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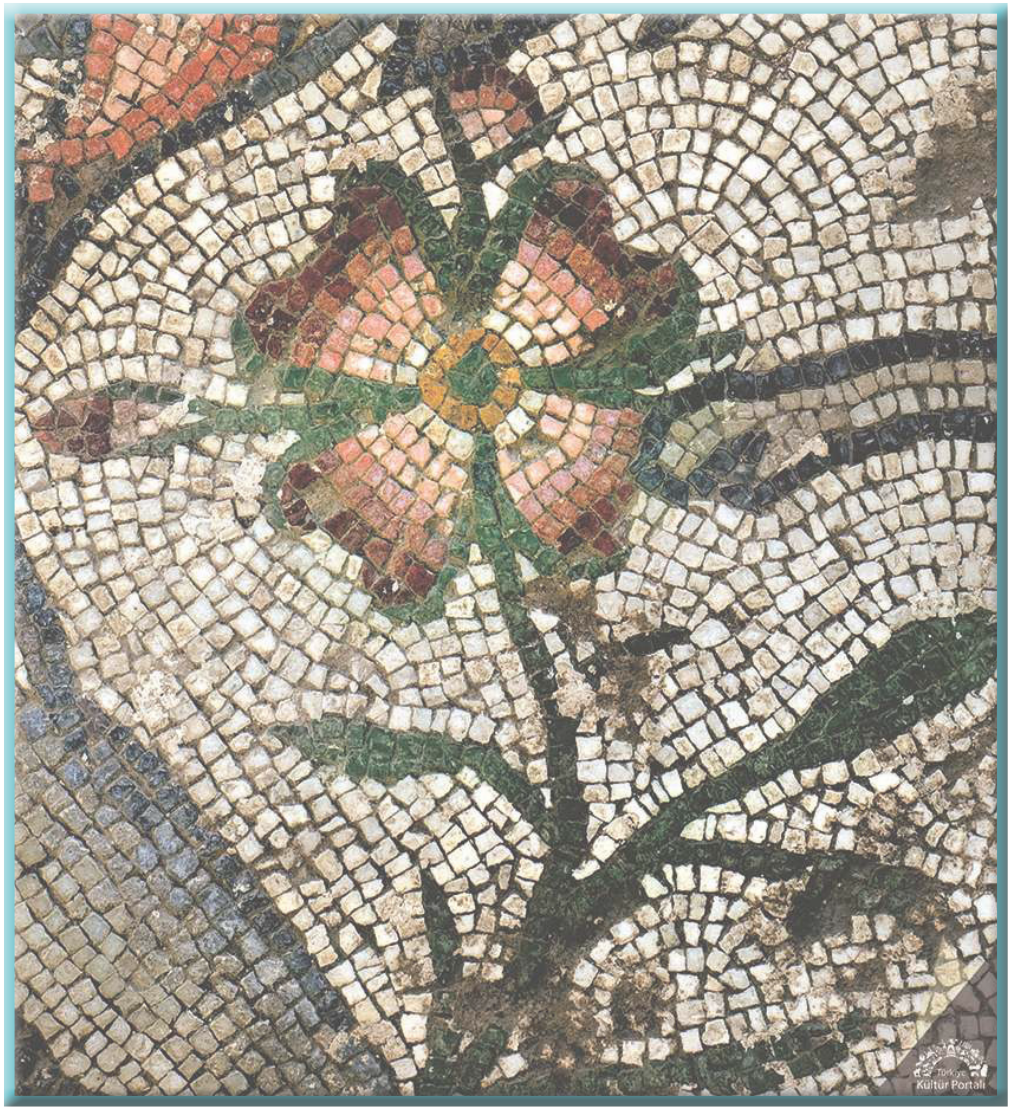
KAHRAMANMARAŞ SÜTÇÜ İMAM ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ



KSU MEDICAL JOURNAL

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Dekanlık Dergi Editörlüğü
46100 Kahramanmaraş

e-posta: tkoca@ksu.edu.tr
Tel: 0344 300 34 08
Faks: 0344 300 34 09

DERGİ DANIŞMA *Kurulu*

AMAÇ

Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Dergisi bilimsel bir dergi olup, tıbbın çeşitli alanlarında araştırma makaleleri, olgu sunumları ve derlemeleri yayınlar

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Introduction

Material and Methods

Results

Discussion

Acknowledgements

References

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Introduction

Case report

Discussion

References

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İÇİNDEKİLER
Contents

Yıl / Year: 2025
Cilt / Volume: 20
Sayı / Number: 3

Araştırma Makaleleri (Research Articles)

Olgu Sunumu (Case Report)

Derleme (Reveiw)

Editöre Mektup (Letter to Editor)

Research Article (Araştırma Makalesi)

Effects of Biceps Tenotomy on The Shoulder Joint in the Treatment of Slap Lesions

Slap Lezyonlarına Uygulanan Biceps Tenotomisinin Omuz Eklemine Etkileri

Caner POYRAZ[1], Vahit YILDIZ[1]

[1] Adnan Menderes University, Faculty of Medicine, Department of Orthopaedics and Traumatology, Aydın, Türkiye

Özet

Amaç: Bu çalışmada izole SLAP (Superior Labrum Anterior To Posterior) lezyonlarında biseps tenotomisi sonrası omuz eklemindeki radyolojik ve klinik değişikliklerin araştırılması amaçlandı.

Gereç ve Yöntemler: Eylül 2015 ile Eylül 2019 tarihleri arasında merkezimizde SLAP lezyonları için omuz artroskopisi yapılan toplam 380 hasta retrospektif olarak analiz edildi. Çalışmaya dahil edilme kriterlerini karşılayan 44 hasta dahil edildi (izole SLAP lezyonu, biseps tenotomisi, omuz instabilitesi yok, ileri omuz artrozu yok, ek omuz patolojisi yok, takip süresi 1 yıldan uzun). Hastaların ameliyat öncesi ve sonrası değerleri klinik ve radyolojik ölçümlerle karşılaştırıldı. Klinik değerlendirmede; UCLA, Constant, VAS, DASH skorlama sistemi ve kas gücü karşılaştırıldı. Radyolojik değerlendirmede; Superior Humeral Migrasyon, Korakohumeral Mesafe, Akromiohumeral Mesafe, Kritik Omuz Açısı, Akromiyal İndeks karşılaştırıldı.

Bulgular: Çalışmaya dahil edilen 44 hastanın 18'i kadın, 26'sı erkekti. Hastaların ortalama yaşı 51 ve ortalama takip süresi 32,2 aydı. Hastaların ameliyat öncesi ölçümlerinde Korakohumeral Mesafe: 11,5 ± 2,4 mm, Humerus Başı Superior Migrasyonu: 3,4 ± 1,0 mm idi. Ameliyat sonrası grup ölçümlerinde Korakohumeral Mesafe: 8,4 ± 1,4 mm, Humerus Başı Superior Migrasyonu: 4,5 ± 1,3 mm. Bu değerler karşılaştırıldığında, SHY ve KH mesafesi değerlerindeki değişiklikler istatistiksel olarak anlamlıydı (p=0,031, p=0,012). Klinik değerlendirmeler kapsamındaki tüm fonksiyonel ölçümlerde ve skorlama sistemlerinde istatistiksel olarak anlamlı iyileşmeler gözlendi.

Sonuç: İzole SLAP lezyonlarının tedavisinde biseps tenotomisi, radyolojik olarak humerusun anterior ve superior translasyonu ile sonuçlandı. Klinik değerlendirmelere göre, tenotomi bu hastalarda ağrının giderilmesine ve fonksiyonun iyileşmesine katkıda bulunmaktadır.

Anahtar Kelimeler: SLAP lezyonu, Biseps Patolojisi, Superior Humeral Oryantasyon, Korakohumeral Mesafe, Biseps Tenotomisi.

Abstract

Objective: This study aimed to investigate the radiologic and clinical changes in the shoulder joint after biceps tenotomy for isolated SLAP (Superior Labrum Anterior to Posterior) lesions.

Material and Methods: A total of 380 patients who underwent shoulder arthroscopy for SLAP lesions between September 2015 and September 2019 in our center were retrospectively analyzed. The study included 44 patients who met the inclusion criteria (isolated SLAP lesion, biceps tenotomy, no shoulder instability, no advanced shoulder arthrosis, no additional shoulder pathology, follow-up period longer than 1 year). Post operative and pre-operative values of the patients were compared with clinical and radiologic measurements. In clinical evaluation; UCLA, Constant, VAS, DASH scoring system and muscle strength were compared. In radiologic evaluation; Superior Humeral Migration, Coracohumeral Distance, Acromiohumeral Distance, Critical Shoulder Angle, Acromial Index were compared.

Results: Among the 44 patients included in the study, 18 were female and 26 were male. The mean age of the patients was 51 years and the mean follow-up period was 32.2 months. In the preoperative measurements of the patients, Coracohumeral Distance: 11.5 ± 2.4 mm, Superior Migration of the Humeral Head: 3.4 ± 1.0 mm. In the postoperative group measurements, Coracohumeral Distance: 8.4 ± 1.4 mm, Superior Migration of the Humeral Head: 4.5 ± 1.3 mm. When these values were compared, the changes in the SHY and KH distance values were statistically significant (p=0.031, p=0.012). Significant improvements were observed in all functional measurements and scoring systems within the scope of clinical evaluations.

Conclusion: Biceps tenotomy in the treatment of isolated SLAP lesions resulted in anterior and superior translation of the humerus radiologically. According to clinical evaluations, tenotomy contributes to pain relief and improved function in these patients.

Keywords: SLAP lesion, Biceps Pathology, Superior Humeral Orientation, Coracohumeral Distance, Biceps Tenotomy.

Correspondence: Vahit YILDIZ, Adnan Menderes University, Faculty of Medicine, Department of Orthopaedics and Traumatology, 09100, Aydın, Türkiye.

Phone: +90 505 293 27 83 **e-mail:** dr.vyildiz44@hotmail.com

ORCID No (Respectively): 0000-0002-3169-2455, 0000-0003-3639-0912

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INTRODUCTION

The effects of the long head of the biceps tendon on shoulder have been described by guesswork and hearsay for a long time. It is known that the biceps tendon is often a source of pain in shoulder pathologies (1). However, there is no consensus on the functions and working mechanism of this tendon. Many authors have suggested that the long head of the biceps tendon is a rudimental structure similar to the palmaris longus tendon in the wrist, while others have reported that the tendon has a critical role in shoulder proprioception and dynamic and static stabilization (2–4).

Recently, SLAP(Superior Labrum Anterior to Posterior) lesions are diagnosed 4 times more frequently due to technological advances and the increase in the popularity of arthroscopic surgery (5). Repetitive traumas are prominent in the etiology of SLAP. It has been reported in the literature that the long head of the biceps tendon causes this trauma with the effect of traction, especially in type 2 SLAP lesions (6). In traditional surgical treatment, it has been shown that the previously reported high success rates in the repair of SLAP lesions with anchor sutures cannot be achieved and the frequency of biceps tenotomy/tenodesis operations has become more frequent (7). In our study, changes in shoulder structure and function in patients who underwent biceps tenotomy were examined. Humeral migration, position of the humeral head in the joint and functional changes were evaluated. It is hypothesized that the humerus will be migrated superiorly with the removal of the depressor effect and the symptoms related to the SLAP lesion will be relieved with the reduction of the traction effect.

MATERIALS AND METHODS

The clinical and radiologic findings of patients who underwent shoulder arthroscopy for isolated SLAP lesions between September 2015 and September 2019 in our clinic were evaluated retrospectively. A total of 380 patients were retrospectively reviewed from the orthopedic arthroscopy archive. Among these patients, 44 patients who underwent biceps tenotomy were included in the study. Patients with a follow-up period of less than 12 months, patients who did not come for follow-up, patients who underwent primary repair or tenodesis of SLAP lesion, patients who did not have MRI examination at postoperative controls, patients who had additional pathology with SLAP lesion, and patients who underwent any previous shoulder operation were excluded from the study. All operations were performed by a single surgeon. All patients included in the study were evaluated clinically, functionally, radiologically and cosmetically. In clinical evaluation; UCLA, Constant, VAS, DASH scoring system and muscle strength were compared with preoperative values.

Radiological measurements

In the radiologic examination of the patients, direct radiographs and preoperative MR imaging were evaluated. The evaluation of the humeral head and glenoid status, presence of defects and comorbid pathologies were evaluated on the radiographs. The presence and degree of SLAP lesion and accompanying soft tissue pathologies were evaluated in MR imaging. X-ray and MR images were repeated at the first postoperative year controls. Preoperative and postoperative radiologic measurements were made on X-ray and MR images. Acromiohumeral Distance, Coracohumeral Distance, Superior Humeral Migration, Critical Shoulder Angle, Acromial Index were evaluated.

