentage, frequency). In the evaluation of the data, t-test, Mauchly's analysis of variance, Bonferroni correction analysis for repeated measures were applied. Chi-square test was used to compare categorical data. A value of P<0.05 was considered statistically significant.

RESULTS

Our study included adult patients aged 18-75 years who were planned for ASA I and II laparoscopic cholecystectomy. We planned to compare the effect of transversus abdominis plan and rectus sheath block on sevoflurane and fentanyl consumption with entropy monitoring in these patients. For this purpose, the ages of the patients included in our study ranged between 22 and 70 years. When demographic data, ASA scores and comorbidities of the patients were compared between the groups, no statistically significant difference was found (P>0.05). Demographic data, ASA scores and patient comorbidity data of the study are shown in Table 1. (Table 1)

There was no statistically significant difference between the mean operation time and pneumoperitoneal pressure of the patients. (P>0.05) (Table 2) When the total amount of inhalation agent consumed during the total case duration was compared between the two groups, it was 27.05±7.43 ml in Group C and 12.25±4.34 mL in Group B, and a statistically significant difference was found between the groups (P<0.05) (Table 2).

The need for additional fentanyl doses during the intraoperative period was required in 30% of the cases. The need for additional fentanyl doses during the intraoperative period and the total amount of fentanyl consumed showed significant differences between the groups. Group C required more additional fentanyl doses intraoperatively than Group B (21 in Group C and 3 in Group B). In total, $115\pm33.62~\mu cg$ and $84\pm22.10~\mu cg$ fentanyl were consumed, respectively, and a statistically significant difference was found between the two groups (P<0.05) (Table 2).

According to our randomized controlled trial results, we demonstrated that preoperative TAP and rectus sheath block combined with general anesthesia reduced the intraoperative opioid and anesthetic agent consumption in laparoscopic cholecystectomy cases. We found that the amount of inhalation anesthetic agents consumed throughout the case, the need for intraoperative additional dose of fentanyl, and the total amount of fentanyl given throughout the case were significantly less in the laparoscopic cholecystectomy group (Group B) with TAP and RC block compared to the laparoscopic cholecystectomy group (Group C) without block (P=0.002, P<0.001, P=0.001).

Table 2. Comparison of clinical information of patients in Group C and Group B

| | Group C (n=40) | Group B (n=40) | P value |
|---|----------------|----------------|---------|
| Total duration of surgery (minute) | 40 (30-50) | 40 (30-50) | 0.213 |
| Pneumoperitoneum pressure (mmHg) | 14 (12-16) | 15 (12-18) | 0.386 |
| Amount of inhalation anesthetic consumed (mL) | 33.5 (19-48) | 13.5 (6-21) | 0.002* |
| Intraoperative need for additional dose of fentanyl | | | |
| (+) | 21 (52.5%) | 3 (7.5%) | <0.001* |
| (-) | 19 (47.5%) | 37 (92.5%) | |
| Total amount of fentanyl (μcg) | 125 (60-190) | 95 (55-135) | 0.001* |

Data are shown as mean±standard deviation or n (%). Group C=control group, Group B=block group.

Mann-Whitney U testi, Student t test

^{*}P<0.05 statistically significant

Table 1. Comparison of SE values of Group C and Group B

| State entropy (SE) | Group C (n=40) | Group B (n=40) | P value |
|--|----------------|------------------|---------|
| Initial | 89.18±3.28 | 88.30±3.08 | 0.724 |
| Before induction | 87.38±4.55 | 88.18±2.77 | 0.042* |
| After induction | 44.75±5.05 | 45.18 ± 5.88 | 0.441 |
| After incision 1st min | 49.45±6.60 | 51.13±6.73 | 0.978 |
| Pnömoperitoneum 5 th min | 45.75±5.53 | 47.28 ± 5.89 | 0.590 |
| Pnömoperitoneum 10 th min | 48.35±5.87 | 48.10±5.62 | 0.946 |
| Pnömoperitoneum 15 th min | 48.48±5.93 | 48.93 ± 5.86 | 0.740 |
| After pneumoperitoneum 1st min | 50.18±8.21 | 53.20±6.34 | 0.840 |
| After extubation | 82.78±7.45 | 82.50 ± 8.25 | 0.838 |
| Postoperative recovery 1st min | 86.43±5.25 | 87.33±2.95 | 0.005 |
| Postoperative recovery 5 th min | 89.30±3.04 | 89.43±2.71 | 0.381 |

Data are shown as mean±standard deviation. Group C=control group, Group B=block group, SE=state entropy, min=minute. Student t test, Paired Samples t test

The pre-induction SE (static entropy, entropy of state) values of Group B were statistically significantly higher than Group C (P=0.042, P<0.05). When SE measurements were compared between the groups, there was no statistically significant difference (P>0.05) between baseline, post-induction, 1st min. after incision, 5th min., 10th min. and 15th min. after pneumoperitoneum, 1st min after pneumoperitoneum,

1st min., and 5th min. after postoperative recovery (Table 3).

When RE (respond entropy) measurements were compared between the groups, there was no statistically significant difference (P>0.05) between baseline, pre-induction and post-induction, 1st min. after incision, 5th min., 10th min. and 15th min. after pneumoperitoneum, 1st min. after pneumoperitoneum, 1st

Table 2. Comparison of RE values of Group C and Group B

| Respond entropy (RE) | Group C (n=40) | Group B (n=40) | P value |
|--|------------------|------------------|---------|
| Initial | 96.88±1.84 | 97.00±2.23 | 0.383 |
| Before induction | 95.53±3.81 | 96.40±2.83 | 0.718 |
| After induction | 46.95 ± 5.19 | 47.80 ± 6.82 | 0.053 |
| After incision 1st min | 51.85 ± 6.68 | 53.00±6.52 | 0.513 |
| Pnömoperitoneum 5 th min | 48.75 ± 5.75 | 49.05 ± 5.78 | 0.874 |
| Pnömoperitoneum 10 th min | 50.78 ± 6.20 | 49.90 ± 6.08 | 0.573 |
| Pnömoperitoneum 15 th min | 50.40 ± 5.67 | 50.68 ± 5.80 | 0.921 |
| After pneumoperitoneum 1st min | 52.50±8.32 | 54.40±7.46 | 0.857 |
| After extubation | 91.65 ± 6.58 | 91.75±7.68 | 0.380 |
| Postoperative recovery 1st min | 94.65±4.17 | 95.78±3.04 | 0.612 |
| Postoperative recovery 5 th min | 96.65±2.15 | 97.23±1.96 | 0.315 |

Data are shown as mean±standard deviation. Group C=control group, Group B=block group, RE=respond entropy, min=minute.

Student t test, Paired Samples t test

^{*}P<0.05 statistically significant

min. after extubation, 1st min. and 5th min. after postoperative recovery (Table 4).

Since there should be no difference between the entropy values to make a statistical comparison between the groups, we were able to achieve this value with the statistical results in Tables 3 and 4.

DISCUSSION

The commonly preferred combination of anesthesia in laparoscopic cholecystectomy cases is induction of general anesthesia followed by maintenance with a combination of inhalation agents and opioids. However, these agents have undesirable effects such as prolonging recovery time, causing postoperative nausea and vomiting, causing intestinal dysfunction and respiratory depression, causing postoperative rebound pain, increasing environmental pollution and increasing health costs [10, 11]. Therefore, minimizing intraoperative consumption of anesthetic and analgesic agents should be a priority for every anesthesiologist [12].

Fascial plane blocks performed after intubation for preemptive analgesia to minimize the trauma of the surgical incision and to reduce the incidence of post-operative chronic pain have become popular [13-15]. TAP and rectus sheath block is a peripheral block method that blocks somatic nerves in the anterior abdominal wall. Bilateral TAP and rectus sheath block has been successfully used for pain control in laparoscopic cholecystectomies [16, 17].

There are a limited number of studies in the literature on intraoperative anesthetic agent consumption in laparoscopic surgeries combining TAP and rectus sheath block with general anesthesia [18, 19]. Our study aimed to evaluate the effect of TAP and RC block on inhalation agent and opioid consumption. In our study, we found that sevoflurane consumption was less in the Group B compared to the Group K at the same depth of anesthesia. At this point, we believe that TAP and rectus sheath block contribute to multimodal analgesia strategies by reducing inhaled gas consumption.

Kokulu *et al*. [19] compared the cost and anesthetic agent consumption in cases with and without TAP block, with intraoperative Target BIS kept at 40-50 in laparoscopic cholecystectomy surgery. They reported that anesthetic agent use decreased in the TAP block group. They did not find a statistical difference

in the amount of intraoperative opioid consumption between the two groups. Contrary to the results of this study, sevoflurane consumption was lower in laparoscopic cholecystectomy cases where we applied TAP and rectus sheath block in our study. In addition, the need for intraoperative additional fentanyl dose and the total amount of fentanyl consumed were found to be lower in Group B. We think that this is due to the preemptive fascial plane blocks. Monitoring the depth of anesthesia with entropy gave us different results.

Karaman et al. [1] studied the intraoperative remifentanil and sevoflurane consumption in the group in which TAP block was combined with patients undergoing total abdominal hysterectomy (TAH) under general anesthesia. They found that total remifentanil and sevoflurane consumption was significantly lower in the group in which TAP block was added. They found that QoR-40 (Quality of Recovery score) was significantly higher in Group TAP patients. They reported that combining TAP block with general anesthesia reduced opioid and anesthetic consumption in TAH cases and provided a better postoperative period. In our study, the total amount of inhalational anesthetic consumed during the case was statistically significantly lower in Group B than in Group K. Our study also obtained similar results with this study.

Bhattacharjee et al. [20] investigated the effect of TAP block and saline infusion after general anesthesia on intraoperative hemodynamic parameters and intraoperative fentanyl consumption in patients undergoing TAH surgery. They found that the heart rate, systolic blood pressure and intraoperative fentanyl requirement during surgery were significantly higher in the saline group compared to the block group. In conclusion, they showed that TAP block combined with general anesthesia before incision reduced intraoperative fentanyl requirement, prevented hemodynamic responses to surgical stimuli and provided appropriate postoperative analgesia. Our study was parallel to this study and the amount of intraoperative additional fentanyl dose administered was statistically significantly higher in Group K compared to Group B.

Opioid agents contribute to postoperative pain by inhibiting nociception. However, due to undesirable side effects, different methods and various drugs are used for postoperative pain management instead of opioids [21]. Regional regional anesthesia is a very popular method in this sense. In our study, we

used a combination of two facial plan blocks for postoperative analgesia.

Insufficient depth of anesthesia may not suppress somatic and autonomic reflexes sufficiently and may be harmful especially in patients with limited cardiac reserve. Excessive depth of anesthesia may also suppress vital functions and may cause complications such as coma and death [3]. To prevent anesthesia complications especially in high-risk patient groups, anesthesia depth measurement should be added to standard monitoring [22]. In our study, we used entropy monitoring, which is considered more recent, to monitor the depth of anesthesia.

The importance of environmentally sustainable health services has also become more on the agenda [23]. The provision of various health services, such as operating rooms, consumables, waste volumes, high energy systems, anesthesia gas systems, etc. causes a considerable amount of greenhouse gas emissions [24]. In the study examining the effect of anesthesia types on carbon footprint, McGain et al. [25] mentioned that general, regional and combined anesthetics have similar effects in terms of CO₂ equivalence in greenhouse gas emissions. However, of the 3 main factors affecting the carbon footprint (disposable equipment, electricity consumption of devices, and drugs used), it is stated that the biggest change can be made through drugs. It has been shown that sevoflurane, one of the inhalation anesthetic agents, occupies a significant place in greenhouse gas emissions, especially in patients undergoing general and combined anesthesia. In a study by Struys et al. [26] on the environmental effects of anesthesia, it was reported that inhalation anesthetics such as nitrogen oxide and halogenated ethers have a serious global warming potential because they are important greenhouse gases. As a result, inhalation anesthetics consumed during the operation were found to cause more than 50% of the peroperative greenhouse gases. Therefore, reducing the amount of inhalation anesthetic agents consumed by measuring the depth of anesthesia is an ethical obligation for every anesthesiologist in these days of global climate change.

One of the Principles of Environmentally Sustainable Anesthesia in the Global Consensus Statement of the World Federation of Societies of Anesthesiologists aims to reduce atmospheric waste of volatile agents to reduce the carbon footprint [27]. However, in the face

of ever-increasing health expenditures, cost control is also important. It should be aimed to identify various strategies to reduce the use of inhalation anesthetic agents due to their high costs [28].

Limitations

Our study was conducted at a single center; conducting multicenter randomized controlled trials with larger numbers of patients under similar standards would raise awareness for reducing consumption of inhalation anesthetic agents.

CONCLUSION

The strengths of our study include the use of the entropy monitor during the operation, the fact that the TAP and rectus sheath block were performed by an experienced anesthesiologist and similar block success was achieved in each block application (we visually monitored the distribution of local anesthesia in the target area simultaneously with ultrasonography and confirmed that the blocks were performed effectively), the same physician performed the data collection phase, and we standardized anesthesia for both groups with patient group selection factors. The weaknesses of our study are that the operations were performed by different surgeons even though the same surgical technique was applied, dermatomal sensory block levels could not be determined after TAP and rectus sheath block, and postoperative analgesia follow-up was not performed in every patient. As a result, we have shown that monitoring the depth of anesthesia of patients undergoing preoperative block may support cost and environmental protection, in addition to less drug use and fewer side effects.

Ethical Statement

This study was approved by the Tekirdağ Namık Kemal University Non-Interventional Clinical Research Ethics Committee on 26.07.2022 with the research protocol number 2022.138.07.05.

Authors' Contribution

Study Conception: EK, CA; Study Design: EK, AG; Supervision: EK, IY; Funding: EK, IY; Materials: EK, AG; Data Collection and/or Processing: EK, BT; Statistical Analysis and/or Data Interpretation: EK,

BT; Literature Review: EK, AG; Manuscript Preparation: EK, IY and Critical Review: EK, CA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Emergency Medicine

Comparison of ultrasound-guided joint reduction with traditional methods in the emergency center

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ABSTRACT

Objectives: This study aimed to compare and analyze the reliability of ultrasound-guided procedures and traditional methods in the reduction of joint dislocations in the emergency department.

Methods: A total of 136 cases were included in the prospective randomized controlled study. The cases were randomized into groups as ultrasound-guided reduction (n=66) and traditional reduction (n=70). The reduction success, time spent for the procedure, complication rates, pain scores and patient satisfaction levels were evaluated. Functional results and osteoarthritis development were also analyzed in long-term follow-up. Chi-square test, Student t-test and Mann-Whitney U test were used in the statistical analysis of the data.

Results: The success rate in the ultrasound reduction group (93.9%) was significantly higher than in the conventional reduction group (71.4%) (P<0.001). The mean reduction time was calculated as 3.2±1.8 minutes in the ultrasound group and 7.6±4.1 minutes in the conventional group (P<0.001). Complication rates were 7.6% in the ultrasound group and 21.4% in the conventional group (P=0.018). While 90.9% anatomical position was achieved in the ultrasound group in post-reduction, this rate remained at 64.3% in the conventional group (P<0.001). In the long-term follow-up, osteoarthritis development (ultrasound: 15.2%, conventional: 35.7%, P=0.012) and functional limitation rates (ultrasound: 10.6%, conventional: 25.7%, P=0.021) were significantly lower in the ultrasound group.

Conclusions: Ultrasound-guided interventions in the reduction of joint dislocations in the emergency department provide higher success rates, shorter treatment times, and lower complication rates than traditional methods. Long-term results also support the superiority of reductions performed with ultrasound guidance. In light of these findings, ultrasound-guided reduction is recommended as the first-line approach in the management of joint dislocations.

Keywords: Joint dislocation, ultrasound, reduction, emergency department, point-of-care ultrasound

oint dislocations are among the most common reasons for emergency department visits and are among the orthopedic emergencies that require rapid intervention. Especially in shoulder joint dislocations, correct diagnosis and selection of reduction

technique are of critical importance. It has been shown that evaluation using ultrasound protocol increases successful reduction rates. A systematic ultrasound examination including acromioclavicular joint, biceps, subscapularis and supraspinatus evaluations offers im-

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portant gains in terms of pre-reduction planning and guidance during the procedure [1].

Therefore, the role of ultrasound in the diagnosis and treatment of joint dislocations is increasing. Recent systematic reviews and meta-analyses have shown that reductions performed under ultrasound guidance are associated with higher success rates and lower complication risks compared to traditional methods. The use of ultrasound provides valuable information, especially in terms of confirming joint position in post-reduction evaluation [2].

With the widespread use of ultrasound in practice, changes have occurred in emergency department treatment algorithms. Contemporary diagnostic approaches show that the use of ultrasound together with traditional methods provides positive results [3]. Three-dimensional imaging techniques provide additional advantages in the analysis of joint morphology and reduction planning, especially in complicated patients [4].

The use of ultrasound provides optimization in patient management in the emergency department. Studies have shown that reductions performed with ultrasound guidance shorten the procedure time and increase patient comfort. Especially with bedside ultrasound application, rapid diagnosis and treatment are provided and the clinical decision-making process is improved [5].

However, it is also emphasized that ultrasound cannot replace clinical examination but should be used as a complementary tool. A comprehensive clinical evaluation forms the basis of reduction success and the best results are obtained when evaluated together with ultrasound findings [6].

The aim of this study was to analyze the effectiveness of ultrasound-guided reduction procedures in the treatment of joint dislocations in the emergency department by comparing them with traditional methods. The study aimed to determine the most appropriate treatment approach for the management of joint dislocations in the emergency department by evaluating the reliability, success rates, procedure times, complication risks, and patient satisfaction levels of ultrasound-guided procedures. In addition, functional results and osteoarthritis development were analyzed in long-term follow-ups to investigate whether ultrasound-guided reductions can be recommended for routine use in clinical practice.

METHODS

Study Design

This prospective randomized controlled trial was planned to compare ultrasound-guided joint reduction in the emergency department with conventional methods. The study protocol was approved by the Adana City Hospital Ethics Committee (Date: April 4, 2025, Number: 12/446) and was conducted according to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Patient Selection and Randomization

The study included 136 patients who presented to the emergency department and required joint reduction. Patients were divided into two groups using a randomization table: ultrasound group (n=66) and conventional group (n=70). Ultrasound group included patients who underwent joint reduction under ultrasound guidance. Ultrasonographic evaluation was performed before, during and after the reduction procedure. Direct radiography was not performed in this group. However, conventional group included patients who underwent traditional manual reduction techniques. Direct radiography was performed before and after reduction.

Inclusion criteria are the following: (1) Diagnosis of acute joint dislocation; (2) Joint displacement requiring reduction. Exclusion criteria included: (1) Open fracture-dislocation, (2) Presence of neurovascular complications, (3) Multiple trauma patients, (4) History of coagulopathy, (5) Pregnant women, and (6) Refusal to participate in the study.

Ultrasound Protocol

In the ultrasound group, joint anatomy was evaluated using a linear probe. The congruence of the joint surfaces, surrounding soft tissue status and vascular structures were examined before reduction. Joint reduction was observed with real-time imaging during reduction. Anatomical congruence was confirmed ultrasonographically after the procedure.

Reduction Techniques

Traditional standard reduction techniques were used in both groups according to the joint type. The need for sedation was assessed according to the pa-

tient's condition. Reduction success was defined as achieving anatomical harmony.

Data Collection and Evaluation Parameters

Primary Outcome Parameters: Reduction success rate, Procedure time, and Complication rates Secondary Outcome Parameters: Patient satisfaction, Cost analysis, Functional scores, and Long-term results

Demographic Data: Age and gender distribution, Comorbidity status, Trauma mechanism, and Time to presentation

Clinical Parameters: Affected joint location, Dislocation type (simple/complex), Amount of displacement before reduction (angular and translational), Need for secondary reduction, and Types of complications (nerve injury, loss of reduction)

Imaging Results: Post-reduction joint congruence (anatomical, acceptable, not reduced)

Functional Assessment: Gartland-Werley score, DASH (Disabilities of the Arm, Shoulder and Hand) score, Pain intensity (VAS 0-10), and Range of motion (degrees)

Long-Term Follow-up (6 months): Time to union, Development of osteoarthritis, and Functional limitation rate

Satisfaction and Cost Analysis: Patient satisfaction (Likert scale 1-5), Preference for repeat procedure, Physician technical difficulty score (VAS 0-10), Procedure cost (USD), Emergency room stay (minutes), and Radiation exposure (zero in USG group, all patients in conventional group)

Subgroup Analyses: Age groups, Simple and complex dislocation groups, and Bone mineral density (DEXA) assessment (only in patients over 65 years of age, n=51).

Sample Size Calculation

Based on pilot data showing a 70% success rate with conventional methods, a sample size of 64 patients per group was calculated to detect a 20% improvement with ultrasound guidance (α =0.05, β =0.20, two-sided test).

Statistical Analysis

Categorical variables were compared using the Chi-square test or Fisher's exact test. Continuous variables were analyzed using the Student t-test for normally distributed data and the Mann-Whitney U test for nonparametric data. Normal distribution was assessed using the Shapiro-Wilk test. All analyses were performed using SPSS version 25.0. A P value of <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Features

A total of 136 patients were included in the study. The mean age in the ultrasound group (n=66) was 42.7±20.8 years, while it was 57.5±15.7 years in the conventional group (n=70) (P=0.003). In the ultrasound group, 69.7% (n=46) of the patients were female and 30.3% (n=20) were male; in the conventional

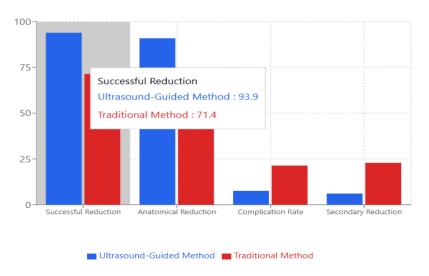


Fig. 1. Comparison of ultrasound-guided versus traditional methods in joint reduction outcomes.

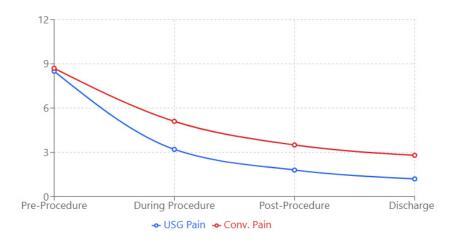


Fig. 2. Pain scores over time (Visual Analog Scale).

group, 74.3% (n=52) were female and 25.7% (n=18) were male (P=0.621). When the affected joint distribution was examined, shoulder involvement was observed in 56.1% of the patients in the ultrasound group, elbow involvement was observed in 18.2% and bilateral involvement was observed in 25.7%; in the conventional group, these rates were 84.3%, 11.4% and 4.3%, respectively (P<0.001) (Fig. 1).

Reduction Success and Complications

The reduction success rate in the ultrasound group was 93.9% (62/66), while it was 71.4% (50/70) in the conventional group (P<0.001). The mean reduction time was measured as 3.2 ± 1.8 minutes in the ultrasound group and 7.6 ± 4.1 minutes in the conventional group (P<0.001). The need for secondary reduction was seen as 6.1% (4/66) in the ultrasound group and 22.9% (16/70) in the conventional group (P=0.004).

When the complication rates were compared, they were found to be 7.6% (5/66) in the ultrasound group and 21.4% (15/70) in the conventional group (P=0.018). Nerve injury was 3.0% (2/66) in the ultrasound group and 8.6% (6/70) in the conventional group; Loss of reduction was observed in 4.5% (3/66) in the ultrasound group and 12.9% (9/70) in the conventional group.

Imaging Results and Functional Assessment

When post-reduction joint congruence was evaluated, 90.9% anatomic and 9.1% acceptable reduction was achieved in the ultrasound group; 64.3% anatomic, 28.6% acceptable and 7.1% non-reducible results were obtained in the conventional group (P<0.001).

In the functional assessment, the Gartland-Werley score was calculated as 2.1±1.8 in the ultrasound

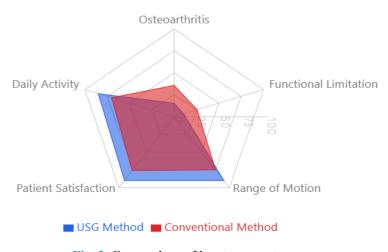


Fig. 3. Comparison of long-term outcomes.

group and 5.6 ± 3.2 in the conventional group (P<0.001). The Disabilities of the Arm, Shoulder and Hand (DASH) score was determined as 12.4 ± 9.1 in the USG group and 28.7 ± 14.6 in the conventional group (P=0.002). Pain intensity assessed by Visual Analog Scale (VAS) was measured as 1.8 ± 0.9 in the ultrasound group and 3.5 ± 1.2 in the conventional group (P<0.001) (Fig. 2).

Long-Term Results and Satisfaction

The mean union time was determined as 8.2 ± 2.1 weeks in the ultrasound group and 10.5 ± 3.4 weeks in the conventional group (P=0.009). Osteoarthritis development was observed as 15.2% (10/66) in the ultrasound group and 35.7% (25/70) in the conventional group (P=0.012). Functional limitation rate was determined as 10.6% (7/66) in the ultrasound group and 25.7% (18/70) in the conventional group (P=0.021) (Fig. 3).

Patient satisfaction (Likert 1-5) was evaluated as 4.5±0.6 in the ultrasound group and 3.8±1.1 in the conventional group (P=0.003). In terms of repeat procedure preference, 90.9% of patients preferred the procedure performed under ultrasound guidance, while this rate was determined as 21.4% in the conventional group (P<0.001). In the physician's technical difficulty assessment (VAS 0-10), the ultrasound group received 3.0±1.2 points, while the conventional group received 6.2±2.0 points (P<0.001).

DISCUSSION

In our study, the effectiveness comparisons of reductions performed with ultrasound guidance and conventional methods in the management of joint dislocations in the emergency department were analyzed. In our study, a success rate of 93.9% was determined in the ultrasound group, while this rate remained at 71.4% in the conventional group (P<0.001). These results are parallel to the 100% sensitivity and specificity rates reported in the systematic review by Gonai *et al.* [7]. Similarly, Attard Biancardi *et al.* [8] demonstrated high diagnostic accuracy of point-of-care ultrasound for shoulder dislocations, supporting our findings of superior reduction success rates with ultrasound guidance. In particular, the significant difference in complication rates (7.6% in the ultrasound group and

21.4% in the conventional group, P=0.018) is similar to the literature findings.

In pain control; VAS scores were significantly lower in the ultrasound group in our study (1.8±0.9 vs. 3.5 ± 1.2 , P<0.001). While no difference was found in pain control between ultrasound and landmark techniques in Owusu-Akyaw's study [9], better pain control was noted in our study in procedures performed under ultrasound guidance. However, Rungsinaporn et al. [10] demonstrated that ultrasound-guided intraarticular lidocaine injection was more effective for pain control, which is consistent with our findings of lower VAS scores in the ultrasound group. In the systematic review by Gawel et al. [11], it was revealed that ultrasound-guided nerve blocks showed lower complication rates (3.9% vs. 24.9%, P<0.001). The inferior accuracy of landmark-guided glenohumeral joint injections reported by Omer et al. [12] further supports the superiority of ultrasound-guided techniques demonstrated in our study. These findings support the low complication rates in our study.

The high success rates reported in the case series by Mohanty et al. [13] confirm the high performance of the ultrasound group in our study. Gottlieb's comprehensive review [14] of reduction techniques emphasizes the importance of technique selection, which aligns with our observation that ultrasound-guided approaches yielded consistently better outcomes. When evaluated from an anatomical perspective, the principles of glenohumeral joint instability emphasized by Ladd et al. [15] reveal the importance of ultrasound guidance. The ultrasound assessment of anterior humeral head translation described by Inoue et al. [16] provides the anatomical basis for our superior joint congruence results in the ultrasound group. However, in our study, post-reduction joint congruence was 90.9% in the anatomical position in the ultrasound group, while this rate was lower in the conventional group and remained at 64.3%.

A significant difference was observed in the procedure time values in our study (3.2±1.8 minutes in the USG group, 7.6±4.1 minutes in the conventional group, P<0.001). The 94.1% USG success rate reported by Gibbons *et al.* [17] is almost the same as the 93.9% rate in our study. The advantages of handheld ultrasound emphasized by Lahr *et al.* [18] support the short procedure times observed in our study. Hunter *et al.* [19] highlighted the expanding role of muscu-

loskeletal ultrasound in shoulder dislocation management, supporting our recommendation for routine ultrasound use in emergency departments.

The effect of POCUS on procedure success [20] was clearly demonstrated in our study. The need for secondary reduction also showed a significant difference, and this rate was 6.1% in the ultrasound group and 22.9% in the conventional group (P=0.004). The high prevalence of rotator cuff pathologies reported by Shapla et al. [21], especially in patients over 40 years of age, supports the importance of ultrasound use in our study. The mean age in our study was recorded as 42.7±20.8 years in the ultrasound group and 57.5±15.7 years in the conventional group. The special conditions in patients over 40 years of age emphasized in the study of Zhou et al. [22] are present in our study, and the importance of ultrasound guidance in this age group is confirmed. Henneberry's POCUS usage principles [23] formed the basis of the protocol applied in our study.

In terms of patient satisfaction, a significant difference was found in our study (4.5±0.6 in the ultrasound group, 3.8±1.1 in the conventional group, P=0.003). Considering Baah's anatomical principles [24], it is observed that USG guidance provides a superior controlled and safe reduction. The recommendations of Mohanty *et al.* [25] regarding peripheral nerve blocks also express the reason for the low complication rates observed in our study.

Limitations

Methodological Limitations

This study is primarily a single-center study, therefore, the generalizability of the results is limited. The fact that the mean age of the patients in the ultrasound group $(42.7 \pm 20.8 \text{ years})$ was significantly lower than that of the patients in the conventional group $(57.5\pm15.7 \text{ years})$ (P=0.003) may have affected the comparisons between the groups.

Limitations Related to the Sample

The size of the study population (n=136) is moderate. The small number of patients, especially in subgroup analyses (e.g. cases with bilateral involvement, 25.7% in the ultrasound group, 4.3% in the conventional group), limited the statistical analysis. The imbalance in gender distribution may also affect the generalizability of the results due to the female predominance.

Technical Limitations

Having emergency medicine specialists experienced in the use of ultrasound may have positively affected the application results. This may lead to the failure to achieve similar success rates (93.9%) in less experienced centers. The low ultrasound-directed radiography incompatibility rate (3.0%) also highlights the importance of operator experience.

Limitations Related to Follow-up

The limited long-term follow-up data has limited the analysis of chronic complications in particular. Long-term outcomes such as osteoarthritis development (15.2% in the ultrasound group, 35.7% in the conventional group) and functional disability rates (10.6% in the ultrasound group, 25.7% in the conventional group) need to be analyzed with a longer follow-up period.

Cost Analysis Limitations

Since the cost-effectiveness analysis was performed only on medical costs; procedure costs (ultrasound group 148.5±32.4 USD, conventional group 234.7±45.8 USD) and indirect costs (labor loss, transportation costs, etc.) were not analyzed.

Recommendations

In future studies: (1) Multicenter studies with larger patient groups should be conducted, (2) More homogeneous groups should be created in terms of age and gender, (3) Studies with longer follow-up periods should be planned, and (4) Comprehensive cost-effectiveness analyses should be conducted.

Recommendations for Clinical Practice

- 1. Ultrasound-guided reduction should be adopted as the first-line approach in the treatment of joint dislocations in emergency departments.
- 2. The use of ultrasound should be routinely performed to evaluate accompanying rotator cuff pathologies, especially in patients over the age of 40.
- 3. The use of ultrasound in post-reduction evaluation should prevent unnecessary radiation exposure and should be accepted as a standard procedure for rapid analysis of procedure success.
- 4. Regular training on the use of ultrasound should be provided in the emergency department and competency levels should be periodically checked.

Recommendations for Future Research

- 1. Multi-center, randomized controlled studies with larger patient populations should be conducted.
- 2. Specific ultrasound protocols should be developed and standardized for different joint dislocations.
- 3. Long-term and prospective cohort studies analyzing functional outcomes over longer periods should be planned.
- 4. Comprehensive health economic evaluations should be performed for cost-effectiveness analyses.

Recommendations for Education and Quality Improvement

- 1. Ultrasound-guided reduction techniques should be added to the curriculum in emergency medicine residency programs and should be given as a standard in education.
- 2. Standard procedures for reduction of dislocations under ultrasound guidance should be developed and quality indicators should be established.
- 3. Regular monitoring should be carried out with continuous quality improvement programs regarding success rates, complication developments and patient satisfaction.
- 4. Multidisciplinary approach should be routinely implemented; treatment protocols should be established among orthopedics, radiology and emergency medicine specialists.