*Acromiohumeral Distance (AH):*Measurement of the shortest distance between the acromion and humeral head in axial views (8,9) **(Figure 1)**.

Coracohumeral Distance (CH): Measurement of the shortest distance between the coracoid process and the tuberculum minus in axial and sagittal sections (10,11) **(Figure 2)**.

Acromial Indeks (AI): The ratio of the distance from the glenoid articular surface to the outer border of the acromion and the distance from the glenoid articular surface to the outer border of the tuberculum majus on true AP radiographs (12) **(Figure 3)**.

Critical Shoulder Angle (KOA): Measurement of the angle between the parallel line placed on the glenoid articular surface and the lower outer corner of the acromion on true AP radiographs (13) **(Figure 4)**.

Superior migration of the humeral head (SHM): Measurement of the distance between the center of the joint face and the center of the humeral head in the sagittal plane (8,14) **(Figure 5)**.

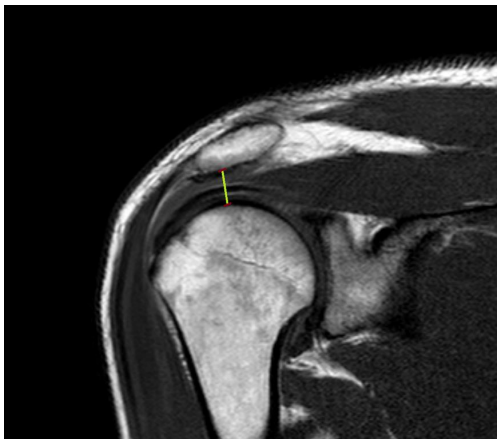

Figure 1. Acromiohumeral distance measurement

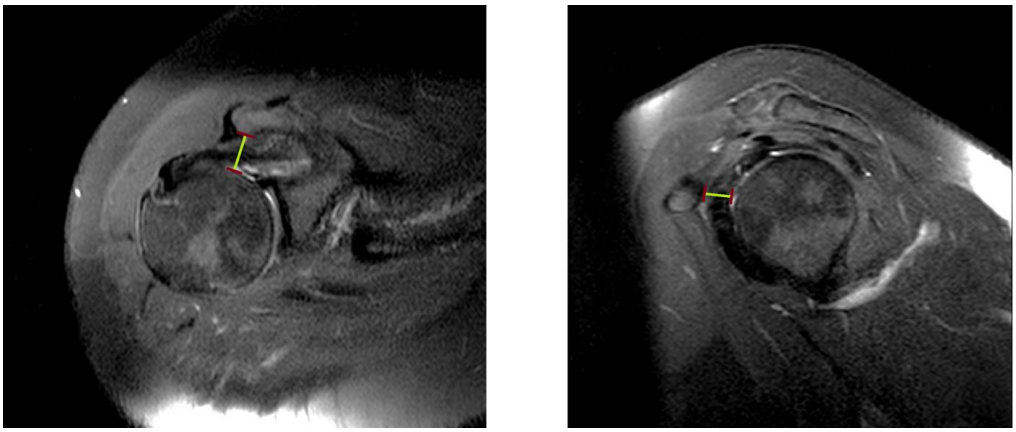

Figure 2. Coracohumeral distance measurement

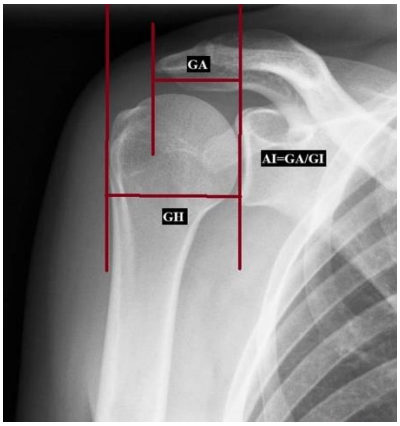

Figure 3. Acromial Index measurement

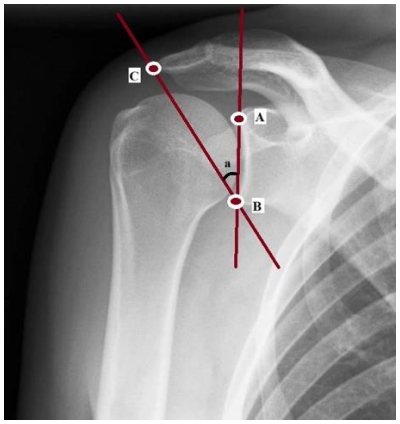

Figure 4. Critical Shoulder Angle measurement

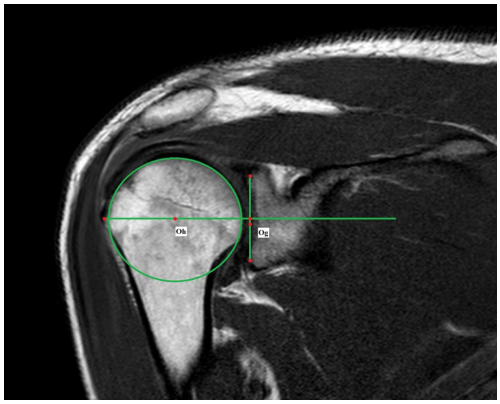

Figure 5. Superior migration of the humeral head (SHM) measurement

Statistical Analysis

IBM SPSS Statistics 26 program was used for statistical analysis of the data. Numerical data were calculated as mean and standard deviation, while categorical data were calculated as frequency and percentage. Descriptive statistics were used to evaluate the data of the patients. The Kolmogorov-Smirnov test was used to evaluate whether the data were normally distributed. Parametric statistical methods were used for normally distributed variables. Paired t test was used as parametric test. Wilcoxon Signed Rank test was applied to variables that did not show normal distribution. The statistical significance limit (p) was evaluated as 0.05.

RESULTS

A total of 380 patients who underwent shoulder arthroscopy for SLAP lesions were retrospectively analyzed from the shoulder archive. Among these patients, 44 were included in the study with isolated SLAP lesions and intact biceps tendon. It was confirmed that biceps tenotomy was performed in all 44 patients included in the study. The mean age of the patients was 51 years (37-65) and the follow-up period was 32.2 months. Eighteen of the patients were female (40.9%) and 26 were male (59.1%). 65.1% of the lesions were on the right shoulder and 34.9% on the left shoulder. The lesions were on the dominant hand side in 31 (70.4%) and on the non-dominant hand side in 13 (29.6%) of the patients **(Table 1)**. The preoperative diagnosis of the patients was confirmed by MRI scans, clinical examination findings, video recordings and intraoperative operative notes.

Table 1. Demographic Data of Patients		
Gender	Female	18 (%40.9)
	Male	26 (%59.1)
Age(year)		Mean: 51,63 (37–65)
Follow-up Period (month)		Mean: 32.2
Affected side	Right	28 (%65)
	Left	16 (%35)

Clinical Results

In the preoperative and postoperative comparative analysis of the patients who underwent arthroscopic biceps tenotomy for SLAP lesion, the preoperative mean Constant Score was 50 (10-70) and the postoperative mean Constant Score was 79.4 (33-99). According to the VAS Scoring system, the preoperative mean value was 6.2 (5-8), while the postoperative mean value was 2.5 (0-4). According to the DASH Scoring system, the preoperative mean value was 13.2 (11-15) and the postoperative mean value was 9.6 (8-11). According to the UCLA Scoring system, the preoperative mean value was 9.0 (6-12) and the postoperative mean value was 29.06 (17-35). There was a statistically significant improvement in all scoring systems after tenotomy compared to preoperative values ($p<0.05$). According to the VAS scoring system, the preoperative mean VAS score was 6.2 (5-8) and the postoperative value was determined as 2.5 (0-4) with a 59.67% improvement **(Table 2)**.

According to the Medical Research Council system, muscle strength levels of the patients were determined in preoperative and postoperative examinations. Accordingly, the mean deltoid muscle strength was 4.01(3-5) preoperatively and 4.64 (4-5) postoperatively. When these values were compared, it was determined that there was a statistically significant increase in deltoid muscle strength after tenotomy ($p<0.05$). Biceps muscle strength was 2.95(2-4) preoperatively and 4.01(3-5) postoperatively. When these values were compared, it was determined that there was a statistically significant increase in biceps muscle strength after tenotomy ($p<0.05$).

In our study, complications such as 'Popeye's Sign', tenderness in the bicipital groove and cramping pain did not occur in a total of 44 patients who underwent tenotomy. Skin reaction developed in a total of 3 patients and was treated with simple medical applications.

Radiological Findings

The preoperative mean AH distance of the patients who underwent biceps tenotomy for SLAP lesion was 6.41 ± 1.29 mm (min-max =3.2-15.1 median=6.8) and the postoperative mean was 6.49 ± 1.07 mm (min-max =2.9-14.8 median=6.5). The preoperative mean CH distance was 11.53 ± 2.44 mm (min-max =2.19-26.1 median=11.3) and the postoperative mean was 8.48 ± 1.41 mm (min-max =1.77-18.9 median=9.9). The preoperative mean of the preoperative SHM was 3.48 ± 1.02 mm (min-max =2.5-12.7 median=4.6) and the postoperative mean was 4.52 ± 1.33 mm (min-max =3.1-16.4 median=4.9). Preoperative mean CSA was 43.50 ± 6.66° (min-max =33°-61° median=43°) and postoperative mean was 43.31 ± 5.98° (min-max =32°-64° median=44°). The mean preoperative AI was 0.50 ± 0.11 (min-max =0.6-1.12 median=0.82) and the mean postoperative AI was 0.53 ± 0.14 (min-max =0.8-1.23 median=0.77).

Table 2. Comparison of Scoring Systems Results			
	Preoperative	**Postoperative**	**p**
Constant Score	50 (10-70)	79.4 (33-99)	($p<0.05$)
VAS	6.2 (5-8)	2.5 (0-4)	($p<0.05$)
DASH	13.2 (11-15)	9.6 (8-11)	($p<0.05$)
UCLA	9.0 (6-12)	29.06 (17-35)	($p<0.05$)

Significant difference was found in SHM and CH values in postoperative measurements when compared to preoperative values in patients who underwent biceps tenotomy operation due to SLAP lesion **(Table 3)**.

DISCUSSION

In our study, we examined the effects on shoulder biomechanics of biceps tenotomy, which is currently used in the surgical treatment of Slap lesions. Tenotomy is preferred by clinicians because of its short operation time, low complication rate and easy applicability. Clinical improvement was evaluated as a decrease in the traction effect on the biceps labrum complex. In addition, it causes migration of the humeral head superiorly and anteriorly.

The initial treatment of SLAP lesions is mostly conservative treatment. Surgical treatment is recommended for patients whose pain does not improve despite conservative treatment and who cannot reach their previous activity level. Arthroscopic SLAP lesion repair, SLAP lesion repair with biceps tenodesis or biceps tenotomy, solely biceps tenotomy are among the treatment options (15,16). The preference between tenodesis and tenotomy operations is based on the patient's age, level of function, being an athlete and cosmetic expectations(15). In a study conducted by Molnar et al. in 2020, SLAP lesions in elite amateur wrestlers were treated using biceps tenodesis and tenotomy method. The data obtained in this study showed that optimum functional performance can be regained in athletes after biceps tenotomy (17). Our preference in our operations is the biceps tenotomy procedure because it offers shorter operation time, earlier rehabilitation opportunities, and we rarely encounter complications mentioned in the literature.