CONCLUSION

The results of our prospective randomized controlled study revealed that reductions performed with ultrasound guidance are significantly superior to traditional methods in the management of joint dislocations in the emergency department. Higher success rates (93.9% vs. 71.4%), shorter procedure times (3.2±1.8 vs. 7.6±4.1 minutes) and lower complication rates (7.6% vs. 21.4%) were demonstrated in reduction treatments performed with ultrasound. Patient satisfaction was significantly higher in the USG group (4.5±0.6 vs. 3.8±1.1), while the preference for repeating the procedure was clearly and distinctly in favor of the treatment performed with ultrasound (90.9% vs. 21.4%).

In the long-term follow-ups of the patients, lower osteoarthritis formation (15.2% vs. 35.7%) and less

functional limitation (10.6% vs. 25.7%) were observed in the ultrasound treatment group. Post-reduction joint congruence was found to be more successful in the ultrasound group (90.9% anatomic reduction) and this was reflected positively in the functional results. In addition, the cost-effectiveness calculation of the procedures performed with ultrasound guidance was calculated more positively than conventional methods (148.5±32.4 vs. 234.7±45.8 USD).

Ethical Statement

The study was approved by the Adana City Training and Research Hospital Scientific Research Ethics Committee (Decision no.: 446 and date: 10.04.2025).

Data Availability Statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request, subject to institutional approval and ethical considerations.

Authors' Contribution

Study Conception: SE, SM, Vİ; Study Design: SE, SM, Vİ; Supervision: SE, SM, Vİ; Funding: SE, SM, Vİ; Materials: SE, SM, Vİ; Data Collection and/or Processing: SE, SM; Statistical Analysis and/or Data Interpretation: SE, SM, Vİ; Literature Review: SE, SM, Vİ; Manuscript Preparation: SE; and Critical Review: SE, SM, Vİ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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General Surgery

Factors influencing fistula formation following perianal abscess treatment

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ABSTRACT

Objectives: Perianal abscesses are frequently encountered in clinical practice and are primarily attributed to a cryptoglandular origin. Despite prompt incision and drainage, a subset of patients still develop anal fistulas. This study aims to identify risk factors associated with fistula formation after perianal abscess management. **Methods:** A total of 145 patients (64 females, 81 males) with perianal abscess were retrospectively reviewed between 2020 and 2024. All underwent urgent incision and drainage under anesthesia. Demographic characteristics, comorbidities, type of surgical intervention, and postoperative outcomes were analyzed. Postoperative complications were assessed at both early (≤30 days) and late (>30 days) time points. Univariate and logistic regression analyses were conducted to determine independent predictors of fistula formation.

Results: The median patient age was 42 years (IQR: 35-50), and 37.9% had at least one comorbidity (17.2% diabetes mellitus, 13.8% hypertension). Intraoperative fistulas were identified in 37.9% of cases and managed via fistulotomy or seton placement when feasible. Early postoperative complications occurred in 24.1% of patients, most of which were minor. Over a median follow-up of 7 months (IQR: 4-12), abscess recurrence was observed in 6.9% and new-onset fistula in 14.5%. Comorbidities such as diabetes mellitus were associated with a higher likelihood of fistula formation. Anal incontinence was documented in 2.8% of patients, most cases resolving spontaneously or with conservative measures.

Conclusions: Although urgent incision and drainage generally yields favorable early outcomes, a notable proportion of patients develop late complications, particularly fistula formation. Close follow-up and tailored surgical strategies, including fistulotomy or seton placement when indicated, may help reduce morbidity. Prospective and multicenter studies with extended follow-up are warranted to further refine treatment protocols and identify high-risk individuals.

Keywords: Perianal abscess, anal fistula, fistulotomy, seton placement, postoperative complications, cryptoglandular disease

norectal infections may present as acute abscesses or chronic anal fistulas, with perianal abscesses ranking among the most frequently encountered conditions in proctological practice [1, 2].

Although perianal abscesses can be associated with various comorbidities, most are attributed to a primary cryptoglandular origin [3]. According to the cryptoglandular theory initially described by Parks and Eisen-

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hammer, obstruction of the anal crypt gland ducts causes infection within the intersphincteric space, which may subsequently spread into the ischioanal fossa or drain into the anal canal [2, 3]. A thorough understanding of anal canal anatomy is therefore critical for accurate diagnosis and effective management, as timely intervention often prevents severe complications such as anal incontinence or recurrence [4, 5]. Nonetheless, certain cases follow a more challenging clinical course, necessitating advanced treatment approaches to minimize morbidity [6-8]. Numerous studies have evaluated outcomes following standard interventions, including incision and drainage, fistulotomy, cavity packing, and postoperative management strategies such as abscess cavity packing [6-8]. However, comparative data on how these strategies influence subsequent fistula formation remain limited, underscoring the need for risk-stratified analyses. Despite these efforts, some patients still experience persistent disease or recurrence [9-11].

Therefore, our study aims to retrospectively investigate the factors influencing fistula development following perianal abscess management, with the ultimate goal of guiding future treatment strategies and improving patient outcomes.

METHODS

This retrospective study was conducted between 2020 and 2024, involving patients diagnosed and treated for perianal abscess at our institution. Abscesses were anatomically classified as simple perianal, ischioanal, or horseshoe based on operative notes and pre-operative imaging. A total of 145 patients, aged between 18 and 75 years, were included in the analysis. The sample comprised 64 females and 81 males. Patient selection was based on the completeness of medical records and the availability of relevant clinical data. Individuals whose records were incomplete or otherwise inadequate were excluded from the study.

All data were obtained from the patients' medical files and the institutional electronic medical record system. For each patient, demographic characteristics (e.g., age and sex) and pertinent clinical information (e.g., comorbidities, surgical procedure type, and postoperative outcomes) were systematically documented. The collected data were de-identified and anonymized to pro-

tect patient confidentiality. This study was approved by the Biruni University Ethics Committee (2024-BİAEK/06-50) and complied with the principles outlined in the Declaration of Helsinki. Written informed consent (where applicable and/or in line with institutional policy for retrospective studies) was obtained to ensure the protection of patient rights and privacy.

Early readmission was defined as an unplanned hospital stay within 30 days of the index operation. Minor complications were adverse events requiring only bedside or outpatient care (e.g., superficial wound infection, self-limited bleeding), whereas major complications necessitated re-operation, imageguided drainage, or intensive-care monitoring.

Statistical Analysis

All statistical analyses were performed using SPSS version 25. Continuous variables were presented as means ± standard deviations, while categorical variables were reported as frequencies and percentages. The chi-square test or Fisher's exact test was used to assess the relationship between categorical variables, and continuous variables were compared using either the Student's t-test or the Mann-Whitney U test, depending on the normality of the data distribution. To identify independent risk factors influencing fistula

Table 1. Baseline demographic and clinical characteristics (n=145)

| Characteristic | Data |
|---------------------------------------|------------|
| Age, years (range) | 18-75 |
| Median age [IQR] | 42 [35-50] |
| Sex Distribution | |
| Female | 64 (44.1%) |
| Male | 81 (55.9%) |
| Comorbidities (≥1) | 55 (37.9%) |
| Diabetes Mellitus | 25 (17.2%) |
| Hypertension | 20 (13.8%) |
| Other (e.g., COPD, CAD) | 10 (6.9%) |
| Mean symptom duration, days (mean±SD) | 6.2±2.4 |
| Total patients analyzed | 145 |

COPD=chronic obstructive pulmonary disease,

CAD=coronary artery disease, IQR=interquartile range,

SD=standard deviation

formation, a logistic regression analysis was conducted. Statistical significance was defined as a P-value of less than 0.05. Variables with P<0.10 on univariate testing were entered into a multivariable logistic-regression model; adjusted odds ratios (OR) with 95 % confidence intervals (CI) are reported.

RESULTS

A total of 145 patients (64 females and 81 males) aged between 18 and 75 years were included in this retrospective evaluation of perianal abscess management conducted from 2020 to 2024. The median age was 42 years (interquartile range 35-50), and 37.9% of all patients reported at least one comorbidity, most frequently diabetes mellitus (17.2%) and hypertension (13.8%). The mean duration of symptoms prior to clinical presentation was 6.2±2.4 days, with pain (98.6%), swelling (87.6%), and erythema (69.0%) constituting the most common complaints (Table 1).

All patients underwent urgent incision and drainage under anesthesia. Intraoperative assessment revealed a clinically identifiable fistula in 55 (37.9%) cases, leading to fistulotomy or seton placement when feasible. Antibiotic prophylaxis was administered to 114 (78.6%)patients. The mean operative time was 33.1±8.2 minutes (Table 2).

Cavity packing was used in 40 (27.6 %) patients. Eight (5.5 %) abscesses were classified as horseshoe; seven of these patients ultimately developed a fistula.

Table 2. Operative details (n=145)

| Parameter | Data |
|---|-------------|
| I&D alone | 70 (48.3%) |
| I&D+Fistulotomy | 50 (34.5%) |
| I&D+Seton placement | 25 (17.2%) |
| Intraoperative Fistula Detection | 55 (37.9%) |
| Antibiotic prophylaxis | 114 (78.6%) |
| Mean operative time (minutes) | 33.1±8.2 |
| Type of anesthesia | |
| General | 120 (82.8%) |
| Spinal or Regional | 25 (17.2%) |

Data are shown as mean±standard deviation or n (%). I&D=incision and drainage

Table 3. Early postoperative outcomes (\leq 30 days) (n=145)

| Outcome | n (%) |
|-------------------------------------|------------|
| No Early complications | 110 (75.9) |
| Minor complications | 20 (13.8) |
| Local infection or wound issues | 12 (8.3) |
| Mild bleeding/hematoma | 8 (5.5) |
| Major complications | 8 (5.5) |
| Severe infection or reoperation | 5 (3.4) |
| Other (e.g., thromboembolic events) | 3 (2.1) |
| Early readmission | 7 (4.8) |
| Mortality | 0 (0.0) |

Within the first 30 days after surgery, 110 (75.9%) patients experienced no complications, whereas 20 (13.8%) developed minor issues such as wound infection or mild bleeding managed conservatively, and 8 (5.5%) had major complications requiring additional intervention (Fig. 1). Early readmission occurred in 7 (4.8%)cases, primarily related to severe infection or re-accumulation of an abscess (Table 3).

Late postoperative outcomes were evaluated beyond 30 days, with a median follow-up period of 7.0 months (interquartile range 4-12) (Fig. 1). As shown in Table 4, 10 (6.9%) patients experienced abscess recurrence, and 21 (14.5%) developed an anal fistula confirmed on examination or imaging. Eleven of those fistulas ultimately required additional surgical intervention, whereas 10 were managed conservatively. Four (2.8%) instances of mild anal incontinence were documented; in two cases, this resolved spontaneously, and in the other two, pelvic floor rehabilitation was recommended. Late readmission occurred in 10 (6.9%)patients, typically related to fistula management or recurrent infection.

Table 5 summarizes baseline and peri-operative characteristics according to fistula status. Compared with patients who remained fistula-free (n=124), those who developed a fistula (n=21) were more likely to have diabetes mellitus (42.9 % vs 12.9 %; p = 0.004), a horseshoe-type abscess (28.6 % vs 1.6 %; P<0.001) and a longer pre-operative symptom duration (median 7 days [IQR 5-9] vs 6 days [IQR 4-7]; P=0.021). Early complications occurred more often in the fistula group, although the difference did not reach statistical

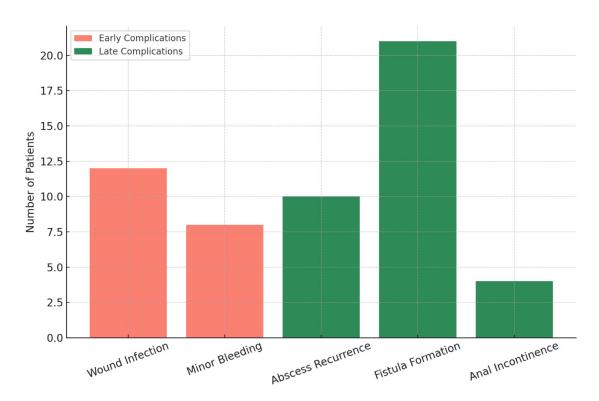


Fig. 1. A stacked bar chart comparing early and late complications by category.

significance (33.3 % vs 16.9 %; P=0.08). The use of postoperative cavity packing was comparable between groups (33.3 % vs 26.6 %; P=0.54).

Multivariable logistic regression confirmed three independent predictors of fistula formation: diabetes mellitus (OR 2.6, 95 % CI 1.1-6.4), horseshoe abscess configuration (OR 3.9, 95 % CI 1.4-11.1) and symptom duration > 7 days (OR 1.8, 95 % CI 1.0-3.3). The median interval from the index operation to fistula diagnosis was 3.2 months (IQR 2.1-4.6).

Transient anal incontinence was observed exclu-

Table 4. Late postoperative outcomes (>30 days) (n=145)

| Outcome | n (%) |
|---|------------|
| No late complications | 100 (69.0) |
| Abscess recurrence | 10 (6.9) |
| Fistula formation | 21 (14.5) |
| Required further surgery | 11 (7.6) |
| Managed conservatively (Seton, etc.) | 10 (6.9) |
| Anal incontinence (temporary or minor) | 4 (2.8) |
| Late readmission | 10 (6.9) |

sively in patients whose procedures involved internal-sphincter division (4/18, 22 %); no incontinence occurred among individuals managed with incision-and-drainage \pm cavity packing alone (0/127).

DISCUSSION

In this retrospective analysis of 145 patients who underwent urgent incision and drainage for perianal abscess between 2020 and 2024, we observed that 37.9% of patients had an intraoperatively detectable fistula, supporting the close relationship between perianal abscess and anal fistula formation [2, 3, 12]. This finding aligns with the cryptoglandular theory, which posits that obstruction of the anal crypt glands leads to infection within the intersphincteric space and can ultimately result in fistula formation [2, 3]. Our results further indicate that, despite the overall safety and effectiveness of incision and drainage (as evidenced by the 75.9% rate of no early complications and zero mortality), some patients still develop late complications, including fistula (14.5%) and abscess recurrence (6.9%), underscoring the importance of meticulous anatomic evaluation and vigilant long-term follow-up

| Variable | Fistula (n=21) | No fistula (n=124) | P value |
|--------------------------------------|----------------|--------------------|---------|
| Median age (years) (IQR) | 43 (36-51) | 42 (35-50) | 0.72 |
| Diabetes mellitus, n (%) | 9 (42.9) | 16 (12.9) | 0.004 |
| Horseshoe abscess, n (%) | 6 (28.6) | 2 (1.6) | < 0.001 |
| Cavity packing used, n (%) | 7 (33.3) | 33 (26.6) | 0.54 |
| Median symptom duration (days) (IQR) | 7 (5-9) | 6 (4-7) | 0.021 |
| Early complication rate, n (%) | 7 (33.3) | 21 (16.9) | 0.08 |

Table 5. Comparison of patients with and without fistula formation

[3-5, 13].

Our multivariable analysis confirmed diabetes mellitus and horseshoe anatomy as strong, independent drivers of fistula development, while cavity packing showed no significant protective or harmful effect. These findings support a tailored approach: aggressive drainage and loose-seton placement for horseshoe abscesses or diabetics, versus sphincter-preserving incision and drainage for low-risk cases.

Comorbidities such as diabetes mellitus and hypertension emerged relatively frequently in our cohort, suggesting that metabolic and vascular factors may impair wound healing and increase susceptibility to infection progression [9, 10, 14]. Patients with such comorbidities may therefore require more aggressive perioperative management (e.g., optimized glucose control, careful infection surveillance) to reduce the risk of adverse outcomes [9, 10, 14]. Although the overall rate of fistula formation in this study (14.5%) is comparable with rates reported in prior literature [6-8], our findings emphasize that the standard incision and drainage procedure alone may not suffice in all cases. A subset of patients needed additional surgical interventions, including fistulotomy or seton placement, either at the time of initial surgery or during follow-up. Such individualized treatment planning including consideration of patient risk factors, anal sphincter integrity, and fistula complexity - is essential to minimize morbidity and optimize healing [6-8, 15].

A subgroup review demonstrated that all four cases of transient incontinence followed procedures that divided the internal sphincter, reinforcing the importance of sphincter-sparing techniques whenever anatomical conditions permit.