The popularity of biceps tenotomy has been increasing, and studies examining the effects of LHBT on the shoulder joint have also been gaining popularity. These studies have found that the biceps long head tendon provides dynamic stabilization to the shoulder joint (18). Superior migration of the humeral head was first studied by Golding in the 1960s. Weiner and Macnabise conducted research on this subject in 1970. Due to dysfunction, rupture or tenotomy of the biceps tendon, it was thought that the removal of the depressor force of the biceps tendon on the humeral head caused superior migration of the humeral head, which resulted in a decrease in the acromiohomeral distance. In this sense, a study conducted in 2005 showed that 379 patients had decreased acromiohumeral distance and fatty degeneration of the infraspinatus muscle after tenotomy/tenodesis (19,20). In their biomechanical studies, Pagnani et al. showed that in isolated anterosuperior labrum lesions, there was no anteroposterior or superoinferior translation of the glenohumeral joint when the supraglenoid origin of the long head of the biceps was intact. However, in cases where the superior labrum is completely torn, in other words, when the biceps-labrum complex becomes unstable, studies have reported a significant increase in superoinferior and anteroposterior translation (21,22). Burkat *et al.* found that anterior and anteroinferior translation increased at 30 and 60 degrees of abduction in simulated SLAP lesions in cadaveric studies. In addition, the authors stated that SLAP lesion repair provides normal biomechanics and contributes to glenohumeral stability (23,24). In the examinations performed in our study, we found statistically significant differences in terms of SHM in patients who underwent tenotomy. In accordance with the literature, the most important outcome of our study was the detection of superior migration of the humeral

Table 3. Comparison of Radiological Results

	Preoperative	**Postoperative**	**p**
Acromiohumeral Distance (AH)	6.41± 1.29 mm	6.49 ± 1.07 mm	(p=0.220)
Coracohumeral Distance (CH)	**11.53±2.44mm**	**8.48 ± 1.41 mm**	**(p=0.012)**
Superior Humeral Migration (SHM)	**3.48±1.02mm**	**4.52 ± 1.33 mm**	**(p=0.031)**
Critical Shoulder Angle (CSA)	43.50±6.66°	43.31 ± 5.98°	(p=0.25).
Acromial Index (AI)	0.50 ± 0.11	0.53 ± 0.14	(p=0.598)

head with the elimination of the depressor function of the long head of the biceps tendon. In a study on biceps tendon rupture conducted in 2019, coracohumeral distance and coracoid indices were evaluated and it was determined that an increase in these distances correlated with biceps rupture (25). According to a clinical study, Alexander et al. reported that isolated biceps tenotomy may increase anterior shoulder instability regardless of whether the superior labrum is intact or not (26). Similar results were obtained in our study by finding that the CH distance was significantly decreased in patients who underwent tenotomy. The finding that the coracohumeral distance was decreased in biceps long head ruptures and tenotomy is a significant result indicating that the biceps long head tendon is an important factor in the anterior stability of the humeral head.

A study by Gill *et al.* in 2001, in which a total of 30 patients were examined and the mean age was 50 years, patients were evaluated in the postoperative period after biceps tenotomy. Patients reported a significant reduction in pain and functional improvement (27). In another study conducted by Boileau et al. in 2007, it was reported that biceps tenotomy/tenodesis treatment would increase athletic performance in athletes due to the elimination of the pain source (28). Szabo et al. reported that tenotomy/tenodesis performed in patients with biceps pathology with rotator cuff pathology, even if it did not provide shoulder strengthening, gave satisfactory results in terms of pain reduction and functional range of motion, while it was simple and had low complication and reoperation rates (20). Earlier studies in the literature have also reported pain and loss of function after tenotomy, and a 1998 study by Carpenter et al. showed a 20% spontaneous loss of forearm supination strength and 8-20% spontaneous loss of elbow flexion strength after tenotomy (29). Koh *et al.* performed biceps tenotomy in 41 patients with biceps pathology. They reported the complications of "Popeye sign", pain during elbow flexion and decreased elbow flexion strength with a rate of 27% in the postoperative period. When contraction pain and elbow flexion strength were compared, there were no significant differences (30). In a similar study, Kelly et al. reported that out of 160 patients who underwent tenotomy, 70% had "Popeye's sign" and 38% complained of pain and loss of strength during flexion at the elbow (31). This finding was not observed in 44 patients of our study. Instability of the shoulder, radiologic osteoarthritis of the glenohumeral joint and loss of strength during flexion of the elbow joint were not found in any of our patients. In parallel with the general consensus in the literature, a statistically significant improvement was observed in Constant scores and functional assessments in patients who underwent biceps long head tenotomy.

The major limitation of our study is the retrospective design. However, we consider that our complication rates were lowered by the limited size of the patient population. Prospective controlled studies with a large patient group on the functions of the long head of the biceps tendon, wich has become the center of attention in recent years, will provide us with more enlightenment on this subject.

According to the data obtained in our study, we observed that the position of the humeral head in the shoulder joint changed after biceps tenotomy for the treatment of SLAP lesions. We determined that the humeral head migrates superiorly and anteriorly after biceps tenotomy and LHBT stabilizes the humeral head in these vectors. We conclude that the clinical relief of pain and improvement in activities of daily life including shoulder, elbow and forearm movements after tenotomy is a result of the reduction of the traction effect on the biceps labrum complex.

Conflict of Interest and Financial Status: Our study has not been financed by an institution and institution. In this study, there is no conflict of interest among the authors on any subject.

Ethical Approval: This study was approved by the Aydın Adnan Menderes University Faculty of Medicine Ethics Committee (date: 01.07.2021/E-53043469-050.04.04-47710/protocol number: 2021-105).

Author contribution: The authors declare that, they have contributed equally to the manuscript.

REFERENCES

1. Manske RC, Voight M, Wolfe C, Page P. Long Head of the Biceps Tendon (LHBT). Int J Sports Phys Ther. 2022 Dec 2;17(7):1205–7.
2. Khazzam M, George MS, Churchill RS, Kuhn JE. Disorders of the long head of biceps tendon. J Shoulder Elbow Surg. 2012 Jan;21(1):136–45.
3. Yu J, Yin Y, Chen W, Mi J. Long Head of the Biceps Tendon Plays a Role in Stress Absorption and Humeral Head Restriction during the Late Cocking and Deceleration Phases of Overhead Throwing: A Finite Element Study. J Shoulder Elbow Surg. 2024 Aug 13;S1058-2746(24)00573-1.
4. Diplock B, Hing W, Marks D. The long head of biceps at the shoulder: a scoping review. BMC Musculoskelet Disord. 2023 Mar 28;24(1):232.
5. Onyekwelu I, Khatib O, Zuckerman JD, Rokito AS, Kwon YW. The rising incidence of arthroscopic superior labrum anterior and posterior (SLAP) repairs. J Shoulder Elbow Surg. 2012 Jun;21(6):728–31.

6. Bey MJ, Elders GJ, Huston LJ, Kuhn JE, Blasier RB, Soslowsky LJ. The mechanism of creation of superior labrum, anterior, and posterior lesions in a dynamic biomechanical model of the shoulder: the role of inferior subluxation. J Shoulder Elbow Surg. 1998;7(4):397–401.
7. Huri G, Hyun YS, Garbis NG, McFarland EG. Treatment of superior labrum anterior posterior lesions: a literature review. Acta Orthop Traumatol Turc. 2014;48(3):290–7.
8. GOLDING FC. The shoulder--the forgotten joint. Br J Radiol. 1962;35(411):149–58.
9. Cetinkaya M, Ataoglu MB, Ozer M, Ayanoglu T, Oner AY, Kanatli U. Do subscapularis tears really result in superior humeral migration? Acta Orthop Traumatol Turc. 2018;52(2):109–14.
10. Balke M, Banerjee M, Greshake O, Hoeher J, Bouillon B, Liem D. The Coracohumeral Distance in Shoulders with Traumatic and Degenerative Subscapularis Tendon Tears. Am J Sports Med. 2016;44(1):198–201.
11. Dey R, Roche S, Rosch T, Mutsvangwa T, Charilaou J, Sivarasu S. Anatomic variations in glenohumeral joint: an interpopulation study. JSES Open Access. 2018;2(1):1–7.
12. Nyffeler RW, Werner CML, Sukthankar A, Schmid MR, Gerber C. Association of a large lateral extension of the acromion with rotator cuff tears. J Bone Jt Surg - Ser A. 2006;88(4):800–5.
13. Moor BK, Bouaicha S, Rothenfluh DA, Sukthankar A, Gerber C. Is there an association between the individual anatomy of the scapula and the development of rotator cuff tears or osteoarthritis of the glenohumeral joint? A radiological study of the critical shoulder angle. Bone Jt J. 2013;95 B(7):935–41.
14. Weiner DS, Macnab I. Superior migration of the humeral head. A radiological aid in the diagnosis of tears of the rotator cuff. J Bone Joint Surg Br. 1970 Aug;52(3):524–7.
15. Hsu SH, Miller SL, Curtis AS. Long head of biceps tendon pathology: management alternatives. Clin Sports Med. 2008 Oct;27(4):747–62.
16. Bicos J. Biomechanics and anatomy of the proximal biceps tendon. Sports Med Arthrosc Rev. 2008 Sep;16(3):111–7.
17. Molnár S, Hunya Z, Pavlik A, Bozsik A, Shadgan B, Maffulli N. SLAP Lesion and Injury of the Proximal Portion of Long Head of Biceps Tendon in Elite Amateur Wrestlers. Indian J Orthop. 2020 May;54(3):310–6.
18. Warner JJ, Bowen MK, Deng X, Torzilli PA, Warren RF. Effect of joint compression on inferior stability of the glenohumeral joint. J Shoulder Elbow Surg. 1999;8(1):31–6.
19. Walch G, Edwards TB, Boulahia A, Nové-Josserand L, Neyton L, Szabo I. Arthroscopic tenotomy of the long head of the biceps in the treatment of rotator cuff tears: clinical and radiographic results of 307 cases. J Shoulder Elbow Surg. 2005;14(3):238–46.
20. Szabó I, Boileau P, Walch G. The proximal biceps as a pain generator and results of tenotomy. Sports Med Arthrosc Rev. 2008 Sep;16(3):180–6.
21. Pagnani MJ, Deng XH, Warren RF, Torzilli PA, Altchek DW. Effect of lesions of the superior portion of the glenoid labrum on glenohumeral translation. J Bone Joint Surg Am. 1995 Jul;77(7):1003–10.
22. Pagnani MJ, Deng XH, Warren RF, Torzilli PA, O'Brien SJ. Role of the long head of the biceps brachii in glenohumeral stability: a biomechanical study in cadavera. J Shoulder Elbow Surg. 1996;5(4):255–62.
23. Burkart A, Debski R, Musahl V, McMahon P, Woo SLY. [Biomechanical tests for type II SLAP lesions of the shoulder joint before and after arthroscopic repair]. Orthopade. 2003 Jul;32(7):600–7.
24. Burkart A, Debski RE, Musahl V, McMahon PJ. Glenohumeral translations are only partially restored after repair of a simulated type II superior labral lesion. Am J Sports Med. 2003;31(1):56–63.
25. Leite MJ, Sá MC, Lopes MJ, Matos RM, Sousa AN, Torres JM. Coracohumeral distance and coracoid overlap as predictors of subscapularis and long head of the biceps injuries. J Shoulder Elbow Surg. 2019 Sep;28(9):1723–7.
26. Alexander S, Southgate DFL, Bull AMJ, Wallace AL. The role of negative intraarticular pressure and the long head of biceps tendon on passive stability of the glenohumeral joint. J Shoulder Elbow Surg. 2013 Jan;22(1):94–101.
27. Gill TJ, McIrvin E, Mair SD, Hawkins RJ. Results of biceps tenotomy for treatment of pathology of the long head of the biceps brachii. J Shoulder Elbow Surg. 2001;10(3):247–9.
28. Boileau P, Baqué F, Valerio L, Ahrens P, Chuinard C, Trojani C. Isolated arthroscopic biceps tenotomy or tenodesis improves symptoms in patients with massive irreparable rotator cuff tears. J Bone Joint Surg Am. 2007 Apr;89(4):747–57.
29. Carpenter JE, Flanagan CL, Thomopoulos S, Yian EH, Soslowsky LJ. The effects of overuse combined with intrinsic or extrinsic alterations in an animal model of rotator cuff tendinosis. Am J Sports Med. 1998;26(6):801–7.
30. Koh KH, Ahn JH, Kim SM, Yoo JC. Treatment of biceps tendon lesions in the setting of rotator cuff tears: prospective cohort study of tenotomy versus tenodesis. Am J Sports Med. 2010 Aug;38(8):1584–90.
31. Kelly AM, Drakos MC, Fealy S, Taylor SA, O'Brien SJ. Arthroscopic release of the long head of the biceps tendon: functional outcome and clinical results. Am J Sports Med. 2005 Feb;33(2):208–13.

Research Article (Araştırma Makalesi)

Examination of Hearing and Blood Pressure in Call Center Operators

Çağrı Merkezi Operatörlerinde İşitme ve Kan Basıncının İncelenmesi

Ayşe BOZAN[1], Mahmut OZKIRIS[1]

[1] Cappadocia University, Institute of Health Sciences, Department of Audiology, Nevsehir, Turkey

Özet

Amaç: Gürültünün tanımı yapılırken öznellik çerçevesinde hoşa gitmeyen, istenmeyen, rahatsız edici ses olarak bahsedilmektedir. Fizyolojik olarak mevcut ses bireyler arası, bireyin sosyal ilişkisi veya bireyin kendi içerisindeki homeostasiyi bozuyorsa o ses artık gürültü olarak tanımlanmaktadır. Çağrı merkezi operatörleri 67-87 dB şiddet aralığında gürültüye maruz kalmaktadır. 80 dB ve üstü şiddette gürültüye maruz kalmak işitme kaybına, sistolik ve diyastolik kan basıncında artışa, kalp atış hızında değişikliğe neden olabilmektedir. Çalışmamızın amacı, çağrı merkezi operatörlerinin kulaklıkla konuşma ile mesleki gürültünün işitme, kan basıncı ve kalp atış hızıyla ilişkisini incelemektir.

Gereç ve Yöntemler: Çalışmada tüm katılımcılara elektronik sfigmomanometre ile sistolik kan basıncı, diyastolik kan basıncı ve kalp atışı ölçümü, odyometri ile işitme eşiklerinin ölçümü yapılmıştır. Çalışmaya 32'si kadın 28'i erkek 60 çağrı merkezi operatörü ve gürültülü ortamda çalışmayan 31'i kadın ve 29'u erkek 60 birey dahil edilmiştir.

Bulgular: Çalışmamızda 1000, 2000, 4000 Hz işitme eşikleri, sistolik kan basıncı, diyastolik kan basıncı ve kalp atışı gruplara göre istatistiksel açıdan anlamlı farklılık göstermektedir ($p<0,05$). Çağrı merkezi operatörlerinin işitme eşikleri 1000, 2000, 4000 ve 8000 Hz'te kontrol grubuna kıyasla bilateral daha yüksek bulunmuştur. Gruplar karşılaştırıldığında sistolik kan basıncı ve diyastolik kan basıncı operatör grubunda bulunan bireylerde daha yüksekken kalp atış hızı ise kontrol grubunda bulunan bireylerde daha yüksek görülmüştür.

Sonuç: Çalışmamızın sonucunda çağrı merkezi operatörlerinde kontrol grubuna kıyasla 1000 Hz ve üstü frekanslarda işitme eşikleri daha yüksek, sistolik ve diyastolik kan basıncı daha yüksek, kalp atış hızı daha düşük gözlenmiştir.

Anahtar Kelimeler: Çağrı merkezi, Kan basıncı, İşitme, Gürültü, Gürültüye bağlı işitme kaybı

Abstract

Objective: This study sought to investigate the relationship between occupational noise exposure and hearing, blood pressure, and heart rate during headset use in call center operators.

Material and Methods: An electronic sphygmomanometer was used to evaluate the heart rates, diastolic blood pressure, and systolic blood pressure of 60 participants working as call center operators and 60 participants with a noiseless working environment; Audiometry was additionally employed to measure the participants' hearing thresholds.

Results: Statistically significant differences were detected between the groups in terms of 1000, 2000, and 4000 Hz hearing thresholds, systolic blood pressure, diastolic blood pressure, and heart rate ($p<0.05$). In comparison to the control group, call center operators were found to have higher bilateral hearing thresholds at 1000, 2000, 4000, and 8000 Hz. Heart rate was higher in the control group, while both the diastolic and systolic blood pressures were higher in the operator group.

Conclusion: As a result of our study, it was found that hearing thresholds at frequencies above 1000 Hz were higher, systolic and diastolic blood pressure were elevated, while heart rate was lower in call center operators compared to the control group.

Keywords: Call Center, Blood Pressure, Hearing, Noise, Noise-Induced Hearing Loss.

Correspondence: Ayşe BOZAN, Kapadokya Üniversitesi Sağlık Bilimleri Enstitüsü, Nevşehir, Türkiye

Phone: +90 544 378 92 66 **e-mail:** aysebozan12@gmail.com

ORCID No (Respectively): 0000-0001-9842-4466; 0000-0002-0682-0144

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INTRODUCTION

When noise is defined, it is considered as an unpleasant, undesirable, or disturbing sound within the framework of subjectivity. Physiologically, if the presence of a particular sound disturbs the relationship between individuals, the relationship of the individuals with their surroundings, or the individual's own homeostasis, that sound is now classified as noise.

Noise can impair both sensory and cognitive auditory functions, leading to physiological and psychological harm in individuals. Furthermore, it can diminish occupational efficiency and motivation, and disturb environmental tranquility, and affect community relations. The proliferation of professions and institutions in today's industrialized world has elevated the demand for call center operators, who facilitate communication between individuals and organizations. Prolonged exposure of call center operators to headset noise may have detrimental effects on both the physical and mental well-being of these workers, akin to other occupations subjected to excessive noise levels. Increased noise intensity exacerbates the magnitude of discomfort and may further impair health. Tomei and his colleagues (2009) examined the non-auditory effects of noise at different intensity levels and observed that noise between 66-85 dB causes physiological effects such as fatigue, sudden reflexes, and neurovegetative effects such as accelerated respiration, increased blood pressure, and heartbeat, along with hearing loss (1). In studies examining the noise exposure experienced by call center operators, Patel and Broughton documented an average noise level ranging from 67 to 84 dBA over an 8-hour shift, whereas Pawlaczyk-Łuszczyńska and colleagues reported levels ranging from 66 to 86 dBA (2,3).

In the literature review conducted in consideration of this information, it was noted that no studies address the concurrent evaluation of blood pressure and hearing among call center operators.

The objective of our study was to examine the association between occupational noise exposure and its impact on hearing, blood pressure, and heart rate among call center operators while utilizing headsets.

MATERIALS AND METHODS

This study was approved by the Cappadocia University Ethics Committee Clinical Research Ethics Committee (Decision No: E-64577500-050.99-62941).

The study comprised 60 call center operators aged between 18 and 45, consisting of 32 women and 28 men, alongside 60 individuals who were not exposed to noisy environments, comprising 31 women and 29 men. A signed "Participant Informed Consent Form" was obtained from all individuals participating in the study.

The participants underwent tympanometry testing using the Interacoustics AT235 immittance device with a 226 Hz probe tone and a pressure range of (+200,-400) daPa, as well as pure tone speech audiometry tests conducted with the Interacoustic AC-33 audiometer device. Pure-tone air conduction hearing thresholds were assessed at frequencies of 125, 250, 500, 1,000, 2,000, 4,000, and 8000 Hz. Pure-tone averages were derived by computing the arithmetic mean of the hearing thresholds measured at 500, 1,000, 2,000, and 4,000 Hz.

Systolic and diastolic blood pressure, as well as heart rate was assessed using the Life Net Medikal Wbp108 sphygmomanometer on the upper arm following a five-minute rest period.

The data collected from the research were transferred to a computerized environment and analyzed using the SPSS 29.0 software package. In the data analysis, the Independent Samples T-test was employed for comparisons between two independent groups when the assumption of normal distribution was satisfied, whereas the Mann-Whitney U Test was employed in cases where this assumption was not met. To observe the link between two numerical variables, the "Pearson Correlation Test" was employed. The accepted threshold for statistical significance in all tests was $p<0.05$.

RESULTS

In the operator group, 53.3% of individuals were female, while in the control group, the proportion was 51.7%. The gender distribution across the groups did not exhibit a statistically significant difference, indicating homogeneity in gender distribution within the groups ($p>0.05$). Concerning the complaint of hearing loss, 93.3% of individuals in the operator group reported experiencing hearing loss, while none of the individuals in the control group reported such complaints. The complaint of hearing loss exhibited a statistically significant difference between the groups ($p<0.05$). Similarly, while the complaint of tinnitus did not demonstrate a significant difference between the groups ($p>0.05$), complaints of fullness in the ear and difficulty comprehending speech exhibited significant differences between the groups ($p<0.05$). The proportion of individuals who did not complain of stuffiness in the ear was 76.7% in the operator group and 90% in the control group. The complaint of "difficulty comprehending speech" was not observed in 85% of the individuals in the operator group and 96.7% of the individuals in the control group **(Tables 1, 2)**.

Table 1. Demographic Characteristics of the Participants

			Group				
			Operator	Control	Total	χ^2	P
Gender	Female	n	32	31	63	0.033	0.855
		%	53.3%	51.7%	52.5%		
	Male	n	28	29	57		
		%	46.7%	48.3%	47.5%		
Complaint of hearing loss	Yes	n	4	0	4	4.138	0.042
		%	6.7%	0.0%	3.3%		
	No	n	56	60	116		
		%	93.3%	100.0%	96.7%		
Tinnitus complaint	Yes	n	16	8	24	3.333	0.068
		%	26.7%	13.3%	20.0%		
	No	n	44	52	96		
		%	73.3%	86.7%	80.0%		
Complaint of fullness in the ear	Yes	n	14	6	20	3.840	0.050
		%	23.3%	10.0%	16.7%		
	No	n	46	54	100		
		%	76.7%	90.0%	83.3%		
Difficulty comprehending speech	Yes	n	9	2	11	4.904	0.027
		%	15.0%	3.3%	9.2%		
	No	n	51	58	109		
		%	85.0%	96.7%	90.8%		
						T	P
Age	Mean±SD		30.17±6.71	30.33±6.72		-0.136	0.892
	Median (Min-Max)		29 (22-45)	29 (20-45)			
Year of Operation	Mean±SD		6.12±6.63	-		-	-
	Median (Min-Max)		4 (1-28)	-			
Weekly working hours	Mean±SD		45.75±8.30	-		-	-
	Median (Min Max)		40 (36-72)	-			
Daily phone or headset conversation duration	Mean±SD		7.62±0.90	2.37±1,15		27.815	<0.001
	Median (Min-Max)		7 (7-10)	2 (1-5)			

*χ^2= Chi-Square Test; t=Independent Sample T Test; p<0.05

The mean ages of both groups did not exhibit a statistically significant difference, indicating homogeneous distribution of ages (p>0.05). The daily phone or headset conversation duration differs statistically significantly depending on the groups. Individuals in the operator group were more likely to have a longer daily phone or headset conversation duration (7.62±0.90) compared to individuals in the control group (2.37±1.15).

The pure-tone air conduction thresholds at 125 Hz, 250 Hz, and 500 Hz did not exhibit a statistically significant difference between the groups (p>0.05). The 1000 Hz right, 2000 Hz right and left, 4000 Hz right and left, and 8000 Hz right and left air conduction thresholds displayed a statistically significant difference between the groups (p<0.05). Upon examining the air conduction thresholds at 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz for both right and left ears, it was observed that the values for individuals in the operator group were higher compared to those in the control group.

The bone conduction hearing thresholds at 500 Hz for both right and left ears did not exhibit a statistically significant difference between the groups (p>0.05). The

Table 2. Variations in the Hearing Thresholds for Bone and Air Conduction Between Groups

		Operator	Control		
		Mean±SD	Mean±SD	t*/U**	P
125 Hz Air Conduction Threshold	Right	8.67±3.17	8.92±3.20	-0.430	0.668
	Left	8.83±3.24	8.25±3.03	1.019	0.310
250 Hz Air Conduction Threshold	Right	8.92±4.02	9.08±3.62	-0.458**	0.647
	Left	9.08±3.38	8.42±3.12	1.122	0.264
500 Hz Air Conduction Threshold	Right	10.67±4.46	11.25±4.08	-0.748	0.456
	Left	10.83±4.43	11.08±4.33	-0.313	0.755
1000 Hz Air Conduction Threshold	Right	16.08±5.22	12.25±5.71	3.841	**<0.001**
	Left	14.50±4.67	11.75±5.27	3.025	0.003
2000 Hz Air Conduction Threshold	Right	24.08±6.28	12.33±5.08	11.270	**<0.001**
	Left	23.92±5.68	12.42±4.83	70.579**	**<0.001**
4000 Hz Air Conduction Threshold	Right	39.33±7.84	13.17±5.89	20.673	**<0.001**
	Left	39.83±7.13	12.83±6.13	22.242	**<0.001**
8000 Hz Air Conduction Threshold	Right	40.50±8.96	13.75±7.17	18.060	**<0.001**
	Left	40.67±9.68	13.83±7.15	17.274	**<0.001**
500 Hz Bone Conduction Threshold	Right	9.42±4.33	9.42±3.69	0.000	1.000
	Left	9.75±4.36	9.50±3.76	0.336	0.737
1000 Hz Bone Conduction Threshold	Right	14.25±4.49	10.75±5.43	3.845	**<0.001**
	Left	14.08±4.65	10.58±5.30	3.848	**<0.001**
2000 Hz Bone Conduction Threshold	Right	22.75±5.56	11.08±4.97	74.298**	**<0.001**
	Left	22.92±5.62	10.92±4.46	77.472**	**<0.001**
4000 Hz Bone Conduction Threshold	Right	38.67±7.80	12.42±5.93	20.745	**<0.001**
	Left	39.00±7.30	11.58±5.71	22.922	**<0.001**

bone conduction hearing thresholds at 1000 Hz, 2000 Hz, and 4000 Hz for both right and left ears exhibited a statistically significant difference between the groups ($p<0.05$). Upon examination of the bone conduction hearing thresholds at 1000 Hz, 2000 Hz, and 4000 Hz for both right and left ears, it was observed that the values for individuals in the operator group were higher compared to those in the control group.