Our observation that most patients experienced no significant early complications (75.9%) with a low

major complication rate (5.5%) reaffirms the safety profile of urgent incision and drainage for perianal abscess [1,7]. However, the fact that severe infection or reoperation occurred in 3.4% of patients highlights the need for close postoperative surveillance and timely intervention when warranted. Furthermore, although we noted a relatively low incidence of anal incontinence (2.8%), it is crucial to remain mindful of this potential complication, particularly when fistulotomy or more extensive sphincter manipulation is required [4, 5]. Where minor incontinence did occur, conservative measures such as pelvic floor rehabilitation appeared beneficial.

Limitations

Because our study was retrospective, data completeness depended on the accuracy of electronic medical records, and certain clinical variables could not be evaluated in detail. Additionally, as this was a single-center experience, the generalizability of our findings may be limited. Future multicenter and prospective studies with longer follow-up periods are needed to better delineate the risk factors associated with fistula development and to refine treatment algorithms [6-8, 9-11]. Future studies should also evaluate quality-of-life outcomes and cost-effectiveness across anatomical subtypes.

CONCLUSION

While urgent incision and drainage is largely successful and safe for perianal abscess management, the relatively high incidence of fistula formation and recurrence in specific patient subsets (e.g., those with diabetes or hypertension) underscores the need for tailored treatment approaches and vigilant follow-up.

Precise anatomical assessment and, when indicated, additional procedures such as fistulotomy or seton placement can improve long-term outcomes. Prospective, large-scale investigations will further clarify risk stratification and foster optimized, individualized management strategies for perianal abscess and associated anal fistulas. Explicit attention to abscess anatomy, metabolic comorbidities, and symptom duration can improve risk-stratification and guide operative decision-making.

Ethical Statement

This study was approved by the Biruni University Scientific Research Ethics Committee (Decision no.: 2024-BİAEK/06-50, date: 20.01.2025).

Authors' Contribution

Study Conception: AH, SNKÇ; Study Design: N/A; Supervision: AH; Funding: AH, SNKÇ; Materials: AH, SNKÇ; Data Collection and/or Processing: AH; Statistical Analysis and/or Data Interpretation: AH; Literature Review: AH; Manuscript Preparation: AH; and Critical Review: AH, SNKÇ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Psychiatry

The relationship between knowledge of cardiovascular disease risk factors and health anxiety among caregivers of patients undergoing open-heart surgery

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ABSTRACT

Objectives: Cardiovascular diseases, characterized by their chronic nature, frequently lead to considerable physical strain and psychological distress in affected individuals. In managing these challenges, the involvement of caregivers plays a pivotal role. The effectiveness and consistency of the care they offer are substantially influenced by both their psychological health and their understanding of the disease's risk profile. This study aims to examine the relationship between caregivers' knowledge of cardiovascular risk factors and their levels of health anxiety while caring for patients recovering from open-heart surgery.

Methods: Participants who were identified as caregivers for individuals undergoing open-heart surgery were assessed using three instruments: a demographic and descriptive questionnaire, the Cardiovascular Disease Risk Factors Knowledge Level Scale (CARRF-KL), and the Health Anxiety Inventory (HAI).

Results: The study included 58 participants, with females comprising 56.9% of the sample. The average score obtained on the Cardiovascular Disease Risk Factors Knowledge Level Scale (CARRF-KL) was 19.16±4.99, whereas the mean score on the Health Anxiety Inventory (HAI) was 21.1±14.84. The analysis showed a statistically significant, positive but weak correlation between the total scores of the Health Anxiety Inventory (HAI) and the Cardiovascular Disease Risk Factors Knowledge Level Scale (CARRF-KL) (r= 0.282, P=0.032). Additionally, participants' education levels were significantly related to their CARRF-KL scores (P<0.001). Conclusions: This research highlights the vital importance of caregivers' knowledge about the disease and their mental health status in providing quality care to patients. Improving caregivers' comprehension of cardiovascular diseases, clearly defining their caregiving roles, and managing their health-related anxieties may enhance the well-being of both caregivers and patients. These findings point to the necessity of implementing specialized educational programs and psychological support services tailored for caregivers in cardiac care environments. Keywords: Cardiovascular disease, risk factors knowledge, health anxiety, caregivers, open heart surgery

ardiovascular disease (CVD) stands as the most widespread non-communicable illness worldwide. According to the World Health Organiza-

tion CVD encompasses a spectrum of disorders involving the heart and vascular system, including but not limited to coronary artery disease, cerebrovascular

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incidents, peripheral artery disease, rheumatic heart conditions, deep vein thrombosis, and pulmonary embolism [1].

In addition to its high incidence, CVD is a leading cause of mortality globally. Deaths attributed to cardiovascular conditions have been increasing steadily, with 17.9 million fatalities recorded in 2016 alone. Projections estimate this figure will rise to 22.2 million by 2030. That same year, CVD was responsible for nearly 31% of all deaths worldwide [2]. Within Turkey, ischemic heart disease (IHD) and cerebrovascular disease ranked as the top two causes of premature death in 2010, according to data from the Institute for Health Metrics and Evaluation [3].

Recognizing and understanding the risk factors associated with CVD is essential for identifying individuals who are at heightened risk, thereby facilitating prompt interventions aimed at risk reduction. Since the mid-1900s, significant advancements have been made in pinpointing major contributors to CVD development, aiding in the effective control of the disease, particularly in developed countries [4]. Key modifiable risk factors-including hypertension, diabetes, obesity, elevated lipid levels, smoking, and physical inactivity—have consistently been associated with higher rates of CVD incidence and mortality [5]. Because many of these factors can be prevented or managed, the onset and worsening of CVD are often avoidable. Consequently, knowledge about these risk factors is fundamental to both preventing and managing cardiovascular conditions [6]. Public health efforts that promote healthy behaviors and raise awareness about CVD symptoms are crucial for early detection, prevention, and better health outcomes [7].

Individuals diagnosed with cardiovascular disease often rely on caregivers due to the emergence of acute complications or the chronic nature of their condition [8]. Caregivers are generally described as those who offer informal, unpaid support to relatives or friends coping with chronic illnesses or disabilities. They form an essential part of the long-term care framework for patients facing both physical and mental health challenges [9]. Their responsibilities encompass aiding patients in daily activities, managing intricate treatment plans, coordinating with healthcare providers, and reducing the likelihood of medical errors [10]. Nevertheless, the caregiving role can impose significant emotional and social strain. Many caregivers report

symptoms such as depression, anxiety, social withdrawal, exhaustion, familial tensions, financial difficulties, and worries regarding their own well-being [11].

Health anxiety can manifest at various stages throughout an individual's life, often triggered by unfamiliar circumstances, unexpected events, bodily sensations, discomfort, or increased exposure to illness-related media content. In many instances, this anxiety is transient, diminishing as physical symptoms resolve or effective treatment is provided. However, in more severe cases, health anxiety persists despite appropriate medical intervention [12]. The experience of losing a loved one has been shown to intensify health-related worries, causing individuals to become overly focused on their own well-being. According to cognitive-behavioral models of health anxiety, people develop beliefs about illness based on both personal experiences and external influences, such as past illness encounters and information obtained from their surroundings. While early life experiences play a foundational role, exposure to health-related content through social media, cultural factors, and interpersonal relationships also significantly shape enduring health perceptions and anxieties [13]. Research examining health perceptions and anxiety among nursing students found that factors including chronic illness presence, history of hospitalization, and family history of chronic disease were linked to elevated health anxiety levels [14].

To the best of current knowledge, there has been no comprehensive study conducted in Turkey that explores the association between caregivers' awareness of CVD risk factors and their levels of health anxiety within the context of caring for patients undergoing open-heart surgery. The aim of this cross-sectional study is to assess caregivers' awareness of cardiovascular disease risk factors and to investigate the relationship between this knowledge and their level of health anxiety.

METHODS

Study Population and Sample

This cross-sectional study was carried out at the cardiovascular surgery outpatient clinic between August and December 2024. Approval was granted by the Ethics Committee for Non-Interventional Studies prior to the commencement of the research. Before enrolling in the study, all participants received detailed information from the researchers regarding the study's objectives and the nature of the questionnaires and scales to be used. Written informed consent was obtained from each participant, with assurances that their data would remain anonymous and be utilized exclusively for research purposes.

Participants were considered eligible if they were caregivers of patients undergoing open-heart surgery, aged 18 years or older, possessed at least a primary school education, and voluntarily consented to take part in the study. Exclusion criteria included diagnoses of intellectual disability, psychotic disorders, or primary/acquired neurological conditions potentially affecting cognitive abilities (such as stroke, dementia, head trauma, or cranial surgery). Additionally, individuals with current alcohol or substance abuse issues, as well as those who declined to provide informed consent, were excluded from the study.

The researchers initiated the process by introducing themselves and confirming that each participant met the criteria for being a caregiver as defined by the study. They then provided a comprehensive explanation of the study's objectives and procedures. In situations where patients had multiple caregivers, the individual who spent the greatest amount of time caring for the patient was selected to participate, ensuring that only one caregiver per patient was included in the study.

The calculated sample size needed to achieve a 95% confidence level (P<0.05) was 50 participants. Initially, 61 caregivers were approached for inclusion in the study. Among them, 2 declined to participate due to time limitations, and 1 was excluded from the analysis because of incomplete or inaccurately completed questionnaires and scales. Consequently, the final sample comprised 58 caregivers.

Data Collection and Analysis

Caregivers received a printed set that included a demographic questionnaire, the Cardiovascular Disease Risk Factors Knowledge Level Scale (CARRF-KL), and the Health Anxiety Inventory (HAI). The administration of these instruments was supervised by a psychiatrist to maintain uniformity and provide assistance when necessary. Completion of the questionnaire took approximately 15 minutes per participant.

Measures

Descriptive Questionnaire Form

The researchers designed a descriptive questionnaire encompassing various socio-demographic and health-related variables. The collected data encompassed variables such as participants' age, sex, educational attainment, marital and employment status, income level, residential setting, their relation to the patient, individual medical background, familial cardiovascular disease history, smoking behavior, physical activity patterns, and anthropometric measurements including body weight and height.

Cardiovascular Diseases Risk Factors Knowledge Level (CARRF-KL)

The Cardiovascular Diseases Risk Factors Knowledge Level (CARRF-KL) scale was developed by adapting 16 items from the Heart Disease Fact Questionnaire (HDFQ) and 4 items from the 40-item Coronary Heart Disease Knowledge Test, both of which were translated into Turkish from their original [15]. Furthermore, eight additional items (numbers 5, 8, 9, 10, 17, 18, 22, and 26) were included to comprehensively evaluate knowledge of CVD risk factors, resulting in a 28-item instrument. This scale was validated for reliability and content validity by Arıkan et al. [16]. The first four items cover general aspects of CVD such as characteristics, preventability, and agerelated factors. Fifteen items target specific risk factors (items 5, 6, 9, 12, 14, 18, 20, 23, 25, 27, 28), while nine items (7, 8, 13, 15, 16, 17, 21, 22, 26) evaluate outcomes associated with behavioral risk changes. Responses are recorded as 'yes,' 'no,' or 'don't know,' with correct answers scored as one point. Of the 28 items, 22 are scored directly, and 6 (items 11, 12, 16, 17, 24, 26) are reverse-scored. The highest attainable score is 28, with higher totals reflecting greater knowledge of cardiovascular risk factors. An internal consistency coefficient (Cronbach's alpha) of 0.76 was obtained, reflecting an acceptable level of reliability for the scale.

The Health Anxiety Inventory (HAI)

The Health Anxiety Inventory (HAI) is a self-administered questionnaire consisting of 18 items, developed to assess individuals' levels of health-related anxiety [13]. Its validity and reliability have been confirmed in prior research [17]. The initial 14 items as-

sess cognitive and behavioral components of health anxiety, while the final 4 items evaluate beliefs related to the presence of serious mental illness. Each item is scored on a 0 to 3 scale, with higher scores indicating increased health anxiety. Total scores range from 0 to 54, where elevated scores represent greater health anxiety. The scale demonstrated strong internal consistency, with a reported Cronbach's alpha of 0.91.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 26 (IBM Corp., 2019). The normality of the data distribution was evaluated using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For variables following a normal distribution, group comparisons based on socio-demographic factors were conducted with independent two-sample t-tests and one-way ANOVA. When ANOVA indicated significant differences, Duncan's post-hoc test was applied. For variables that did not meet normality assumptions, the Mann-Whitney U and Kruskal-Wallis H tests were utilized to assess differences across socio-demographic categories. A Bonferroni-corrected Z test was utilized to assess differences in total CARRF-KL and HAI scores across comorbidity categories with multiple response options. Spearman's rho correlation coefficient was used to investigate relationships between non-normally distributed variables - such as age, BMI, duration of the patient's illness, and time since surgery - and the scores on the CARRF-KL and HAI scales. Additionally, correlations between total and subscale scores of the CARRF-KL and HAI were examined using Spearman's rho. Results were reported as mean±standard deviation for normally distributed data, median (range) for non-normally distributed data, and frequency (percentage) for categorical variables. Statistical significance was determined at a threshold of P<0.05.

RESULTS

The study included 58 participants with a mean age of 49.34 years, ranging from 22 to 75 years. Females comprised 56.9% of the sample. The average body mass index (BMI) was 26.86, with values spanning from 18.5 to 40.2. Regarding marital status, the ma-

Table 1. Sociodemographic and clinic characteristics of the participants

| Characteristics Data | |
|---|--|
| (n=5X) | |
| (n=58) Age (years) 49.34±11.58 | |
| Gender, n (%) | |
| Female 33 (56.9) | |
| Male 25 (43.1) | |
| BMI (kg/m ²) 26.86±4.55 | |
| Marital status, n (%) | |
| Single 7 (12.1) | |
| Married 51 (87.9) | |
| Education Status, n (%) | |
| Illiterate 4 (6.9) | |
| Primary-secondary school 30 (51.7) | |
| • | |
| High School 16 (27.6) | |
| University 8 (13.8) | |
| Economic Status, n (%) | |
| Low 5 (8.6) | |
| Middle 43 (74.1) | |
| High 10 (17.2) | |
| Occupation, n (%) | |
| Housewife 25 (43.1) | |
| Labourer 5 (8.6) | |
| Officer 5 (8.6) | |
| Self-employment 5 (8.6) | |
| Retired 15 (25.9) | |
| Other 3 (5.2) | |
| Place of residence, n (%) | |
| Village 13 (22.4) | |
| District 15 (25.9) | |
| Province centre 30 (51.7) | |
| Comorbidity*, n (%) | |
| Allergy 1 (1.7) | |
| DM 11 (19) | |
| Goiter 4 (6.9) | |
| Hyperlipidaemia 2 (3.4) | |
| COPD 3 (5.2) | |
| CVD 8 (13.8) | |
| Psoriasis 2 (3.4) | |
| None 29 (50) | |

Eur Res J. 2025;11(4):800-808 Dolapoğlu *et al*

Table 1 contunied. Sociodemographic and clinic characteristics of the participants

| Characteristics | Data |
|---|---|
| | (n=58) |
| Smoking, n (%) | _ |
| Did not smoke | 23 (39.7) |
| Quit smoking | 13 (22.4) |
| Still smoking | 22 (37.9) |
| Alcohol, n (%) | |
| Did not drink | 45 (77.6) |
| Quit drinking | 6 (10.3) |
| Still drinking | 7 (12.1) |
| Dietary Practices, n (%) | |
| No | 44 (75.9) |
| Yes | 14 (24.1) |
| Exercise, n (%) | |
| No sport at all | 35 (60.3) |
| Occasionally | 20 (34.5) |
| Regularly | 2 (3.4) |
| Yes | 1 (1.7) |
| Death in the family due to CVD, n (%) | |
| No | 28 (48.3) |
| Yes | 30 (51.7) |
| Duration of illness of the patient | 65.37±107.25 |
| under care (month) | |
| Time elapsed since the date of | 8.34 ± 20.21 |
| surgery of the patient under care (month) | |
| | • |

Data are shown as mean±standard deciation or n (%). BMI=Body mass index, COPD=Chronic obstructive pulmonary disease, CVD=Cardiovascular disease, DM=Diabetes mellitus

jority (87.9%) were married. Educationally, 51.7% had completed either primary or secondary school. Most participants (74.1%) reported a middle-income level, and 46.6% lived with their spouses. In terms of occupation, 43.1% identified as housewives, and 51.7% resided in urban settings. Half of the participants reported no comorbid conditions, while 19% had diabetes mellitus. Lifestyle behaviors revealed that 37.9% were smokers, 12.1% consumed alcohol, 24.1% followed a diet, and 34.5% engaged in exercise sporadi-

cally. Only 31% had received information regarding cardiovascular disease (CVD), whereas 51.7% had experienced a family loss related to CVD. The average duration of illness for the patients under their care was 65.3 months, with an average of 8.24 months elapsed since the patients' surgery (Table 1).

A significant difference was identified in the total CARRF-KL scores across educational levels (P<0.001). Illiterate participants had a mean score of 11.25, whereas those with primary to secondary education averaged 17.93. Participants with a high school education scored an average of 21, and university graduates achieved a mean score of 24. These findings suggest a positive association between higher education levels and increased CARRF-KL scores. Additionally, nutritional status was significantly related to CARRF-KL scores (P=0.036); individuals not adhering to a diet had a mean score of 18.39, while those following a diet scored higher, with a mean of 21.57. Moreover, a weak but statistically significant negative correlation was found between age and total CARRF-KL score (r = -0.285, P = 0.030). Similarly, a negative weak correlation was observed between BMI and the CARRF-KL subscale measuring changes in risk behaviors (r = -0.285, P = 0.030) (Table 2).

Based on the results obtained, no statistically significant associations were observed between participants' socio-demographic characteristics and their HAI scores (P>0.05). The mean score for the CARRF-KL subscale assessing knowledge of disease characteristics, preventability, and age-related factors was 2.48. Participants' average score on the risk factors subscale was 11.1, while the mean score for the risk behavior change subscale was 5.57. The overall mean total score on the CARRF-KL scale was 19.16, and the mean HAI score was 21.1 (Table 3).

A weak but statistically significant positive correlation was identified between participants' HAI scores and the CARRF-KL subscale related to disease characteristics, preventability, and age factors (r=0.262, P=0.047). Similarly, a significant positive weak correlation was found between the overall HAI scores and total CARRF-KL scores (r=0.282, P=0.032). In contrast, no significant associations emerged between HAI scores and the CARRF-KL subscales measuring risk factors and changes in risk behaviors (P>0.05) (Table 4).

^{*}Multiple response

Table 2. Examination of the relationship between age, BMI, duration of the patient's illness, time since surgery, and participants' CARRF-KL and HAI scores

| | | Age | BMI | Duration of illness of the patient under care (month) | Time elapsed since the date of surgery of the patient under care (month) |
|--|---------|--------|--------|---|---|
| CARRF-KL (Properties, Preservability, Age Factor) | r | -0.224 | -0.187 | -0.030 | -0.131 |
| | P value | 0.090 | 0.160 | 0.826 | 0.327 |
| CARRF-KL (Risk Factors) | r | -0.294 | -0.166 | 0.113 | -0.019 |
| | P value | 0.025 | 0.213 | 0.399 | 0.887 |
| CARRF-KL (Change in Risk Behaviour) | r | -0.185 | -0.285 | 0.085 | -0.256 |
| | P value | 0.164 | 0.030 | 0.524 | 0.053 |
| CARRF-KL (Total) | r | -0.285 | -0.250 | 0.059 | -0.193 |
| | P value | 0.030 | 0.059 | 0.662 | 0.147 |
| HAI | r | -0.160 | -0.078 | 0.032 | 0.101 |
| | P value | 0.231 | 0.560 | 0.810 | 0.449 |

CARRF-KL=Cardiovascular Diseases Risk Factors Knowledge Level, HAI=Health Anxiety Inventory r=Spearman's rho correlation coefficient

DISCUSSION

The study included 58 participants, of whom 56.9% were female. The average total score on the CARRF-KL was 19.16±4.99, while the mean score on the HAI was 21.1±14.84. A weak but statistically significant positive correlation was identified between the total scores of the HAI and CARRF-KL (r=0.282, P=0.032). Additionally, significant differences in CARRF-KL scores were found across educational levels (P<0.001), with higher education associated with

greater knowledge scores. This cross-sectional study sought to assess caregivers' awareness of cardiovascular disease risk factors and to analyze the connection between this knowledge and levels of health anxiety.

In our study, the average total score on the CARRF-KL was 19.16. Kazim *et al.* [18] reported that around 71.5% of their participants demonstrated adequate knowledge of cardiovascular disease risk factors. Conversely, lower levels of CVD awareness were observed in studies conducted in Lebanon (47.3%) and Saudi Arabia (47.1%) [19, 20]. These variations in knowledge

Table 3. Distribution of total and subscale scores of the CARRF-KL and mean HAI scores among participants

| | Mean±SD | Median (min-max) |
|---|-----------------|------------------|
| CARRF-KL (Properties, Preservability, Age Factor) | 2.48±1.16 | 2 (0-4) |
| CARRF-KL (Risk Factors) | 11.1±2.52 | 12 (3-15) |
| CARRF-KL (Change in Risk Behaviour) | 5.57 ± 2.14 | 6 (1-9) |
| CARRF-KL (Total) | 19.16±4.99 | 19.5 (7-27) |
| HAI | 21.1±14.84 | 16.5 (0-51) |

CARRF-KL=Cardiovascular Diseases Risk Factors Knowledge Level, HAI=Health Anxiety Inventory, SD=Standard deviation

Eur Res J. 2025;11(4):800-808 Dolapoğlu *et al*

Table 4. Examination of the relationship between participants' HAI scores and the total and subscale scores of the CARRF-KL

| | HA | |
|---|-------|---------|
| | r | P value |
| CARRF-KL (Properties, Preservability, Age Factor) | 0.262 | 0.047 |
| CARRF-KL (Risk Factors) | 0.220 | 0.097 |
| CARRF-KL (Change in Risk Behaviour) | 0.229 | 0.084 |
| CARRF-KL (Total) | 0.282 | 0.032 |

CARRF-KL=Cardiovascular Diseases Risk Factors Knowledge Level, HAI=Health Anxiety Inventory r=Spearman's rho correlation coefficient

levels might be explained by differences in participants' educational backgrounds as well as the distinct measurement instruments employed across studies.

Our findings revealed a statistically significant variation in CARRF-KL total scores according to participants' educational levels (P<0.001). Specifically, illiterate individuals had a mean score of 11.25, those with primary or secondary education scored 17.93 on average, high school graduates achieved a mean of 21, and participants with a university degree obtained an average score of 24. This pattern demonstrates a clear positive association between education level and knowledge of cardiovascular disease risk factors. These results align with prior research indicating that higher education correlates with increased awareness of CVD risk factors [18].

A previous research has not identified any statistically significant differences between male and female caregivers in terms of health anxiety levels [21]. In line with these results, our study similarly found no statistically significant associations between participants' socio-demographic variables and their scores on the Health Anxiety Inventory (HAI) (P>0.05).

Multiple studies investigating factors affecting caregivers' knowledge have identified a tendency for younger individuals to demonstrate greater awareness [22, 23]. Consistent with this, our findings revealed a statistically significant, albeit weak, negative correlation between participant age and the total CARRF-KL score (r= -0.285, P=0.030). This relationship may reflect the greater propensity of younger adults to access health information via the internet and social media. In terms of lifestyle habits, 37.9% of participants reported smoking, 12.1% consumed alcohol, 24.1%

were adhering to a diet, and 34.5% engaged in physical activity intermittently. These results correspond with similar observations reported in studies by Koohi and Khalili [24] and Kazim *et al.* [18], conducted in Iran and the United Arab Emirates, respectively.

Our findings demonstrated a statistically significant difference in the total CARRF-KL scores according to participants' dietary habits (P=0.036). Specifically, those not adhering to a diet had a mean score of 18.39, whereas participants who were following a diet achieved a higher mean score of 21.57. Furthermore, a statistically significant weak negative correlation was observed between participants' body mass index (BMI) and their scores on the CARRF-KL subscale measuring changes in risk behaviors (r= -0.285, P=0.030).

These findings indicate that participants who possess sufficient knowledge may play an active role in preventing modifiable risk factors. Supporting this, Pallangyo *et al.* [25] reported that individuals with higher health concerns tend to have greater health-related knowledge. Similarly, our study identified a statistically significant positive yet weak correlation between participants' HAI scores and their total scores on the CARRF-KL scale (r=0.282, P=0.032). This relationship could be explained by the motivating effect of anxiety, which may encourage individuals to seek health information and thereby enhance their knowledge.

Limitations

This study has a some limitations. Firstly, the cross-sectional design precludes the establishment of causal inferences between the variables examined. Secondly, the single-center nature of the study limits

the external validity and generalizability of the findings. Lastly, the utilization of self-administered questionnaires may have introduced recall bias, potentially affecting the accuracy of the collected data.

CONCLUSION

To the best of our knowledge, this is the first study to explore the association between caregivers' knowledge of cardiovascular disease (CVD) risk factors and their levels of health anxiety. This study demonstrates that caregivers' knowledge of the disease and their psychological well-being play a crucial role in the effective management of patient care. By identifying gaps in knowledge and their association with healthrelated anxiety, the findings may contribute to the development of targeted educational programs and psychosocial support interventions. Increasing caregivers' knowledge about CVD and providing them with tools to manage their health-related concerns effectively can foster improvements in both their wellbeing and the health outcomes of the patients they support.

Ethical Statement

The study was approved by the Balikesir University Health Sciences Non-Interventional Research Ethics Committee (Approval Date: 06.08.2024; Approval Number: 2024/130). All participants provided their informed consent.

Authors' Contribution

Study Conception: ND, AD; Study Design: ND, AD; Supervision: ND, AD; Funding: N/A; Materials: ND; Data Collection and/or Processing: SA, EB; Statistical Analysis and/or Data Interpretation: EB, SA; Literature Review: ND, SA, EB; Manuscript Preparation: ND; and Critical Review: ND, AD.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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Clinical Oncology

The efficacy of benzydamine on cancer treatmentinduced oral mucositis: A systematic review of randomised controlled trials

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ABSTRACT

Objectives: Mucositis is a well-known complication of oncological therapies, severely affecting the quality of life of patients. Benzydamine appears to be a promising option for the treatment of this condition, particularly in the management of oral mucositis. We can learn more about the potential use of benzydamine for oral mucositis by examining the available published research and what we know from clinical trials that have used this agent. This systematic review aims to evaluate the efficacy of benzydamine for the prevention and treatment of oral mucositis induced by cancer therapy through Randomized Controlled Trials.

Methods: A systematic literature review was performed across seven databases. After screening, this systematic review included nine articles that had been published between 2013 and 2023. The review was conducted in accordance with the Cochrane guidelines (2023). Bias risk is assessed using the Cochrane Collaboration Risk of Bias Assessment Tool. The studies differed in the number of participants, from 26 to 120, giving a total of 593 participants analyzed. The articles in the studies used Benzydamine, herbal formulation, sodium bicarbonate, povidone-iodine, and low-level laser.

Results: Results showed that benzydamine was effective to varying extents. Several studies provided statistically important improvements while others showed no statistically important variations.

Conclusions: This extensive literature review and clinical study offer insight into how benzydamine may work in the management of oral mucositis.

Keywords: Chemotherapy, radiotherapy, oral mucositis, benzydamine, systematic review

ancer treatment, including chemotherapy (CT) and radiotherapy (RT), is often associated with a range of adverse effects that significantly impact patients' quality of life and adherence to treatment. These adverse effects include cardiotoxicity, nephrotoxicity, myelosuppression, neurotoxicity, hepatotoxicity, gastrointestinal toxicity, mucositis, and alopecia [1-3]. Gastrointestinal issues, including oral

mucositis (OM), are particularly common and may lead to early discontinuation of treatment, affecting overall outcomes [4, 5]. OM causes the oral mucosa to become inflamed and ulcerated, which can be painful, make it hard to eat and talk, cause secondary infections, and raise the risk of systemic complications [6, 7]. If not effectively managed, severe OM can result in treatment delays, dose reductions, and even dis-

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continuation of cancer therapy, which may ultimately affect patient outcomes [8].

OM usually happens because CT and RT have direct cytotoxic effects on epithelial cells, which cause inflammation and damage to the tissue. The five steps in the pathophysiology of OM are starting the process, increasing inflammatory pathways, signal amplification, ulceration, and healing [9]. In particular, 40-75% of patients receiving CT or RT for head and neck cancers (HNC) develop OM, with incidence rates reaching 90% in patients receiving concurrent CT [10]. Standardized tools, like the World Health Organization Oral Toxicity Scale (WHO OTS) and the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE) [11, 12], are often used to measure how bad OM is.

Researchers have explored various strategies for the prevention and management of OM due to its significant clinical impact. Topical pain killers, anti-inflammatory drugs, cryotherapy, photobiomodulation (also known as low-level laser therapy, or LLLT), and protective coatings are some of the current ways to treat the condition [13]. Despite these efforts, there is no universally accepted standard treatment for OM, and existing interventions provide only partial symptom relief. This highlights the necessity for innovative, evidence-based therapies to ensure efficient patient care [14].

An anti-inflammatory drug (NSAID), benzydamine hydrochloride (HCl), possesses pain-relieving, anti-inflammatory, and antimicrobial properties [15]. It may be an effective treatment for OM. Benzydamine takes effect by inhibiting the synthesis of pro-inflammatory cytokines (TNF- α , IL-1 β) and altering prostaglandin biosynthesis. Then, it will hydrate the oral mucosa to help decrease oral pain and swelling [16]. Some medical groups, such as the Multinational Association of Supportive Care in Cancer (MASCC) and International Society of Oral Oncology (ISOO), recommend the use of benzydamine mouthwash for people receiving moderate-dose RT (≤50 Gray [Gy]) without concurrent CT [17]. However, its role when given as part of combination treatments is not clear and requires further exploration, ideally in Randomized Controlled Trials (RCTs).

This systematic review aims to critically appraise the effectiveness of benzydamine for the management of OM due to cancer treatment by pooling findings from RCTs. Organizing the existing evidence should help clarify what medicinal action benzydamine can provide and how it could feature in management plans of OM.

METHODS

This study followed Cochrane guidance (2023) and was registered in PROSPERO (International Prospective Register of Systematic Reviews) as CRD42023494747 [20].

Study Design

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The specific research question was developed based on the PICO (Population, Intervention, Comparison, and Outcome) framework to guarantee both clarity and systematic ordering [19]:

- (1) Population (P): Adult patients (\geq 18 years) undergoing CT and/or RT for cancer.
- (2) Intervention (I): Mouth rinse with Benzydamine HCl, a NSAID, for OM management.
- (3) Comparison (C): Control or comparative interventions, e.g., placebo (or) alternative such as herbal therapies, sodium bicarbonate, povidone-iodine, and LLLT.
- (4) Outcome (O): Efficacy of benzydamine to reduce OM severity, duration, and impact on quality of life.

Guided by this framework, the main research question was: "Does benzydamine HCl reduce the severity and/or improve the management of OM in adult cancer patients undergoing CT and/or RT?

Search Strategy

This was followed by a systematic search of the literature using seven major databases, which included MEDLINE, PubMed, Science Direct, Scopus, Springer Link, Taylor & Francis, and Web of Science. The search was restricted to RCTs before 2023. The keywords and medical subject headings (MeSH) terms were as follows: "Oral mucositis," "Benzydamine," "Non-steroidal anti-inflammatory agents," "Cancer treatment," "Oncology treatment," "Radiotherapy," "Chemotherapy," "Randomized controlled trials"

Two researchers (DG, ZY) independently screened all records for inclusion and resolved inconsistencies by consensus with a third reviewer (FT).

Eligibility Criteria

The eligibility criteria for this systematic review were determined using the PICO framework to develop a structured selection process. Eligibility criteria included RCTs that assessed the efficacy of benzydamine in treating OM in adult cancer patients. Studies had to compare benzydamine against placebo or other treatment and report quantifiable outcome measures, including OM severity, duration, pain levels, or quality of life. Furthermore, studies published in languages other than English or before 2012 were excluded to align with the goals of the study.

On the other hand, nonrandomized trials, retrospective analyses, case reports, and reviews were excluded, as these study designs do not provide sufficient evidence for this review. Studies that involved either animal models or OM not related to cancer were excluded, as we were primarily interested in understanding the potential role of benzydamine in cancer-related mucositis. Additionally, studies in languages other than English were excluded due to practical limitations of translation and interpretation.

Study Selection Process

Study selection was performed in three steps:

- (1) Identification articles were obtained from seven databases according to the pre-specified search strategy.
- (2) Screening: Titles and abstracts were screened for relevance by two independent reviewers (DG, ZY) after omitting duplicates.
- (3) Screening, eligibility, and inclusion: All full-text articles were screened to determine eligibility, and the inclusion of articles was reached by consensus with a third reviewer (FT).