Blood pressure and heart rate values exhibited a statistically significant difference between the groups ($p<.05$). Systolic blood pressure and diastolic blood pressure values were found to be higher in individuals in the operator group. Heart rate values were higher in individuals in the control group **(Table 3)**.

Table 3. Comparison of Blood Pressure and Heart Rate Values Among Groups

		Mean±SD	Median (Min-Max)	t	P
Systolic Blood Pressure	Operator	130.00±9.34	130 (102-146)	6.227	**<0.001**
	Control	116.58±13.67	116.5 (86-154)		
Diastolic Blood Pressure	Operator	83.93±8.01	85 (57-101)	5.035	**<0.001**
	Control	75.12±10.95	74 (59-107)		
Heart Rate	Operator	82.57±11,54	81.5 (58-115)	-2.327	**0.022**
	Control	87.97±13.78	87.5 (62-135)		

*t=Independent Samples t Test

DISCUSSION

Occupational noise-induced hearing loss develops over time due to years of exposure to continuous or intermittent noise. Continuous noise is more damaging than intermittent noise because it does not allow auditory structures to rest (4,5).

In the study conducted to identify modifiable and non-modifiable risk factors for noise exposure, the modifiable risk factors were identified as follows: voluntary exposure to noise, neglect of ear protection, smoking, lack of exercise, tooth loss, poor diet, cardiovascular disease, and diabetes. Non-modifiable risk factors included age, race, genetic predisposition, and gender (6,7).

Occupational noise-induced hearing loss typically manifests as symmetrical and bilateral. It is primarily characterized by notch formation, especially at 4000 Hz, and a decrease in thresholds at adjacent frequencies (3000 and 6000 Hz), with a slight improvement at 8000 Hz.

Call center operators are required to consistently utilize headphones within the work environment as an integral aspect of their job responsibilities. In environments characterized by background noise and inadequate sound isolation, operators may elevate the headphone volume output level to facilitate speech comprehension. The intensity level of background noise may not be severe enough to directly cause hearing loss; however, the continuous use of high-intensity sound coupled with manual increases in sound output can lead to hearing loss over time (8).

Patel and Broughton assessed the daily noise exposure of 150 call center operators employed in the banking, online ordering, and telecommunications sectors, utilizing a dosimeter affixed to a mannequin wearing headphones. The noises to which call center operators are exposed were determined to include call sound, fax sound, routing sound, and hold music sound. The intensity of the conversation sound was measured in the range of 72-82 dBA. The maximum noise level was recorded at 83 dBA for fax audio, 95 dBA for routing audio, and 88 dBA for music-on-hold audio. The average noise level ranged from 67 to 84 dBA, while the maximum noise level ranged from 67 to 87 dBA. Out of 150 operators, 3 were found to be exposed to noise levels exceeding 85 dBA (2).

Pawlaczyk-Łuszczyńska and colleagues researched the noise intensity levels and hearing thresholds of call center operators. The headset noise exposure level of call center operators was measured using an artificial ear, revealing that operators were exposed to noise levels ranging from 66 to 86 dB for 8 hours a day. Approximately 12% of operators were measured to be exposed to average noise levels exceeding 85 dB, while 38% were exposed to levels exceeding 80 dB. While 50% of the operators exhibited bilateral normal hearing in the frequency range of 250-8000 Hz, 73% experienced hearing loss in the extended high frequencies range of 9000-16000 Hz. Less than 10% of the operators exhibited hearing loss at both high frequencies and speech frequencies, while 37% experienced a permanent threshold shift at high frequencies (3,9).

The average noise intensity to which call center operators were exposed during working hours was measured in the range of 67-87 dB according to Patel and Broughton's study, and in the range of 66-86 dB according to Pawlaczyk-Łuszczyńska and colleagues' study. According to a study by Tomei and colleagues, noise levels exceeding 66 dB are associated with hearing loss. Based on this, it can be inferred that call center operators are subjected to noise levels that have the potential to induce hearing loss, as well as elevate blood pressure, heart rate, and respiratory rate.

Martin and colleagues investigated the impact of noise levels ranging from 85 to 90 dB on hearing thresholds. The prevalence of hearing loss was higher among workers than among controls in all age groups. Among foundry workers aged over 50, the prevalence of hearing loss ranged from 14% to 32%, compared to 4% in a control group of the same age range. Workers over 50 years of age exhibited hearing thresholds below 30 dB at 500, 1000, and 2000 Hz, with hearing loss exceeding 50 dB at 3000, 4000, and 6000 Hz (10).

In our study, similar to the investigation by Martin and colleagues, a statistically significant difference was observed between the operator and control groups in hearing thresholds at 1000, 2000, 4000, and 8000 Hz. In our study, the disparity in hearing thresholds between the groups at 4000 and 6000 Hz was greater than the difference at 1000 and 2000 Hz, similar to the findings reported by Martin and colleagues ($p<0.05$).

When speech frequencies were taken into account in our investigation, the control group members' 500, 1000, 2000, and 4000 Hz air and bone conduction hearing thresholds were found to be within the normal range. Hearing thresholds at 500 Hz air and bone conduction do not differ between the groups. It was observed that the operator group had significantly greater air and bone conduction hearing thresholds at 1000, 2000, and 4000 Hz in comparison to the control group ($p<0.05$). In call center operators, airway and bone conduction hearing thresholds at frequencies of 1000, 2000, and 4000 Hz closely align with a difference of less than 5 dB, suggesting sensorineural type hearing loss at these frequencies (11,12).

In our study, the right ear's air conduction Sound Sensitivity Observation (SSO) was obtained as 22.54±4.77, Speech Reception Threshold (SRT) was 21.27±4.49, and Speech Discrimination Score (SDS) was 98.87±2.09. Meanwhile, in the left ear, the air conduction SSO was 22.27±4.28, SRT was 21.44 ±4.28, and SDS was 98.87±2.09 in the operator group. In the control group, the right ear's air conduction SSO was 12.42±4.28; SRT was 16.33±5.51, and SDS was 100.00 ± 0.00. Similarly, in the left ear, the air conduction SSO was 12.25±4.00; SRT was 16.25±5.34, and SDS was 100.00±0.00. In the control group, the right ear's air conduction SSO was 12.42±4.28; SRT was 16.33±5.51, and SDS was 100.00±0.00. Similarly, in the left ear, the air conduction SSO was 12.25±4.00; SRT was 16.25±5.34, and SDS was 100.00 ± 0.00. The decrease in speech discrimination scores in the operator group compared to the control group supports the finding of sensorineural hearing loss in this group.

Somma and colleagues examined the hearing thresholds of cement workers in 2008 while they worked in noisy surroundings with levels exceeding 85 dB. The study included 184 male cement workers and 98 control individuals working in a quiet setting. Participants were divided into groups depending on their age. A pure tone audiometry test was applied in the range of 125-8000 Hz. In all groups, the hearing thresholds of cement workers at frequencies of 3-8 kHz were found to be significantly higher than those of the control group. For the youngest age group (21–30 years old), there was a 5 dB difference between the worker and control groups' hearing thresholds between 3–8 kHz; for the oldest age group (51–60 years old), there was a 2 dB difference. Between 3-8 kHz, a 5 dB difference was observed between the hearing thresholds of the worker and control groups in the youngest age group, aged 21-30 years, and a 2 dB difference was observed between the hearing thresholds of the worker and control groups in the oldest age group, aged 51-60 years. In both groups, hearing loss increases significantly with age, but this rise was observed more prominently in cement workers (13,14).

Our research reveals that the contact center operators' and the control groups' hearing thresholds rise noticeably with age ($p<0.05$). Nonetheless, compared to the control group, operators' hearing thresholds rise more with age. This demonstrates that older operators who are exposed to industrial noise lose their hearing. As demonstrated by Somma and colleagues' study, occupational noise accelerates the aging-related loss of hearing in call center workers.

In our study, a positive relationship was observed between the years of working in the call center and the hearing thresholds of call center operators ($p<0.05$). Hearing loss rises with the number of working years. Nevertheless, no significant correlation was found when examining the association between operators' hearing thresholds and their weekly working hours. This suggests that our study's findings about the long-term effects of call center employment on hearing (15).

It is known that the physiology of hearing differs in men and women. Wang and colleagues examined the effect of gender on noise-induced hearing loss and applied an audiometry test to 1140 female and 1140 male shipyard workers between the ages of 18-60. At frequencies of 3, 4, 6, and 8 kHz, the prevalence of hearing loss was 13.8% in women and 34.4% in men as well. A significant difference was observed at low frequencies (8).

The operator group in our study consisted of 32 female and 28 male individuals, while the control group consisted of 31 female and 29 male individuals. Similar to Wang and colleagues' study, our analysis of the influence of gender on hearing revealed that men's hearing thresholds were greater than women's in both the operator and control groups. However, this increase exhibited a significant difference between genders only in the 1000 Hz hearing thresholds among the operator group and the 125 Hz hearing thresholds within the control group ($p<0.05$).

Tekin and colleagues conducted a study to examine the effects of noise exposure on the cardiovascular system of mine workers. In this study, the systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), oxygen saturation rate, rhythm rate, and pulse values of 100 male workers were examined. Workers were measured three times using a COMEN Star 8000 bedside monitor. The first measurement was taken before the introduction of noise, the second measurement was taken after all the machines were turned on and the noise was present, and the third measurement was taken after all the machines were turned off and the noise was eliminated. The increase in SBP and DBP values in the second measurement compared to the third measurement is statistically significant. No significant difference was observed in blood pressure, oxygen saturation rate, rhythm rate, and pulse values (17).

In our study, the average SBP in the operator group was 130.00±9.34, while the DBP was 83.93±8.01, and the HR was 82.57±11.54. In contrast, the average SBP in the control group was 116.58±13.67, the DBP was 75.12±10.95, and the HR was 87.97±13.78. There is a significant difference between SBP, DBP, and HR groups ($p<0.05$). When comparing the SBP, DBP, and HR values between the groups, the HR value was higher in the control group, while the SBP and DBP values were higher in the operator group, consistent with the findings of Tekin and colleagues.

Abbate and colleagues looked into how exposure to noise affects the cardiovascular system. In the study, 757 male employees of oil distribution and refining companies were split into three groups based on the amount of noise participants were exposed to: low, medium, and high. Their SBP, DBP, and HR values were also looked at. The study included 200 workers who were classified as low exposure (noise level less than 80 dBA), 212 drivers who were classified as medium exposure (noise level between 80 and 85 dBA), and 345 workers who were classified as high exposure (noise level between 85 and 90 dBA). Although there was a statistically significant positive correlation between the groups' noise exposure levels and SBP and DBP values, there was no such correlation with the HR value. Simultaneously, SBP, DBP, and HR values increase linearly with the age and working years of employees (18,19).

In our study, similar to the findings of Abbate et al., a significant positive relationship was observed between age and SBP and DBP values in the operator group, but no relationship was observed with HR ($p<0.05$). As age increases, systolic and diastolic blood pressure increases in operators. In the control group, there was no correlation seen between age and heart rate or blood pressure. In our study, similar to Abbate and colleague's findings, a significant positive correlation was observed between the working years of call center operators and blood pressure ($p<0.05$). By increasing working years, the SBP, DBP, and HR values of operators rise. While the effect of weekly working hours on blood pressure was not observed in call center operators, the increase in SBP, DBP, and KA values as the working years increase reveals the long-term effect of occupational noise on operators.

Wiinberg and colleagues looked into how gender variations affected blood pressure in 1995. In the study, the ambulatory blood pressure of normotensive individuals, both male and female, between the ages of 20-79, was measured for 24 hours. Participants were divided into groups based on their age. Ambulatory blood pressure was measured every 15 minutes between 07:00 and 22:59, and every 30 minutes between 23:00 and 06:59. It was determined to be statistically significant that SBP rises with age and is higher in males than in women. In the 50–59 age group, DBP values only increased with age in men and women. There was no gender difference in these values. Blood pressure values obtained at night were 15% lower than those measured during the day. As a result of the study, it was noted that SBP values were higher in men compared to women, whereas DBP values remained unaffected by gender (20).

In our study, statistically significant differences were observed in SBP values between the operator and control groups based on gender ($p<0.05$). The mean SBP among women in the operator group (127.38±8.68) was observed to be lower compared to that among men (133.00±9.31). The mean SBP among women in the control group (113.23±15.94) was observed to be lower compared to that among men (120.17±9.79). In our study, similar to the findings of Wiinberg and colleagues, the mean SDB was higher in men than in women in both the operator and control groups. There were no significant differences in DBP and HR values between individuals in the operator and control groups based on gender ($p>0.05$).

In our study, it was observed that call center operators exhibited higher hearing thresholds at frequencies of 1000 Hz and above, as well as higher SDB and DBP values, and lower HR values compared to the control group.

A significant positive correlation was observed between age and hearing thresholds in both operator and control groups. The increase in hearing thresholds with advancing age was more pronounced in the operator group compared to the control group.

In call center operators, a significant positive correlation was found between age and SBP and DBP, while no correlation was observed with HR. As age increases, there is a concurrent increase in both SBP and DBP values within the operator group. In the control group, no significant relationships were observed between age and SBP, DBP, and HR values.

It was observed a significant positive relationship between the duration of employment in the call center and both blood pressure levels and hearing thresholds among operators. The hearing thresholds, SBP, DBP, and HR values of call center operators were observed to increase with prolonged years of employment.

A significant difference was observed in the average SBP between genders in both the operator and control groups. In the operator group, it was observed that SBP values were higher in men compared to women.

Ethics Committee Approval: This study was approved by the Cappadocia University Clinical Research Ethics Committee (Decision No: E-64577500-050.99-62941) on December 27, 2023.

Participant Consent: A signed "Participant Informed Consent Form" was obtained from all individuals participating in the study.

Author Contributions: Conceptualization – AB, MÖ; Design – AB, MÖ; Supervision – MÖ; Materials – AB; Data Collection and/or Processing – AB; Analysis and/or Interpretation – MÖ; Literature Review – AB; Writing – AB, MÖ; Critical Review – MÖ.

Conflict of Interest: Each of the authors has contributed to, read, and approved this manuscript. None of the authors has any conflict of interest, financial or otherwise.

This manuscript is original, and it, or any part of it, has not been previously published; nor is it under consideration for publication elsewhere.

REFERENCES

1. Tomei G, Anzani MF, Casale T, Tomei F, Piccoli F, Cerratti D, et al. Effetti extrauditivi del rumore. G Ital Med Lav Erg. 2009;31(1):37-48.
2. Patel JA, Broughton K. Assessment of the noise exposure of call centre operators. Annals of Occupational Hygiene. 2002;46(8):653-661.
3. Pawlaczyk-Łuszczyńska M, Zamojska-Daniszewska M, Zaborowski K, Dudarewicz, A. Evaluation of noise exposure and hearing threshold levels among call centre operators. Archives of Acoustics. 2019;44(4):747-759.
4. Mirza R, Kirchner DB, Dobie RA, Crawford J, ACOEM. Task Force on Occupational Hearing Loss. Occupational noise-induced hearing loss. Journal of occupational and environmental medicine. 2018;60(9):e498-e501.
5. Themann CL, Masterson EA, Peterson JS, Murphy WJ. Preventing Occupational Hearing Loss: 50 Years of Research and Recommendations from the National Institute for Occupational Safety and Health. In Seminars in Hearing. 2023.
6. Daniel E. Noise and hearing loss: a review. Journal of School Health. 2007;77(5):225-231.
7. Fagan JJ. Open access publishing of textbooks and guidelines for otolaryngologists in developing countries. 2019;3(3).
8. Temügan E, Ünsal S. Saf ses hava yolu odyometri. Odyolojide Temel Kavramlar ve Yaklaşımlar. Nobel Tıp Kitapevi. 2015;s.155-162.
9. Olagbemi DO, Asoegwu CN, Somefun AO, Nwawolo CC. Otologic symptoms and hearing thresholds among a cohort of call center operators in Lagos. The Egyptian Journal of Otolaryngology. 2022;38(1), 1-6.
10. Martin RH, Gibson ES, Lockington JN. Occupational hearing loss between 85 and 90 dBA. Journal of Occupational and Environmental Medicine. 1975;17(1):13-18.
11. Purdy S, & Williams W. Guideline for diagnosing occupational noise-induced hearing loss. Part 3: Audiometric standards, Purdy & Williams: Guidelines for audiometry for diagnosis of NIHL. 2012.
12. Kaya M, & Gündüz M. İşitme sistemi anatomi ve fizyolojisi. Odyolojide Temel Kavramlar ve Yaklaşımlar. Eds: Gündüz M, Karabulut H. Nobel Tıp Kitapevi, 2015;61-85.
13. Somma G, Pietroiusti A, Magrini A, Coppeta L, Ancona C, Gardi S, et al. Extended high-frequency audiometry and noise induced hearing loss in cement workers. American Journal of Industrial Medicine. 2008;51(6):452-462.
14. Kozlowski E. İletişim platformları için tasarlanmış kulaklıkların gürültü parametreleri. Uluslararası Çevre Araştırmaları ve Halk Sağlığı Dergisi. 2022;19(6):3369.
15. Gates GA, Schmid P, Kujawa SG, Nam BH, D'Agostino R. Longitudinal threshold changes in older men with audiometric notches. Hearing research. 2000; 141(1-2):220-228.
16. Wang Q, Wang X, Yang L, Han K, Huang Z, Wu H. Sex differences in noise-induced hearing loss: a cross-sectional study in China. Biology of sex Differences. 2021;12:1-10.
17. Tekin A, Nalbant MO, Orhan M, Tekin F, Suvaydan F, Berki K, et al. Türkiye Soma Havzasında Yeraltı Maden İşçilerinin Maruz Kaldıkları Gürültü Etkilerinin İstatistiksel Analizi. Journal of Engineering Sciences. 2023;11(2):449-458.
18. Abbate C, Giorgianni C, Munao F, Costa C, Brecciaroli R, Barbaro M. Effects of noise on functional cardiovascular parameters: a follow-up study. Giornale italiano di medicina del lavoro ed ergonomia. 2002;24(1):43-48.
19. Kalantary S, Dehghani A, Yekaninejad MS, Omidi L, Rahimzadeh M. The effects of occupational noise on blood pressure and heart rate of workers in an automotive parts industry. ARYA atherosclerosis. 2015;11(4):215.
20. Wiinberg N, Høegholm A, Christensen HR, Bang LE, Mikkelsen KL, Nielsen PE, et al. 24-h ambulatory blood pressure in 352 normal Danish subjects, related to age and gender. American journal of hypertension. 1995;8(10):978-986.

Research Article (Araştırma makalesi)

Evaluation of Sputum Eosinophil Level and Presence of Charcot-Leyden Crystals in Patients with Airway Hyperreactivity

Havayolu Hiperreaktivitesi Olan Hastalarda Balgamda Eozinofil Düzeyi ve Charcot-Leyden Kristal Varlığının Değerlendirilmesi

Sümeyra ALKIS KOCTURK[1], Hatice SAHIN[2]

[1] Sütçü Imam University, Faculty of Medicine, Department of Clinical Microbiology, Kahramanmaraş, Türkiye
[2] Sütçü Imam University, Faculty of Medicine, Department of Pulmonary Medicine, Kahramanmaraş, Türkiye

Özet

Amaç: Bu araştırmanın amacı, eozinofilinin bronş hiperreaktivitesine neden olan bağımsız bir faktör olup olmadığını veya balgamdaki varlığının bu durumda tamamlayıcı bir rol oynayıp oynamadığını özellikle astım vakalarında araştırmaktır.

Gereç ve Yöntemler: Veriler, Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Hastanesi Göğüs Hastalıkları servisine yatan 100 kişiden oluşan bir örneklemden elde edildi ve bronş hiperreaktivitesi ile karakterize edilen vakalara odaklanıldı. 30 astımlı, 34 astım dışı solunum hastalığı grubu ve 36 kontrol grubu hastasından oluşan üç grup oluşturuldu. Hastaların ilk servise yatırıldığı anda balgam örnekleri toplandı. Bu nedenle önceden var olan hastalıkların bulgusu olarak da eozinofili ortaya çıkabileceği gözönünde bulunduruldu.

Bulgular: Açıklamak gerekirse; eozinofili oranını üç grupta tanımlandı ve ayrıca smear incelemesinde Charcoat- Leyden kristallerinin varlığını araştırıldı. Çalışmanın sonuçları, astımlılarda eozinofili oranının daha belirgin (%16,6) olduğunu ve geçmiş sonuçları tekrarladığını göstermekteydi. Astımlı olmayan hasta grubundan elde edilen sonuçlar, eozinofili hasta yüzdesinin astımlılardan daha az olduğunu doğrulamaktaydı (%13,3). Hipotezlerle tutarlı olarak kontrol grubu en az yüzdeye (%8,8) sahipti.

Sonuç: Çalışmada eozinofili ile Charcoat Leyden kristallerinin varlığı arasındaki ilişki incelendi. Tüm çabalarımıza rağmen incelenen smearlerin hiçbirinde kristal yapı tespit edilmediğinden herhangi bir korrelasyon görülemedi.

Anahtar kelimeler: Astım, Bronşiyal Hiperreaktivite, Eosinofili.

Abstract

Objective: The focus of this research is to clarify whether eosinophilia is an independent factor in causing bronchial hyperreactivity or if its presence in sputum plays a supplementary role in this condition; especially in asthma.

Material and Methods: Data was obtained from a sample of 100 individuals in the respiratory care unit, concentrating on cases characterized by bronchial hyperreactivity. We made three groups with 30 asthmatics, 34 non-asthmatic respiratory disease group and 36 control group patients. We decided to get the patients' sputum when they were internalized first. Eosinophilia can therefore occur in addition to pre-existing illnesses.

Results: To explain; we defined the ratio of eosinophilia in three groups and also searched for the presence of Charcot-Leyden crystals out of smear examination. The results of the study demonstrate eosinophilia ratio among asthmatics was more prominent (16.6%), replicating past findings. Results from the non-asthmatic patient group confirm that percentage of patients with eosinophilia was lower than that of asthmatics (13.3%). Consistent with hypotheses, control group had the least percentage (8.8%).

Conclusion: The study examined the relation between eosinophilia and the presence of Charcot-Leyden crystals. Despite our efforts, we were unable to observe any signs of coexistence, as no crystal structures were detected in any of the smears examined.

Keywords: Asthma, Bronchial Hyperreactivity, Eosinophilia.

Correspondence: Sümeyra ALKIS KOCTURK, Sütçü İmam Üniversitesi Tıp Fakültesi Klinik Mikrobiyoloji, Kahramanmaraş, Türkiye

Phone: +90 531 866 10 75 **e-mail:** sumeyrakocturk@yahoo.com

ORCID No (Respectively): 0000-0001-9316-794X, 0000-0002-3317-3640

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INTRODUCTION

Inflammation of the airways is an important cause of respiratory diseases such as asthma, chronic obstructive pulmonary disease or chronic cough. Therefore, the collection of airway samples is an essential step for both research and clinical purposes. As a result, sputum sampling is popular as a safe, non-invasive alternative to bronchoscopy, which carries the risk of asthma exacerbation (1,2). Sputum induction is a technique that involves the induction and subsequent processing of expectoration primarily for the analysis of inflammatory cells in the airways in order to understand the underlying mechanism of various inflammatory diseases as asthma. Asthma is a chronic respiratory disease characterized by a persistent inflammatory process in which eosinophils play an important role (3).

Approximately when Osler released his initial textbook, The Principles and Practice of Medicine, highlighting the role of inflammation in asthma, Gollasch discovered eosinophils in the sputum of asthma patients. Afterwards, eosinophils were included of the characteristic process of asthma (4). The percentage of eosinophils in sputum in airway inflammation is a good marker for assessing prognosis in asthma patients. Validation and characterization of biomarkers are crucial for their successful use and should also confirm sensitivity, specificity, and productivity. We are searching if there is a statistically significant correlation between the disease and the eosinophil count in sputum (5). Treatments aimed at normalizing the eosinophil count in sputum may help prevent asthma attacks, and the eosinophil count in the blood is also related to the frequency of attacks. Therefore, the stratification of severe asthmatics as a basis for treatment decisions is complex. Therefore, reliable and sensitive biomarkers such as sputum samples are a valuable tool for physicians (5).