A PRISMA flow diagram illustrated the process of study selection, with the number of included/excluded studies at each stage of the process.

Data Extraction and Risk of Bias Assessment

- (1) A standardized data extraction pro forma was used to obtain:
 - (2) Study details (author, year, country)
 - (3) Sample size and patient features.

- (4) Intervention details (e.g., dosage, duration, route).
 - (5) Comparator interventions.
- (6) Primary and secondary outcomes (OM severity, pain, quality of life).
- (7) What statistical analysis was performed? Bias risk assessment was conducted applying the Cochrane Collaboration Risk of Bias (RoB2) tool, which assesses bias in five domains:
 - (1) Randomization process
 - (2) Anomalies from planned interventions
 - (3) Missing outcome data
 - (4) Measurement of outcomes
 - (5) Selective reporting bias.

Each study was rated as low risk, some concerns, or high risk of bias. Bias was assessed independently by two reviewers (DG, ZY), and disagreements were resolved by FT.

Ethical Considerations

This systematic review was focused on previously published papers and did not involve any direct human or animal participants. Thus, ethical approval was not required.

Statistical Analysis

Qualitative synthesis was performed to summarize the study findings. Because of heterogeneity in study designs, interventions, and outcome measures, a metaanalysis was not conducted. Results were descriptively analyzed by evaluating the effect of benzydamine in comparison with control interventions.

RESULTS

Study Selection

The first database search yielded 1,564 articles from MEDLINE (n=22), PubMed (n=339), Science Direct (n=171), Scopus (n=619), Springer Link (n=228), Taylor & Francis (n=147), and Web of Science (n=38). The titles and abstracts of the remaining articles, after removing duplicates, were screened for relevancy. Fifteen studies were found eligible for full-text review; however, full texts could not be retrieved for 2 studies [21, 22]. After full-text evaluation, four further studies were excluded for inappropriate study design [23, 24], lack of randomization [15], or inclu-

sion of participants under 18 years of age [25]. As a result, this systematic review included nine RCTs published between 2013 and 2023. Study selection is demonstrated in the PRISMA flow diagram (Fig. 1).

Characteristics of Included Studies

The nine studies included had a total of 593 participants (ranging from 26 to 120 per study). Three studies were conducted in Iran, three in India, two in Thailand, and one in Egypt. The studies evaluated therapeutic interventions such as benzydamine, herbal formulations (turmeric, sumac-rose water, curcumin,

aloe vera), sodium bicarbonate, povidone-iodine, and LLLT. There was variability in assessment tools, intervention duration, and primary outcomes between studies, limiting comparability (Table 1).

Interventional Methods and Study Findings

The studies included in the systematic review investigated various intervention strategies for OM in malignant tumors. Results: In one study from Iran (2023), 56 RT patients were randomized to receive either benzydamine 0.15% mouthwash or sumac-rose water spray, administered 4--8 times/day. High-grade

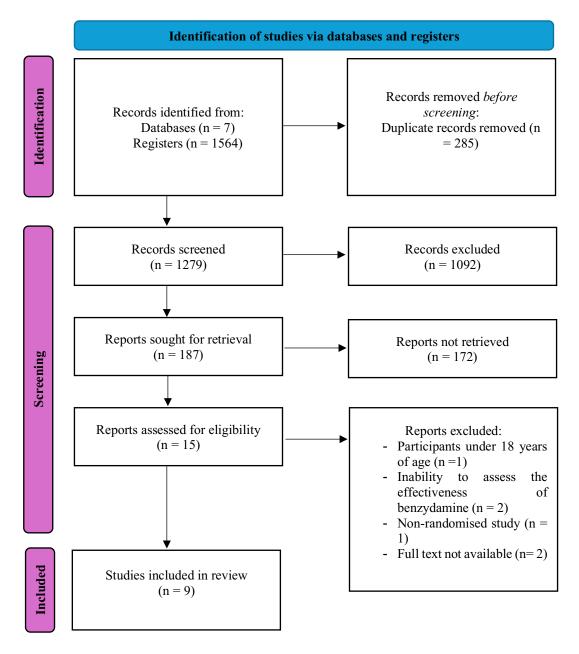


Fig. 1. PRISMA flow diagram for the studies.

| Author Stud Ameri et al. [26] Phas | Study design | Sample size | 1 | | | | T. t. monthon | Control | | |
|---|-------------------------------------|---|--|----------------------------------|-------------------------------|--|--|---|--|--|
| | | | OM assessment tool and assessment period | Primary outcome measures | Secondary outcome measures | Administration | Intervention | Coluctor | Type of cancer treatment | Kesulis |
| | Phase II, triple- blind, RCT | HNC n=56 | RTOG grading | OM occurrence, site and grade | OP grade | Rinse mouth with mouthwash 4 to 8 times a day, starting one day before treatment and continuing until one week after treatment has finished. | Sumac-rose water 30 ml spray bottle | Benzydamine 0.15% | Total RT dose of 50 Gy or more | - |
| | | -Sumak-rose group n=28 | OP numerical rating scale | | Quality of life | | | | CT during RT in both groups | In the intervention group, the occurrence of OP (P=0.001) and high-grade OM (P<0.05) was delayed. |
| | | -Benzydamine group n=28 | EORTC QLQ AILH&N 35 | | | | | | Ď. | At the fifth week of therapy and beyond, the control group had more high-grade OM, worse quality of life, and significantly higher proportions of involved subsites (P-0.05). |
| | | | Patients were evaluated on the first treatment day, then weekly and one week after the end of treatment. | | | | | | | The control group had a higher mean OP score during the whole therapy period. In the third week of therapy, this difference became statistically significant (P=0.01). |
| Chitapanarux et al. Muli [27] | Multi-centre, RCT | Non-metastatic HNC n=60 | OMAS | OM severity | Pain intensity | Rinsing with 15 ml of solution for two minutes four times a daily, starting before therapy and continuing until two weeks after the end of therapy | Benzydamine 0.15% | Sodium bicarbonate, two teaspoons of baking soda with one lite of water | At least 60 Gy platinum-based CT with RT | The median value of OMAS scores was found to be statistically significantly lower than the intervention group every week between the second and eighth weeks of treatment (P=0.01). The transition of the property of the prop |
| | | Benzydamine group | Pain score (0-10) | | | | | | | |
| | | m bicarbonate n=30 | Patients were assessed before therapy, weekly during therapy, at the end of therapy and 4 weeks after therapy. | | | | | | | |
| Kannarunimit et al. Pros [28] RCT | Prospective RCT | HNC curatively treated with concurrent CT n=71 | OMAS | OM grade | | Rinsing the mouth for 30 seconds 4 times a day starting from the first day of therapy | Benzydamine | Povidone-iodine 0.1% | Radiation dose totalled 66-70 Gy | The intervention group presented more OM occurrence (P<0.05). |
| | | Benzydamine group n=37 | NCI-CTCAE version 5.0 | | | | | | | The incidence of OM grade III-IV according to NCI-CTCAE version 5.0 was 51.4% in the intervention group and 56.5% in the control group during the assessment period (PC-0.03). At the same mucositis grade, the highest incidence of OM according to this scale occurred at the 7th week of the rapy (P-0.01). |
| | | Povidone iodine group n=34 | Patients were assessed once a week for 7 weeks and 4 weeks following completion of treatment | | | | | | | |
| Mohamed et al. RCT [29] | F | HNC treated or not treated with RT n=90 | WHO OTS | OM seventy | OP intensity | Rinsing the mouth with alcohol- free mouthwashes twice a day among the oral hygiene recommendations in the first | Benzydamine | Oral care | Radiation dose is 70 Gy in total in 7 weeks, 5 days a week | According to WHO OTS, fewer OM scores were recorded in group 3 during the hempty period, this the difference between the groups was not significant at week 4 (P=0.05), highly spirificant differences were recorded at weeks 2 and 6 (P=0.001) and week 7 (P=0.002). |
| | | In the first group, oral care n=30 | NCI-CTCAE | | | Each In the second group, rinsing the mouth with 15 ml of berzydamine solution 4-8 times a day with 2 minutes until the end of treatment | LLT | | RT alone or in combination with CT | The third group showed lower NCI-CTCAE scores throughout therapy. The difference between the groups was highly significant at weeks 3, 4 and 5 (P-0.05) and weeks 2, 6 and 7 (P-0.001). |
| | | In the second group, benzydamine 0.15% n=30 | VAS | | | Laser irradiation three times a week during therapy to the third group | | | | In the third group, pain scores were lower during therapy. |
| | | In the third group, LLLT n=30 | Patients were assessed before therapy and every week until the therapy was completed. | | | | | | | |
| Rastogi et al. [30] Non- pros RCT | Non-blinded, prospective, RCT | HNC n=120 | WHO OTS | OM grade | | Rinsing the inside of the mouth with 10 ml of mouthwash for at least 1 minute 4-6 times a day during treatment | SW+Benzydamine 0.15% | SW (half a tablespoon salt per 1 litre water) | Radiation dose ≥60 Gy | According to WHO OTS (p=0.05) and NCI-CTCAE version 4.0 (P=0.05), group A patients had more grade III OM than group B patients. |
| | | SW+Benzydamine 0.15%: | NCI-CTCAE version 4.0 | | | | | | | According to WHO OTS (p>0.05) and NCI-CTCAE version 4.0 (P>0.05), the degree of OM between groups C and D was not statistically significant. |
| | | -Group B (RT) n=30 | Patients were assessed weekly during therapy and up to 4 weeks after completion of therapy. | | | | | | | |
| | | -Group D (CT) n=30 | | | | | | | | |
| | | SW mouthwashes: -Group A (RT) n=30 | | | | | | | | |
| | | -Group C (CT) n=30 | | | | | | | | |

Table 1 contunied. Characteristics of studies included

| Author | Study design | Sample size | OM assessment tool and assessment period | Primary outcome measures | Secondary outcome measures | Administration | Intervention | Control | Type of cancer treatment | Results |
|---------------------------|-------------------------------------|---------------------------|---|-------------------------------|-------------------------------|---|------------------------------|----------------------|---|---|
| Sahebjamee et al. [31] | Triple-blind, HNC n=26 RCT | HNC n=26 | WHO OTS | OM grade | | Rinsing the mouth 3 times a daily with 5 ml of solution from the first day of treatment until the end of treatment | Aloe vera | Benzydamine 0.15% | RT dose of at least 50 Gy in a single fraction | Mucositis grade and changes in mucositis grade over time were not significantly different between the two groups (P>0.05). |
| | | Aloe vera group n=13 | Patients were assessed once before therapy, then once a week during the 6-week therapy period, totalling 8 times. | | | | | | | |
| | | Benzydamine group n=13 | | | | | | | | |
| Shah et al. [32] | Parallel-am, triple-blind RCT | HNC n=68 | WHO OTS | OM prevention and severity | 1 | Rinsing the mouth three times a daily for six weeks with 10 ml of solution | Curcumin 0.1 | Benzydamine 0.15% | Radiation dose 60-70 Gy | In the intervention group, the risk of immediate onset of OM was found to be 50% lower than in the control group and delayed the onset of mucositis by 2 weeks (p=0.001). |
| | | Benzydamine group n=35 | Patients were assessed until the end of the 6th week. | | | | | | | Both mouthwashes were equally effective in preventing the onset of severe forms of OM. |
| | | | | | | | | | | |
| Sheibani et al. [17] | Double-blind, RCT | HNC n=51 | OM degree scale (4-point scale) | OM severity | ı | Rinsing the mouth with 15 ml of solution for 2 minutes 4-8 times a day for 2 weeks, starting from before therapy until 2 weeks after the end of therapy | Benzydamine Placebo 0.15% | Placebo | Radiation dose≥5000 cGy, 5 days per week | OM severity did not differ between the two groups until the end of the third week and after the study was completed (p=0.05). |
| | | Benzydamine group n=26 | Patients were assessed before therapy and weekly until 2 weeks after the completion of therapy. | | | | | | | At the end of the fourth week, the mean OM score of the control group was statistically higher than the intervention group (P=0.01). |
| | | Placebo group n=25 | | | | | | | | |
| Thomas et al. [33] | RCT | HNC n=44 | ОНАТ | Oral health status | Oral dysfunction | Rinsing the mouth with 10 ml solution 6 times a day during the therapy period | Turmeric | Benzydamine | Radiation dose 60 to 70 Gy for 6 to 7 weeks | The baseline OHAT scores between the two groups differed significantly (p>0.05). |
| | | Turmeric group N=21 | WHO OTS | OM grade | | | | | | There were found differences significantly between the intervention and control groups in regard to the content of order (p=0.001), oral health status ($p=0.001$) and oral dysfunctions ($P=0.001$). |
| | | Benzydamine group n=23 | Oral Mucositis Symptom (PROMS) scale | | | | | | | |
| | | | Xerostomia Short Form Inventory | | | | | | | |
| | | | Patients were assessed before treatment started and weekly up until the end of treatment. | | | | | | | |

laser therapy, NCI-CTCAE= National Cancer Institute's Common Terminology Criteria for Adverse Events, OHAT= Oral Health Assessment Tool, OM=oral mucositis, OMAS=Oral Mucositis Assessment Scale, OP=oral pain, PROMS= International Prospective Register of Systematic Reviews, RCT=randomized controlles trial, RT=radiotherapy, RTOG=Radiation Therapy Oncology Group, SW=saline water, VAS= Visual Analogue Scale, WHO OTS= World Health Organization Oral Toxicity Scale CT=chemotherapy, EORTC QLQ= European Organisation for Research and Treatment of Cancer Quality of Life Scale, Gy=gray, H&N=head and neck, HNC=head and neck cancer, LLLT=low-level

OM was statistically significantly more frequent in the benzydamine group, while sumac-rose water significantly delayed the onset of OM and improved quality of life (P<0.05) [26]. An older trial from Thailand (2018) evaluated the use of benzydamine 0.15% mouthwash compared to sodium bicarbonate solution in 60 chemoradiotherapy patients. Benzydamine was found to be effective in reducing OM severity and decreasing the need for antifungal medication (P<0.01) [27]. Benzydamine 0.15%, in comparison to a mask scheme (povidone-iodine 0.1%, four times daily), was applied in another research done in Thailand (2023) with 71 HNC patients and RT. In addition, the povidone-iodine group was more effective in preventing severe OM (grade III-IV) (P<0.05) [28].

A study conducted in Egypt (2022) assessed the comparative effectiveness of benzydamine mouthwash (administered 4-8 times daily) and LLLT (administered three times weekly) in 90 patients undergoing RT, with or without CT. The findings indicated that LLLT provided superior efficacy in reducing OM severity and pain levels (P<0.001) [29]. Another study from India (2017) included 120 patients

receiving ≥60 Gy RT, randomized to either benzy-damine plus saline or saline alone, administered 4-6 times daily. The results showed that benzydamine significantly reduced the incidence of grade III OM (P<0.05) [30]. In a trial conducted in Iran (2015), 26 HNC patients receiving RT were randomized to receive either benzydamine 0.15% or aloe vera mouthwash, used three times daily. The results indicated no significant difference in OM severity between the two groups (P>0.05) [31].

An Indian study (2020) compared benzydamine 0.15% with curcumin mouthwash administered three times daily in 68 patients on RT. The results showed that curcumin is more potent in delaying the onset of OM and for reducing severity (P<0.001) [32]. Another RCT was published by Prasad *et al.* [17] (2015) in India and looked at benzydamine 0.15% versus placebo mouthwash in 51 patients receiving RT. Result: Significant delay to the onset of severe OM with benzydamine use (P=0.01) [17]. Finally, one study from India (2023) compared benzydamine 0.15% vs. turmeric mouthwash in 44 patients receiving RT. Results suggested that turmeric showed more efficacy as compared to placebo

| randomization process | from intended interventions | missing outcome data | measurement of the autcome | selection of the reported result | Overall risk of bias |
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Fig. 2. Results from RoB 2 bias analysis of RCTs.

in decreasing the overall severity of OM and improving oral health in patients (P=0.001) [33].

Measurement Tools Used and Effectiveness of the Application

The included studies of this systematic review used a variety of standardized assessment tools to assess OM severity, pain, and quality of life. Of the instruments used to assess grading, WHO OTS was employed in five studies [17, 26-28, 30] and NCI-CTCAE versions 4.0 & 5.0 were used in four studies [28, 29, 31, 32]. Two studies utilized the Oral Mucositis Assessment Scale (OMAS) [29, 31] and one study used the Radiation Therapy Oncology Group (RTOG) Scale [33]. Moreover, two studies contained the Visual Analogue Scale (VAS) for pain [27, 32] and one paper contained the European Organisation for Research and Treatment of Cancer Quality of Life Scale (EORTC QLQ-H&N35) [29]. One study performed an assessment using the Oral Health Assessment Tool (OHAT) [33]. The diversity in measurement tools underscores variations in study methodology, which may account for differences in reported outcomes.

Effectiveness of Benzydamine

Benzydamine had variable efficacy on OM in different studies. In two studies, the authors showed that benzydamine was effective for OM, reducing OM severity and delaying the onset of severe OM [17, 27]. However, five of them found that benzydamine did not have statistically significant advantages over different drugs, including sumac-rose water, povidone-iodine, LLLT, turmeric, or curcumin [26, 28, 29, 32, 32]. Benzydamine was as effective as other interventions, including aloe vera and saline mouthwash, in two further studies with no difference in outcomes [30, 31]. These observations imply that whilst benzydamine underlines some potential advantages, its efficacy remains heterogeneous and is likely influenced by treatment regimen, patient demographics, and assessment criteria.

Risk of Bias in Included Studies

We used the RoB 2 tool to evaluate the risk of bias among the nine included studies (Fig. 2). When bias across studies was assessed, six studies were judged to have a low risk of bias [27-31, 33] and three with a moderate risk of bias [17, 26, 32]. The randomization

process was appropriate in eight studies, and the risk of bias was low. In one study, the lack of stratified randomization was identified as a potential effect modifier of the study outcome [26]. These include bias in most of the studies due to methodological issues that were experienced in the course of conducting the studies themselves [17, 26, 29-31, 33]. Three studies tested other interventions with a potential impact on the development of OM, which increases the risk of deviation from the interventions received as planned [27, 28, 32]. One study was judged to have a high risk of bias concerning missing outcome data because of lost to follow-up or exclusion from the planned analysis [32]. One additional study did not provide information on the validity and reliability of the OM rating scale applied, which raises concerns regarding measurement bias [17]. In contrast, the overall risk of bias due to selective reporting was low for all included studies, suggesting that the outcome measures reported were in accordance with study protocols.

DISCUSSION

This systematic review includes data from several studies assessing the potential efficacy of benzydamine in the management of OM caused by RT or CT during HNC therapy. In related studies, benzydamine was compared with different substances such as sumac-rose water, curcumin, turmeric, aloe vera, sodium bicarbonate solution, povidone-iodine, and LLLT, and its effects on the OM severity, pain, quality of life, and other associated factors were analyzed. Sumac-rose mixture use was associated with lower grade OM and better quality of life than benzydamine [26]. Curcumin reduced the risk of OM onset and delayed it compared to benzydamine [32]. Compared with benzydamine, turmeric mouthwash is more effective in decreasing OM severity [33]. Aloe vera mouthwash and benzydamine mouthwash were found to have similar effects in OM management [31]. This may suggest that natural mixtures may be effective in OM management beyond benzydamine. The findings suggest that while benzydamine is a relatively effective agent in the management of OM, some alternative interventions may also achieve similar or marked results. Although benzydamine is recognized as a standard, alternative methods can be used when the individual circumstances and preferences of patients are taken into account.

Recent systematic reviews and meta-analyses have also evaluated the role of benzydamine in managing OM. A 2021 systematic review by Nicolatou-Galitis *et al.* found that benzydamine is effective in reducing the severity and delaying the onset of OM, particularly in patients receiving moderate-dose RT [15]. Another meta-analysis by Peng *et al.* (2022) comparing various OM interventions identified LLLT and benzydamine as two of the most effective options in OM prevention and treatment [8]. However, discrepancies among individual studies have raised concerns about the consistency of benzydamine's efficacy, particularly in combination treatment protocols.

LLLT has been demonstrated to be effective in reducing OM severity compared with benzydamine [29]. This shows that the alternative therapy method may be effective in achieving better results than benzydamine. Povidone-iodine was associated with less radiation therapy-induced OM compared to benzydamine, and povidone-iodine was generally more effective in the last week of CT therapy [28]. When compared with benzydamine sodium bicarbonate solution, benzydamine was reported to be more effective in decreasing the OM severity and also reduced the need for oral antifungal medication [27]. These findings align with previous meta-analyses that suggest benzydamine may be beneficial as part of a broader OM management strategy, but its standalone efficacy remains variable [15, 16].

In the included studies, it may be difficult to make a direct generalization about the duration of benzydamine application. Because each study seems to have used different protocols and application periods. Comparing the results between these different application periods will be important in determining which method is more effective. The period of benzydamine application was continued throughout cancer treatment in six studies, while in three studies it started before cancer treatment and continued for some time after therapy ended. Benzydamine has been found to be effective in the mouthwash protocol applied starting before cancer treatment and continuing for a while after therapy [17, 27]. However, further research is needed to determine the optimal timing and duration of benzydamine administration. In addition, metaanalyses recommend at least 3 to 8 rinses per day, but

the effect of frequency on efficacy remains unclear [15]. In the included studies, it can be stated that the number of daily applications was not considered as a determining factor in benzydamine efficacy. For example, one of the two studies in which benzidamine was administered 4-8 times a day showed the positive effect of benzidamine on OM [17], while the other failed to show the effectiveness of benzidamine [26]. However, further research is needed to set a definitive standard in this regard. In addition, the individual condition and tolerance of patients may also influence differences in the period of application. In general, studies show that regular use of benzydamine over a period of time is relatively efficient in reducing OM severity.

In the included studies, the measurements used to assess the efficacy of benzydamine were performed through a variety of scales and assessment tools. These measurement tools include scales such as RTOG, numerical pain assessment scale, EORTC QLQ All-H&N 35, OMAS, OP score, NCI-CTCAE Version 4.0 and 5.0, WHO OTS, OHAT, and VAS. These measurement tools allow assessment in different areas such as OM severity, OP, quality of life, and oral health. The use of these measurement tools plays an important role in the interpretation of the results. However, the use of different measurement tools in studies and inconsistency in reaching similar results may make it difficult to reach a definite conclusion about the effectiveness of benzydamine. When the results of the studies were analyzed, it was reported that benzydamine was effective in two studies, it was not effective in five studies, and there was no significant difference in two studies. This difference may be due to the measurement tools used. In addition, factors such as sensitivity and reliability in the measurement tools used may also cause differences in results. In two included studies, OMAS was used to assess the efficacy of benzydamine. However, there are conflicting findings regarding OMAS results among studies. For example, one study reported a positive effect of benzidamine on OMAS scores [27], while the other failed to demonstrate the effectiveness of benzidamine [28]. In conclusion, it was noted that there is diversity among studies assessing the efficacy of benzydamine in terms of the measurement tools used, population characteristics, and therapy protocols. This diversity should be taken into account to understand and compare the results on the efficacy of benzydamine. Researchers may

endeavor to obtain more precise results by using standardized measurement tools in future studies.

The risk of bias was analyzed in nine included studies. According to the findings, the risk of bias due to the randomisation process was found to be low in most of the assessed studies, indicating that the groups in the studies were balanced at baseline. In particular, it is important to note that three studies were considered at high risk of deviating from the intended interventions due to the inclusion of additional interventions. This means that the results of the study may be influenced by other factors and that there may be difficulties in fully assessing the efficacy of benzydamine. One study found an increased risk of missing outcome data due to patients being lost to follow-up and excluded from the analysis. This may affect the results of the studies and reduce the generalizability of the results. In one study, the validity and reliability of the OM rating scale were not reported, and therefore the bias risk in the measurement of the outcome was considered high. This may call into doubt the reliability of the results obtained.

CONCLUSION

This systematic review evaluated the effectiveness of benzydamine in managing OM induced by cancer treatment, particularly RT and CT. The findings from nine RCTs demonstrated inconsistent results regarding its efficacy. While some studies reported that benzydamine could reduce the severity of OM and delay its onset, others found no statistically significant advantage over alternative interventions such as povidone-iodine, sumac-rose water, LLLT, turmeric, and curcumin-based mouthwashes.

The variability in study methodologies, intervention protocols, and outcome assessment tools likely contributed to these inconsistent findings. Some studies initiated benzydamine prophylactically before cancer treatment, while others applied it only during therapy. Furthermore, the frequency of mouth rinses per day and duration of treatment differed across studies, influencing the reported outcomes. The measurement tools used to assess OM severity and pain levels also varied, leading to potential differences in reported efficacy.

Despite these discrepancies, benzydamine remains a widely used and recommended agent, particularly for patients undergoing moderate-dose RT without concurrent CT. However, the findings suggest that alternative treatments may offer similar or superior benefits in certain clinical settings. Future large-scale, well-designed RCTs with standardized treatment protocols and uniform assessment tools are needed to establish the definitive role of benzydamine in OM management.

Ethical Statement

This systematic review was focused on previously published papers and did not involve any direct human or animal participants. Thus, ethical approval was not required.

Authors' Contribution

Study Conception: DG, ZY, FT; Study Design: DG, ZY; Supervision: FT; Funding: N/A; Materials: DG; Data Collection and/or Processing: DG, ZY; Statistical Analysis and/or Data Interpretation: DG, ZY; Literature Review: DG, ZY; Manuscript Preparation: DG, ZY, FT and Critical Review: DG, ZY, FT.

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Medical Pathology

Artificial intelligence, machine learning, and radiomics in lung cancer classification

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ABSTRACT

Lung cancer is a highly heterogeneous disease that presents significant challenges in accurate diagnosis and classification due to its diverse histological and molecular characteristics. Traditional diagnostic methods, while valuable, are often limited by invasiveness, subjectivity, and an inability to fully capture tumor complexity. Recent advancements in artificial intelligence (AI), machine learning, and radiomics have transformed the field, offering enhanced precision, efficiency, and objectivity in lung cancer classification. These technologies enable detailed analyses of imaging data, histopathological findings, and molecular profiles, facilitating improved subtype identification, outcome prediction, and personalized treatment strategies. Cytopathology remains a cornerstone of lung cancer diagnostics, particularly for small biopsies and cytological samples, which are often the only materials available in advanced stages. The integration of AI-driven methods into cytopathology and radiomics workflows has shown substantial potential to overcome the limitations of traditional approaches, reduce interobserver variability, and accelerate the diagnostic process. This review underscores the transformative role of AI and radiomics in lung cancer management, highlighting their synergy in advancing precision oncology. As ongoing research continues to refine these methodologies, the future of lung cancer care is poised for significant advancements, offering improved diagnostic accuracy, personalized therapies, and better patient outcomes.

Keywords: Lung cancer, heterogeneity, cytopathology, artificial intelligence

Stem cells implicated in the development of lung carcinoma are primarily derived from four key proliferative cell types within the airways: basal cells, Clara cells, Type II pneumocytes, and neuroendocrine cells associated with the Amine Precursor Uptake and Decarboxylation (APUD) system. Furthermore, it has been proposed that lung tumors may

originate not only from these proliferative cells but also from an undifferentiated progenitor or stem cell that acts as a precursor [1, 2]. These undifferentiated cells are thought to be distinct from basal or reserve cells. Evidence suggests that such cells are absent in the normal adult respiratory epithelium and may only emerge following damage to proliferative cells [1].

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While hyperplastic, metaplastic, and dysplastic epithelial anomalies, including carcinoma in situ, are now well-characterized morphologically, the precise histogenetic pathways underlying lung carcinoma remain uncertain [3]. Tumorigenesis is an evolutionary process, driven by ongoing genetic mutations and selective pressures in a Darwinian manner [4, 5]. As hyperproliferation occurs during tumor progression, increased genetic instability fosters the development of a diverse population of cancer cells, referred to as clonal subpopulations (Fig. 1) [5, 6]. As hyperproliferation occurs during tumor progression, increased genetic instability facilitates the emergence of a heterogeneous population of cancer cells, referred to as clonal subpopulations (Fig. 1) [5, 7]. The first, the monoclonal (linear) model, proposes that tumor evolution occurs in a sequential and orderly manner. Mutations in oncogenes and tumor suppressor genes drive successive rounds of clonal expansion, with each new mutation leading to the dominance of a single, more advanced clone [8]. This model envisions tumor progression as a straightforward linear process.

In contrast, the multiclonal model presents a more complex and dynamic framework. While all tumor cells originate from a single initiated cell, tumor evolution involves the coexistence of genetically diverse clones [9, 10]. Over time, the population sizes of these clones may fluctuate - some expanding, others remaining stable, and some becoming extinct. This ongoing interplay creates a "messy" evolutionary pathway, where tumors at advanced stages may eventually be dominated by a single clone. In both models, the intensity of color represents the degree of tumor progression, while different colors symbolize distinct clones [5].

The microenvironment within tumors is inherently heterogeneous. Variations in factors such as vascular density, the infiltration of normal cells, and the composition of the extracellular matrix contribute to this complexity. This heterogeneity may explain the emergence of diverse phenotypes among tumor cells, influenced by their specific local environments. Importantly, this intra-tumor heterogeneity extends beyond individual cell phenotypes to encompass a range of phenotypic features, including gene expression (e.g., surface mark-

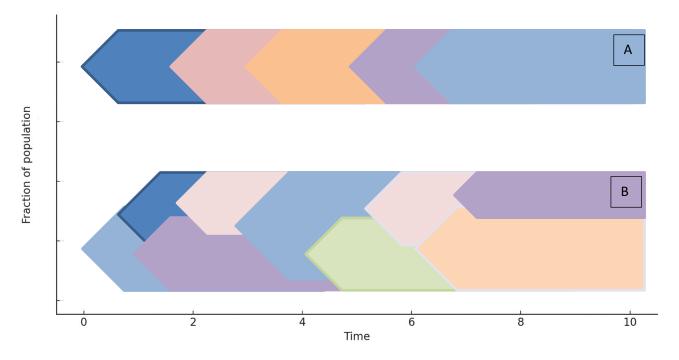


Fig. 1. Tumor evolution can be modeled as either a linear or a multiclonal process. The linear (monoclonal) model (A) depicts tumor progression as an orderly sequence of clonal expansions driven by successive mutations, with each new mutation producing a dominant, more advanced clone. In contrast, the multiclonal model (B) describes a more dynamic and complex process, where genetically diverse clones coexist, compete, and fluctuate in size, leading to a non-linear evolutionary pathway. While advanced tumors may eventually be dominated by a single clone, this occurs after significant periods of clonal diversity. Both models highlight the interplay between order and randomness in tumor progression (Adapted with modifications from: Marusyk A, Polyak K. Tumor heterogeneity: Causes and consequences. Biochim Biophys Acta. 2010;1805(1):105-117. doi: 10.1016/j.bbcan.2009.11.002 [5]).

ers, growth factor and hormone receptors), metabolic activity, motility, angiogenesis, proliferation, immune response, and metastatic potential [5, 7, 9].

The interplay between genetic alterations and morphological phenotypes is well-documented in lung carcinoma. For example, in pleomorphic carcinomas with heterogeneous differentiation, molecular heterogeneity has been linked to Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) mutation status, alterations in gene copy number, and differences in protein expression and phosphorylation levels [9, 11]. Beyond pleomorphic carcinomas, lung carcinomas are characterized by significant histological heterogeneity. Different phenotypic patterns and levels of differentiation are often observed between microscopic fields and histological sections. Approximately 50% of tumors exhibit multiple major histological subtypes [11].

Lung carcinomas are typically classified based on their most differentiated component, while the degree of differentiation is assessed based on the least differentiated regions. This dual criterion complicates the classification of individual tumors [9, 12]. For instance, a predominantly undifferentiated tumor with squamous cell carcinoma (LUSC), or lung cancer subtypes such as adenocarcinoma (LUAD) features is commonly classified as poorly differentiated LUSC or LUAD [13, 14].

This pronounced phenotypic variability is particularly relevant in the analysis of small biopsies and cytological samples, which are often the only available diagnostic material at advanced stages of lung cancer [5, 12]. These small samples provide a limited representation of the tumor's histological and genetic diversity. Their ability to reflect the clonal composition and the quantitative distribution of different growth patterns and tumor subtypes is constrained by the sample's origin, size, and location [7].

Despite these limitations, cytological diagnostics remain a vital tool in clinical practice. For example, touch imprints performed by thoracic surgeons have been shown to achieve sensitivity and specificity comparable to histological methods in lung cancer diagnostics [15].