The Charcot-Leyden crystal (CLC) protein was first observed in 1853 by Jean-Martin Charcot in a leukemia patient and later detected by Ernst Leyden in 1872 in the sputum of asthma patients. The Charcot-Leyden crystals, named after him, are rhombic lysophospholipase crystals (hexagonal, bipyramidal) of up to 50 µm in length, which are produced by eosinophils (6). With the disruption of epithelial integrity, the eosinophils in the bronchial mucosa migrate into the bronchial lumen. The lysophospholipase enzyme released by the eosinophils crystallizes in vitro and in vivo. These crystals, which are found in the sputum of patients with airway hyperreactivity, are called "Charcot-Leyden crystals"(6). A protein called galectin-10, which is distributed in the inner and outer regions of the cell membrane, accounts for 10% of the eosinophil protein concentration. When the local Gal-10 concentration exceeds the threshold concentration resulting from the accumulation of these proteins released by eosinophil degranulation, crystallization begins and Charcot-Leyden crystals form (6). If the CLCs were easy to see; the crystals can be examined directly by light and phase contrast microscopy. Because Gal-10 in CLCs contains aromatic residues, it can also be examined directly by fluorescence microscopy (6). May-Grünwald and Papanicolaou staining of the CLCs show colour blue and orange, respectively. CLCs can also occur in eosinophilic diseases such as asthma, allergic reactions, fungal and helminthic infections and rarely in hematologic and neoplastic diseases. These crystals can also be detected in stool examined for parasites, in respiratory secretions or, more rarely, in tissue biopsies (6). We are trying to answer the question here is to decide whether eosinophilia is an independent factor for bronchial hyperreactivity disorders. Eosinophilia causing symptoms manifesting in addition to pre-existing conditions, masked as a worsening (7).

MATERIALS AND METHODS

Study design

In this prospective study, patients with bronchial hyperreactivity and cough were examined between June 2024 to September 2024. The clinical history, diagnosis as well as accompanying diseases were recorded. In the present study, the inclusion criteria were as follows: (1) between 16 and 80 years of age; (2) bronchial hyperreactivity as the symptom of internalization to service; (3) patients had sputum examination. Corticosteroids and specific biological agents have demonstrated positive results in eosinophilia, so we exclude the patients receiving corticosteroids. We collected the data from routine examined sputum samples received from the respiratory diseases ward.

In our study, the examination of sputum samples coming to the Medical Microbiology Laboratory, sputum smear samples were examined using May Grünwald and Gram staining methods. Gram stain revealed the quality of sputum and presence of PMNL in smears (more than 25 PMNL, less than 10 epithelial cells). Presence of Charcot-Leyden Crystals and percentage of eosinophils in Giemsa-stained smears were investigated. The dependent variable of the study was eosinophil percentage and the presence of crystals in the participants. While the presence of airway hyperreactivity in the participants would be investigated with the diagnosis they held in hospital, and demographic data would constitute the independent variable.

For each sputum sample, the number of PMNL per field of view (10 × objective) were recorded. Sputum samples were classified as good quality by three different criteria: (i) <10 epithelial cell (ii) <10 SEC or >25 PMNL. A magnification of 10 to 10 x 10 was used as a measure of the validity and quality of the sputum samples taken. Attention is paid to the presence of fewer epithelial cells and more than 25 polymorphonuclear leukocytes. In addition, the participants in the research group are asthma patients, and the control groups are patients with respiratory pathology but not asthma, and other pathologies referred to the hospital. taken to ensure that they have similar demographic characteristics, and overlapping clusters were used. After ethics committee approval, since the sputum samples coming to the laboratory for routine examination were examined, sputum samples were not taken; therefore, patients would not be asked to provide an informed consent form. Financial support to be provided by the researchers and used for the expenses of the dyes.

Statistical analysis

Frequency (%) was given for categorical variables, mean ± standard deviation, and median (minimum-maximum) for continuous variables. When examining whether there was a statistically significant difference between the eosinophil percentage and the asthma and non-asthmatic groups, the Mann-Whitney U test was used since the assumption of normal distribution was not met. Statistical significance level was accepted as $p<0.05$. Evaluation of the data was done using the SPSS 11.5 for Windows program.

The study followed the international principles of Helsinki and was approved by the Local Ethics Committee (date 04.11.2024/protocol no: 259).

RESULTS

30 patients were all asthmatics. 34 of the patients in our study were not asthmatic but had respiratory pathology; 36 were non-asthmatic and had non-respiratory pathology. Out of non-asthmatic respiratory tract pathologies, upper respiratory tract infections, chronic cough, bronchiectasis, chronic obstructive pulmonary disease, and pleural effusion were present. Nonrespiratory pathologies were coronary heart disease, hypertension, diabetes mellitus, and rheumatoid arthritis.

No correlation was found between age and sputum eosinophilia; the mean age among 34 asthmatic patients was 54, and patients having other respiratory pathologies had a mean age of 58. The third group had a mean age of 54. In studies that took gender into account, the value was found to be higher in women than in men, but in our study, among all groups, all eosinophilia diagnosis in sputum was found in men. Demographic variables such as gender and ethnicity are thought to be responsible for the different values found in various studies on sputum eosinophilia. In our study, all members' ethnicity was the same, and gender couldn't be accounted for because all patients were men, other for 5 women.

What about the difference among groups? The eosinophil counts are used to detect eosinophilic airway inflammation in our study. Eosinophilia in patients with asthma was found in %1 in 5 asthmatic patients (%16.6), %3 in 4 of patients with other respiratory pathologies (%13.3); including chronic obstructive pulmonary disease exacerbation, pulmonary carcinomas, and pneumonia. Moreover, the control group containing non-asthmatic and non-respiratory pathology patients had % 1 of counted eosinophils in 3 of the patients (%8.8).

DISCUSSION

Every day, many patients with lung diseases and numerous complaints are treated both in the outpatient clinic and on the ward. They are usually admitted to the hospital with complaints related to the diagnosis of pneumonia. They may be chronic obstructive pulmonary disease or mainly asthmatic patients. Sputum examination could be used to monitor asthma and could be performed with limited resources. It is a simple, non-invasive and inexpensive method (1). The sputum cell counting by 400 non-tumour cells; the percentage of eosinophilic cells (Eos%) about 2.5% was defined as eosinophilia in the sputum (8). We had the data by smear examination, stained with May Grünwald, after we decided the sputum was a sample taken properly and was qualified. In the sputum of asthmatics, we found 16.6 % having eosinophilia, and in other respiratory pathologies, found to be 13.3%; in the control group, patients with eosinophilic sputum were 8.8%. We found higher percentages in asthmatics, supporting older studies sharing the idea of reduced eosinophil apoptosis and sputum eosinophil load were correlated with the severity of asthma (9).

Patients with eosinophilia with other respiratory pathologies were pneumonias; we thought that all cell types are increasing in number in infections, so the eosinophils. Some diseases exhibit eosinophilia and are referred to as eosinophilic lung diseases of known or

unknown origin. The percentage of eosinophils in peripheral blood can also be determined; bronchoalveolar lavage fluid and sputum are important samples of the assessment (3). We attempt to answer the question of whether eosinophilia is an independent causative factor or the presence of eosinophilia in sputum is an additional causative factor to bronchial hyperresponsiveness disorders that may have existed prior to the finding of eosinophilia. So we decided to get the patients' sputum when they were internalized first. The symptoms caused by eosinophilia can therefore occur in addition to pre-existing illnesses and be masked as an exacerbation. In a study held in Turkey among the general population, blood eosinophil count was measured in 18-79-year-old people; the mean eosinophil count value was 140 eos/μL, and percentiles were not reported. Eosinophilia at 2.59% is an average rate (10).

In our control group, the least extent of eosinophilia was observed; usually, expectorated sputum is examined for specialization of cell types and to measure the presence of inflammation in the airways. We used smear examination for this process(1). Also, laboratory processing of sputum was significantly important to get results right. According to recent studies, the eosinophil counts of our population are also compared with other populations. It is also unclear whether there is a correlation between the disease and the eosinophil count; also, there may be diurnal variation in sputum as in blood. In eosinophilic asthma, a subtype of asthma characterized by an increased concentration of eosinophils in the airways, peripheral blood and sputum, a complex interplay of factors plays a role in the progression of the disease. Although a standard definition of eosinophilic asthma remains not clear, eosinophilic asthma is often indicated by peripheral blood eosinophil counts that surpass specific benchmarks, such as >150 cells/μL, >300 cells/μL, or >400 cells/μL in peripheral blood (1) and eosinophil counts in sputum of greater than 2 to 3% describes eosinophilic asthma in clinical studies (11).

In a study conducted among the Korean population, the cut-off for sputum eosinophilia was 3.5% (1). In another wide study, blood eosinophil count has moderate accuracy in predicting eosinophils in the sputum of 3% or more in asthma patients. Patients with stable COPD Show that blood eosinophil count at a threshold of 0.3/L could help determine the sputum eosinophilia(12). Balazs et al. found that blood eosinophil count is a good surrogate for identifying sputum eosinophilia (>3%) in stable COPD. Nevertheless, the role of peripheral eosinophil count in predicting sputum eosinophilia in patients with chronic cough is still unclear (13).

The limitations of our study indicate that better methods are needed to assess the involvement of eosinophils in the disease. The cell count in induced sputum is the most reliable method for detecting eosinophilic airway inflammation. However, the induced sputum test is not universally applicable due to its time-consuming and labour-intensive procedures. In addition, some patients with chronic cough have a dry cough, making it difficult to obtain sufficient sputum for cell differential analysis. Therefore, it is difficult to find a simple and reliable biomarker for the prediction of eosinophilic airway inflammation by sputum examination that has clinical significance for chronic cough (1).

Ethics: The study followed the international principles of Helsinki and was approved by the Local Ethics Committee (date 04.11.2024/protocol no: 259).

Author Contribution and Conflicts of Interest: The authors contributed equally to the study and have no conflicts of interest to declare.

REFERENCES

1. Kim M., et al. Reference ranges for induced sputum eosinophil counts in Korean adult population. Asia Pacific Allergy 2014;4(3): 149- 155.
2. Kim, Mi-Yeong; Jo, Eun-Jung; Lee, Seung-Eun; Lee, Suh-Young, Song, Woo-Jung, et al. Reference ranges for induced sputum eosinophil counts in Korean adult population. Asia Pacific Allergy 4(3):p 149-155, July 2014. DOI: 10.5415/apallergy.2014.4.3.149.
3. Yeon Joo Jeong, MD. Eosinophilic lung diseases: A clinical, radiologic, and pathologic review. RadioGraphics 2007; 27:617–639.
4. Hargreave FE, et al. Induced sputum and response to glucocorticoids. Journal of Allergy and Clinical Immunology 1998; 102(5): S102-S105.
5. Gurcay N., et al. The role and importance of transbronchial biopsy in the diagnosis of eosinophilic lung diseases. J Curr Pathol. 2019;3:154-156. doi: 10.5146/jcpath.2019.61.
6. Su J. A Brief History of Charcot-Leyden Crystal Protein/Galectin-10 Research. Molecules. 2018;23(11):2931. doi: 10.3390/molecules23112931. PMID: 30424011; PMCID: PMC6278384.
7. Thomsen GN, et al. The multidisciplinary approach to eosinophilia. Front. Oncol., 18 May 2023, Sec.Hematologic Malignancies, Volume 13-2023.
8. Yi F, Fang Z, Liang H, Huang L, Jiang M, Feng Z, et al. Diagnostic accuracy of blood eosinophils in comparison to other common biomarkers for identifying sputum eosinophilia in patients with chronic cough. World Allergy Organ J. 2023 Sep 28;16(9):100819. doi: 10.1016/j.waojou.2023.100819. PMID: 37811398; PMCID: PMC10558844.
9. Barcellos VA.,et al. Asthma control and sputum eosinophils in adult patients: a cross-sectional study in southern Brazil. Scientifc Reports 2023:13;21464.

10. Yılmaz SF, Erdal S, Bakıcı Z, et al. Investigation of the normal values of some haematological parameters of the adults living in the central region of Sivas. Erciyes Med J. 2003;25:1-10.
11. Hussain M, Liu G. Eosinophilic Asthma: Pathophysiology and Therapeutic Horizons. Cells. 2024 Feb 23;13(5):384. doi: 10.3390/cells13050384. PMID: 38474348; PMCID: PMC10931088
12. Fang Yi, Zhangfu Fang, Hanwen Liang, Lianrong Huang, Mei Jiang, Zien Feng, et al. "Diagnostic accuracy of blood eosinophils in comparison to other common biomarkers for identifying sputum eosinophilia in patients with chronic cough", World Allergy Organization Journal, 2023.
13. Soter S., et al. Predicting Sputum Eosinophilia in Exacerbations of COPD Using Exhaled Nitric Oxide. Inflammation 2013;36(5).