PRECISION IN LUNG CARCINOMA CLASSI-FICATION

Histological and Molecular Insights

Lung carcinomas display significant histological and molecular heterogeneity, necessitating precise classification for effective clinical management. Accurate diagnosis relies on histopathological analysis of tumor tissues, where classification is often guided by the most differentiated component and assessed using the least differentiated regions [11]. This dual criterion can complicate tumor categorization, particularly for adenocarcinomas and squamous cell carcinomas that exhibit mixed features. Research underscores the variability in patient outcomes and therapeutic responses across lung cancer subtypes, with each subtype exhibiting distinct genetic and phenotypic profiles [16]. For example, adenocarcinomas with micropapillary or solid growth patterns are strongly associated with aggressive behavior and poorer prognoses. Furthermore, LUAD histology serves as an independent predictor of lymph node metastasis, emphasizing the need for tailored therapeutic approaches [11, 17].

Recent advancements have introduced mathematical models that integrate immunohistochemistry and LUAD subtypes to predict lymph node metastasis more effectively [18, 19]. Molecular profiling, such as the evaluation of KRAS and Epidermal Growth Factor Receptor (EGFR) mutations, complements histological assessments and improves the classification of lung adenocarcinomas. In particular, cases with solid or micropapillary patterns have shown distinct molecular alterations that influence prognosis and guide therapeutic decisions. Comprehensive histopathological evaluations ensure accurate tumor classification, enabling personalized treatment strategies and improving patient outcomes [16, 20].

RADIOMICS AND AI INTEGRATION Transforming Lung Cancer Diagnosis and Care

Radiomics, driven by advancements in Machine Learning, is revolutionizing lung cancer diagnosis and classification through the analysis of imaging modalities such as Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Positron Emission Tomography (PET). By extracting and analyzing high-dimensional imaging data, radiomics reveals critical connections between imaging features and tumor pathophysiology. Recent innovations, including the ProNet and iMRRN models, utilize deep learning to enhance the classification accuracy of LUAD, LUSC,

and small-cell lung cancer (SCLC), significantly improving diagnostic precision [21, 22].

One prominent application is PET-CT radiomics, which links FDG uptake patterns to aggressive tumor behaviors, facilitating subtype differentiation and enabling more accurate prognosis predictions. This non-invasive approach complements traditional histopathological analyses by providing detailed insights into tumor biology21. Despite the promising progress, challenges remain [23, 24].

Future developments in radiomics emphasize the integration of AI with molecular profiling to refine lung cancer subtyping further and enable truly personalized treatment strategies. By combining radiomic insights with genomic and immunologic data, researchers and clinicians can develop robust, patient-specific models for prognosis and therapy selection. As radiomics evolves, its potential to transform lung cancer care becomes increasingly evident, paving the way for more precise and effective clinical management [23, 24].

INTEGRATION OF AI WITH DIGITAL PATHOLOGY IN PERSONALIZED MEDICINE

The integration of AI and radiomics has significantly improved the speed and accuracy of lung cancer classification, enabling personalized medicine. Radiomics algorithms, validated using PET/CT and MRI, effectively distinguish NSCLC subtypes and support predictive models like CT-based nomograms for classifying SCLC and NSCLC [25, 26].

Digital pathology's telepathology capabilities allow pathologists in remote locations to access high-resolution images for second opinions or to collaborate with AI models trained on diverse datasets. Such implementations have been critical in studies where digital slides were shared across institutions to validate predictive AI models for cancer classification, ensuring consistency and reproducibility across clinical settings [26, 27].

However, challenges such as the high cost of scanners, technical issues with calibration, and the need for robust hardware infrastructure remain [6, 28]. Integration with laboratory information systems and collaboration between pathologists and AI developers are essential to overcome these barriers. For example, in one study, pathologists guided AI model training to

improve tumor segmentation and subtype classification, demonstrating the importance of interdisciplinary efforts [26]. With a success rate of over 90% in rapid remote diagnosis, diagnostic and therapeutic decisions can be made in a timely manner based on findings from rapid remote online evaluations. A quality-assured rapid remote online evaluation process enables the assessment of both the quantitative and qualitative suitability of obtained cellular samples for further standard, immunocytochemical, and molecular pathological analyses. An interdisciplinary understanding of the clinical problem and morphological findings minimizes friction among disciplines and serves as an essential prerequisite for customized diagnostics [29-32].

This synergy between AI and digital pathology not only streamlines diagnostics but also supports personalized treatment strategies by linking histological and molecular data to therapeutic responses. As technology evolves, this integration holds immense potential to transform cancer care, making it more accurate, accessible, and tailored to individual patient needs.

ADVANCING PRECISION MEDICINE The Future of Digital Pathology and AI Integration

The future of digital pathology and AI integration lies in advancing precision medicine through enhanced diagnostic accuracy, efficiency, and accessibility. Emerging techniques, such as self-supervised learning, enable the extraction of histomorphological patterns from whole-slide images (WSIs) without the need for manual annotations, providing insights into tumor heterogeneity and clinical outcomes [26]. AI-powered radiomics models, validated using PET/CT and MRI data, are increasingly being used to predict lung cancer subtypes and assess treatment responses [27, 33].

Digital pathology is also expected to expand its role in telemedicine, enabling real-time consultations and collaborative diagnostics across the globe. These advancements will depend on robust infrastructure, seamless integration with laboratory information systems, and standardization of workflows to ensure reproducibility and reliability [6, 28]. Furthermore, combining AI-driven pathology insights with genomic and transcriptomic data will open new avenues for personalized treatment strategies, bridging the gap between molecular profiling and clinical application [26].

As these technologies evolve, their integration into clinical workflows will redefine diagnostic paradigms, offering scalable, cost-effective, and patient-centric solutions in oncology and beyond.

With ongoing research, lung cancer management is on the cusp of transformative advancements. The integration of molecular profiling with digital pathology and AI is paving the way for unprecedented accuracy in therapeutic decision-making. These innovations bring the potential for enhanced patient outcomes and signify a shift toward precision oncology, where treatment is tailored to the unique biological characteristics of each individual's cancer [26, 33].

UNDERSTANDING THE LIMITATIONS OF AI AND MACHINE LEARNING IN LUNG CANCER DIAGNOSIS

Artificial intelligence and machine learning are often praised for their potential to revolutionise health-care, and lung cancer diagnosis is no exception. However, the reality on the ground is more nuanced [34]. Many AI models are trained on limited datasets—often from a single hospital or demographic—which means they might not perform reliably when faced with patients from different backgrounds [35]. I've seen examples where a model works impressively in the lab, only to fall short in a real hospital setting.

Another concern that comes up frequently in clinical discussions is the "black box" nature of these systems. While deep learning algorithms can achieve high accuracy, they rarely offer explanations that make sense to medical professionals [35, 36]. And in medicine, if you can't explain a diagnosis, it's hard to trust it—let alone act on it.

There's also the question of bias. If a dataset underrepresents certain groups - say, women, minorities, or rare cancer subtypes - the resulting model might be less accurate for those patients. That's not just a technical issue; it's a real-world risk [35, 36].

So what's the way forward? First, we need larger, more diverse datasets, ideally pooled from different regions and healthcare systems. But that's not enough. We also need tools that can explain their reasoning, at least at a level that doctors can understand. And perhaps most importantly, clinicians must be properly trained—not just in how to use these systems, but in when not to trust them [35, 17].

AI can and should be a partner in cancer care—but it has to earn that role through transparency, reliability, and collaboration with the people who treat patients every day.

CONCLUSION

The integration of AI, Machine Learning, and radiomics into lung cancer classification represents a paradigm shift in oncology. These technologies not only address the limitations of traditional methods but also provide a more objective, efficient, and precise framework for diagnosis. By leveraging the vast potential of AI and radiomics, clinicians can reduce subjectivity, accelerate the diagnostic process, and implement personalized treatment strategies tailored to each patient's unique tumor profile. As ongoing research continues to refine these approaches, the future of lung cancer management appears poised for significant advancements, offering hope for improved patient outcomes and a new era in precision oncology.

Ethical Statement

Ethical approval is not required for this study. There are no human or animal elements in the study. This review was carried out by a brief literature screening. Informed consent has not been collected specifically for the patient samples included in this study.

Data Availability Statement

The corresponding author can provide the data supporting the study's conclusions upon reasonable request.

Authors' Contribution

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Conflict of interest

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Cardiovascular Surgery

Management of giant popliteal artery aneurysm using in situ saphenous vein bypass: A case report

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ABSTRACT

Popliteal artery aneurysm is the most common type of peripheral artery aneurysm. These lesions are associated with atherosclerotic disease and other arterial aneurysms. The timing and approach of surgery are critical for limb preservation and reducing the risk of amputation in symptomatic cases. This case report presents our surgical approach, technique, and graft selection for a 75-year-old female patient with swelling and pain in the leg due to a giant popliteal artery aneurysm complicated by thrombosis. We bypassed the superficial femoral artery to the distal popliteal artery below the knee, using the in situ saphenous vein. We excluded the enlarged segment by ligating it at the anastomosis sites. In situ bypass is considered a highly effective method with excellent patency rates that minimizes surgical trauma in the treatment of popliteal aneurysms extending below the knee. **Keywords:** Giant aneurysm, popliteal artery aneurysm, in situ bypass

Popliteal artery aneurysm (PAA) is the most frequently encountered peripheral arterial aneurysm, though its prevalence remains relatively low at less than 0.1% in the general population [1]. Typically affecting elderly men, PAA is closely linked to atherosclerotic disease and the presence of other arterial aneurysms [2, 3]. If left untreated, giant or complicated PAAs can lead to severe consequences, including limb-threatening ischemia or amputation [4]. In this report, we discuss a rare case of a giant PAA managed successfully with an in situ saphenous vein bypass, highlighting the surgical considerations and technical approach involved.

CASE PRESENTATION

A 75-year-old female with a history of diabetes melli-

tus and chronic kidney disease, presented with left thigh pain that had been aggravated in sitting or squatting positions for the previous six months. The patient was admitted to the emergency department with leg pain. She described a painful, firm, mass-like lesion on her thigh. In the last two days, she complained of numbness and pain extending to her foot. On examination, a large pulsatile mass was detected in the popliteal region. Peripheral pulses were absent on palpation and weakly detected via handheld vascular Doppler. The patient was subsequently interned for further investigation and treatment.

Computed tomographic angiography revealed a thrombosed popliteal artery aneurysm with a maximal diameter of 13.88 cm, with post-aneurysmal distal vascular occlusion in the left popliteal artery. Mild atherosclerotic changes were noted in the right popliteal artery. Fig. 1. illustrates the thrombosed aneurysm and

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associated occlusions. Mild atherosclerotic calcifications were observed in the lower iliofemoral arteries without significant aneurysmal changes.

Surgical Technique

The surgery was performed under general anesthesia with the patient placed in a supine position and the knee flexed. The femoral artery was explored through an inguinal incision and turned with a nylon tie. An incision was made to access the popliteal region from the posteromedial level of the sartorius muscle to the adductor space. A third incision was made along the posterior tibial border from the lower aspect of the medial condyle below the knee. The deep fascia was opened, and the medial head of the gastrocnemius muscle was gently retracted posteriorly to enhance access to the vascular structures. Double ligation of the aneurysm was performed at the sites of anastomoses (proximal superficial femoral artery and distal popliteal artery). The aneurysm sac was opened, the thrombus was evacuated, the retrograde bleeding collateral artery ends were subsequently ligated and the sac was reduced in size and subsequently closed.

A bypass from the superficial femoral artery (end-to-side) to the distal popliteal artery (end-to-side) just below the knee was performed using the saphenous vein. A valvotomy was carried out to disrupt vein valves that could impede flow. The retrograde bleeding collateral artery ends were subsequently ligated.

Postoperatively, the patient exhibited good pulsation in the posterior tibial and dorsalis pedis arteries. The pulsatile mass associated with the popliteal artery aneurysm has disappeared. Fig. 2. shows that the leg diameter completely returns to normal in the aneurysm region after the operation. The patient was discharged two days postoperatively and ambulated without assistance. At three months, the patient reported no pain or claudication.

DISCUSSION

Despite being the most prevalent type of peripheral artery aneurysm, the occurrence of PAA remains rare, with a prevalence of less than 0.001% [1-6]. Its incidence rises significantly in males aged 65 to 80, reaching approximately 1% within this demographic [2-8].

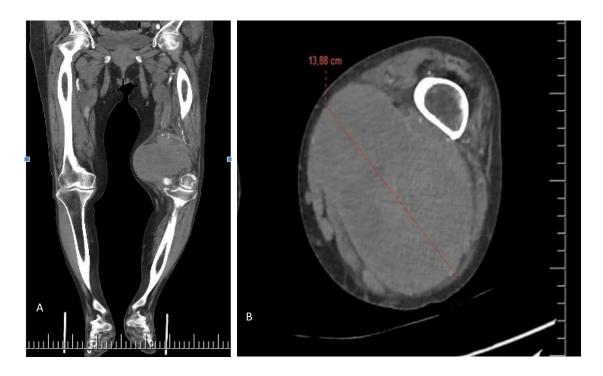


Fig. 1. The left superficial femoral artery was observed to be totally occluded after the level of origin, and a total thrombosed aneurysm was present in the distal part. The diameter of the aneurysm was measured approximately 13.88 cm. (A) Longitudinal, (B) Cross-sectional view.

Eur Res J. 2025;11(4):828-831 Yümün and Haşimoğlu



Fig. 2. Aneurysm had reduced in size and mass of the aneurysm had disappeared.

The normal diameter of the popliteal artery varies based on gender, age, and body surface, typically measuring less than 8 mm. Aneurysms are defined as a dilation of 50% above normal. Though no formal size criteria exist for 'giant PAA,' this case's 14 cm diameter justifies the designation.

The primary etiological factor for PAA is atherosclerosis; however, other causes, including popliteal artery entrapment syndrome, inflammatory arteritis, and pseudoaneurysms, have also been documented [9]. The major complications associated with PAAs include embolization, compression, and an increased risk of deep vein thrombosis. Rupture, though a potentially catastrophic event occurs in less than 2% of cases [1, 2, 7]. Surgical intervention is often recommended for asymptomatic aneurysms larger than 20 mm to prevent future complications.

Indications for surgery include acute ischemia, chronic ischemic symptoms, claudication, resting pain, and tissue loss. For asymptomatic patients, factors influencing surgery include aneurysm size, thrombus, previous thromboembolism, surgical risks, and outcomes [9].

The current gold standard for PAA repair involves the exclusion of the aneurysmal segment combined with bypass using an autologous vein graft. In the presented case, the bypass procedure utilized the proximal superficial femoral artery as the inflow and the distal popliteal artery below the knee as the outflow. An in situ saphenous vein bypass was chosen due to its superior long-term patency and suitability for extensive reconstructions in cases involving complex PAAs extending below the knee. The adequate diameter of the saphenous vein (approximately 8 mm) and its minimal associated surgical trauma further supported this decision.

Traditional surgical approaches include a medial route with aneurysm ligation and bypass, or a posterior approach that provides direct visualization of the aneurysm, followed by resection and reconstruction using vein or prosthetic grafts [8]. In this particular case, given the thrombosis of the proximal superficial femoral artery and the popliteal artery, a segmental bypass was performed. The aneurysmal segment was safely excluded by proximal ligation at the anastomosis sites. This approach ensured effective management of the aneurysm while preserving limb viability and minimizing postoperative complications.

CONCLUSION

In symptomatic popliteal artery aneurysms, the surgical approach is determined based on the aneurysm size and the presence of concomitant occlusive vascular disease. Surgical intervention is crucial for managing hyperextended aneurysms to prevent limb ischemia and preserve function. The use of an autogenous venous graft remains the gold standard for vascular occlusions extending below the knee. Especially in-situ saphenous vein grafts continue to be a reliable option for complex cases. This case underscores the importance of timely surgical intervention in symptomatic giant PAA to prevent limb ischemia, enhance postoperative recovery, and maintain long-term graft patency.

Ethical Statement

This case study was approved by Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital Clinical Research Ethics Committee (Decision date: 08.03.2024, decision no: 89).

Patient' Consent

Patient was informed about the purpose of the case report, and informed consent was obtained from the patient for this publication.

Authors' Contribution

Study Conception: GY; Study Design: GY; Supervision GY, HH; Funding: GY; Materials: GY, HH; Data Collection and/or Processing: HH; Statistical Analysis and/or Data Interpretation: GY; Literature Review: GY; Manuscript Preparation: GY, HH and Critical Review: HH.

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