Research Article (Araştırma Makalesi)

Evaluation of the Relationship between Morphological Measurements of the Knee and Anterior Cruciate Ligament Injuries, along with Meniscus Injuries

Diz Morfolojik Ölçümleri ile Ön Çapraz Bağ Yaralanmaları ve Menisküs Yaralanmaları Arasındaki İlişkinin Değerlendirilmesi

Begüm INCEDEMIR UNDEY[1], Ayfer METIN TELLIOGLU[1], Elif AYDIN[2], Yasemin DURUM POLAT[3]

[1] Aydın Adnan Menderes University, Faculty of Medicine, Department of Anatomy, Aydın, Türkiye
[2] Adnan Menderes University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Aydın, Türkiye
[3]Aydın Adnan Menderes University, Faculty of Medicine, Department of Radiology, Aydın, Türkiye

Özet

Amaç: Bu çalışma, izole lig. cruciatum anterius yaralanmalı olgular, lig. cruciatum anterius ve menisküs yaralanmasının birlikte olduğu olgular ve sağlıklı bireylerde diz ekleminin kemik yapılarındaki morfolojik ölçümleri ve yapısal farklılıkları karşılaştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Çalışmada, lig. cruciatum anterius yaralanması tanısı almış 200 bireyin ve 110 sağlıklı olgunun manyetik rezonans görüntüleri değerlendirilmiştir. Görüntüler menisküs yaralanması açısından da değerlendirilmiş ve bireyler, lig. cruciatum anterius'un izole ve menisküs ile birlikte yaralandığı iki gruba ayrılmıştır. Lig. cruciatum anterius ve menisküs yaralanması için risk faktörü olduğu düşünülen kemik yapı ölçümleri değerlendirilmiş ve bu ölçümler çalışma grupları ile kontrol grubu arasında istatistiksel olarak karşılaştırılmıştır.

Bulgular: Çalışmada, lig. cruciatum anterius'un izole ve menisküs ile birlikte yaralandığı gruplarda; condylus medialis genişliği, condylus lateralis genişliği, bikondiler genişlik, eminentia intercondylaris genişliği, tibia genişliği, patella uzunluğu, ligamentum patellae uzunluğu, patella facies articularis ve sulcus trochlearis açıları anlamlı olarak daha fazla bulunmuştur. Bununla birlikte; fossa intercondylaris şekil indeksi, fossa intercondylaris indeksi, tibial medial eğim, sulcus trochlearis derinliği, trochlear faset asimetrisi, sulcus trochlearis-tuberositas tibia mesafesi ve patellar tilt değerleri bu gruplarda anlamlı olarak daha düşük tespit edilmiştir.

Sonuç: Diz eklemine ait morfometrik ölçümleri klinik uygulamalarda değerlendirmenin, hastanın lig. cruciatum anterius ve menisküs yaralanma riskinin belirlenmesine katkı sağlayacağını düşünmekteyiz

Anahtar Kelimeler: Diz Eklemi, Diz Yaralanmaları, Ligamentum Cruciatum Anterius Yaralanmaları, Menisküs, Manyetik Rezonans Görüntüleme

Abstract

Objective: This study aims to compare the morphological measurements and structural differences in the bony structures of the knee joint among cases with isolated anterior cruciate ligament (ACL) injury, cases with both ACL and meniscus injury, and healthy individuals.

Material and Methods: In our study, knee magnetic resonance imaging records of 200 individuals diagnosed with a ligamentum cruciatum anterius injury and 110 individuals reported as having a normal knee (a total of 310 individuals) were analyzed. The images were also examined in terms of meniscus injury; they were divided into two groups: isolated ligamentum cruciatum anterius injury and combined injury groups involving the anterior cruciate ligament and meniscus. Measurements of bone structures that were presumed to be risk factors for ligamentum cruciatum anterius and meniscus injury were evaluated. These measurements were compared statistically between the two study groups with the control group.

Results: In our study, condylus medialis width, condylus lateralis width, bicondylae width, eminentia intercondylaris width, tibia width, patellar length, ligamentum patellae length, patella facies articularis angle, and sulcus trochlearis angle values were significantly higher in both isolated ligamentum cruciatum anterius injuries and combined injury of ligamentum cruciatum anterius and meniscus. Furthermore, the fossa intercondylaris shape index, the fossa intercondylaris index, the tibial medial slope, the sulcus trochlearis depth, the trochlear facet asymmetry, the sulcus trochlearis and tuberositas tibia distance, and the patellar tilt values were significantly lower in both isolated ligamentum cruciatum anterius injuries and combined injury of ligamentum cruciatum anterius and meniscus.

Conclusion: We think that by evaluating these measurements in daily clinical practice, it can be determined whether the patient is at risk for ligamentum cruciatum anterius and meniscus injuries.

Keywords: Knee Joint, Knee Injuries, Anterior Cruciate Ligament Injuries, Meniscus, Magnetic Resonance Imaging

Correspondence: Ayfer METIN TELLIOGLU, Aydın Adnan Menderes University, Faculty of Medicine, Department of Anatomy, Aydın, Türkiye

Phone: +90 505 229 15 35 **e-mail:** ayfer.tellioglu@adu.edu.tr

ORCID No (Respectively): 0000-0002-2018-9184, 0000-0002-3720-1936, 0000-0002-1874-955X, 00000-0002-4452-6632

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INTRODUCTION

The knee joint is the largest in the body. In addition to flexion-extension movement, it also allows rotational movements, albeit to a small extent. The ligamentum cruciatum anterius (anterior cruciate ligament = ACL) extends from the inner surface of the condylus lateralis of the femur to the area intercondylaris, a structure that belongs to the tibia. This ligament also runs diagonally from posterior lateral to anterior medial (1).

Menisci, which are mostly composed of fibrous cartilage, serve to reduce the inconsistency between the articular surfaces in the knee joint. The meniscus medialis (MM) is more oval and C-shaped when viewed from above, while the slightly smaller meniscus lateralis (ML) is more rounded (2).

Anterior cruciate ligament injuries are one of the most common injuries of the knee region; therefore, they are of high clinical and surgical importance. Although anterior cruciate ligament injuries are mostly related to trauma, anatomical differences between individuals may make some individuals more vulnerable to anterior cruciate ligament injuries. MM is more prone to injury because it is more strongly fixed and heterogeneous in shape. Lesions of the MM, anterior cruciate ligament, and the collateral tibial ligament, called the unhappy triad, often appear together in different combinations (3).

Anatomical studies investigating the relationship between anterior cruciate ligament injuries and bone morphology have focused more on the intercondylar fossa (intercondylar notch), femoral condyles, and tibial plateau, and the link between a narrow intercondylar fossa and ACL injury has been clearly demonstrated. In recent years, femoral trochlear dysplasia (TD) has been frequently investigated as a potential risk factor for ACL injuries. TD is a condition in which the distal femur loses its normal concave shape, and the patella cannot adapt to the convex articular surface. There are also studies reporting that TD causes an increase in ACL load (3).

Studies in which tibial, femoral, and patellar variation and morphological changes are handled separately and associated with ACL injuries are available in the literature. However, there is no in-depth study in which all bone structures involved in the joint are considered holistically, and variations in different structures are associated with each other, ACL and meniscus injuries. In our study, we aim to reveal the morphological measurements and variations in the bone structures involved in the knee joint in a comparative way in the group with ACL injury, the group with combined ACL and meniscus injury, and the control group.

MATERIALS AND METHODS

Our study includes 200 patients who were referred to Aydın Adnan Menderes University Radiology Department for knee magnetic resonance ımaging (MRI) between 1 June 2015 and 1 June 2021 and were diagnosed with ACL injuries according to MRI reports, and 110 patients reported as normal knee MRI (a total of 310 patients). The records were reviewed through our hospital PACS (Picture Archiving and Communication Systems) Sectra Workstation IDS7 Version 23.2.2.5087 2021. Before the study, the approval of the Non-Interventional Clinical Research Ethics Committee dated 17.09.2021 and numbered E-53043469-050.04.04.-76301 was obtained.

The subjects to be included in the study have completed bone development between the ages of 18-60 and have no congenital, traumatic (except anterior cruciate ligament and meniscus injuries) or inflammatory knee diseases, no bone fractures, dislocation or space-occupying lesions in the bones or other tissues joining the knee joint, no signs of osteoarthritis, and no evidence of previous surgery in the knee region. In addition, images with problems, such as the presence of artifacts in the regions where the measurement is planned, were also excluded from the study.

The images were divided into two groups according to the presence or absence of accompanying meniscal injury. In addition, images interpreted as normal MRI of the knee, which will be included in the Control Group, were also taken from the archive.

The gender of the subjects, the age at the time of imaging, and the type of knee injury were recorded. Length measurements were recorded in millimeters, and angle measurements were recorded in degrees.

Radiological Evaluation and Measurements

In the evaluation of images, axial, coronal, and sagittal sections of magnetic resonance (MR) images taken in the extension position were examined. T1 and T2 sequences were analyzed together to evaluate the ACL, menisci, and bony structures in and around the knee joint. All measurements were obtained by a radiologist with 12 years of experience.

Measurements Used to Evaluate Patella Morphology

Patellar length (PL) and patellar ligament length (PLL) were also measured on the longest axis of the patella in the sagittal section; the Insall Salvati Index (ISI), which is the PLL/PL value, was also obtained (4). Patellar width (PW) and Patellar facies articularis (facet)

angle (Wiberg angle) (WA) were measured in the axial section where the patella is widest (5) **(Figure 1)**.

Measurements Used to Evaluate Femur Morphology

Measurements of medial condyl width (MCW), lateral condyl width (LCW), bicondylar width (BW), and intercondylar notch width (NW) were obtained in the coronal section. The intercondylar notch index (NI) is obtained by dividing NW by BW (6). Intercondylar notch depth (ND) and intercondylar notch angle (NA) were measured as in the coronal section. Intercondylar notch shape index (NSI) was obtained by dividing NW by ND (7). Sulcus trochlearis depth (STD) was measured in the axial section, and Trochlear facet asymmetry (TFA) was calculated (8,9), **(Figure 2)**.

Intercondylar notch morphological classification (NMC): It was made by morphologically separating the intercondylary fossa into three types. Type A: narrow fossa intercondylaris; Type U: wide fossa intercondylaris; wide and Type W: double apex fossa intercondylaris (10) **(Figure 3)**.

Measurements Used to Evaluate Tibia Morphology

Tibia width (TW) and eminentia interconylaris width (EIW) were measured in the coronal section (Figure 4). Eminentia intercondylaris width index (EWI) was calculated by dividing EIW by TW (11), Medial tibial slope (MTS), Lateral tibial slope (LTS), and Medial tibial depth (MTD) were measured in the midsagittal section (6) **(Figure 4)**.

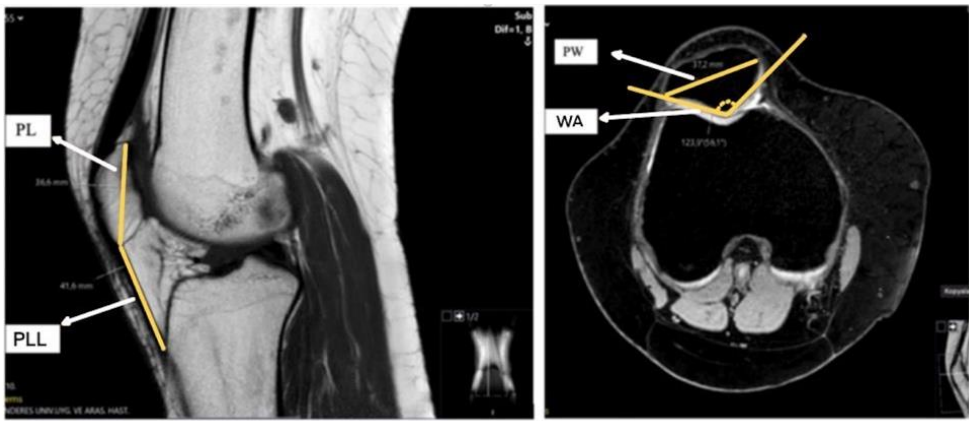

Figure 1. A: PL, PLL, and ISI measurement in the sagittal section of the right knee **B:** PW value and WA measurements of the patella in the axial section of the right knee

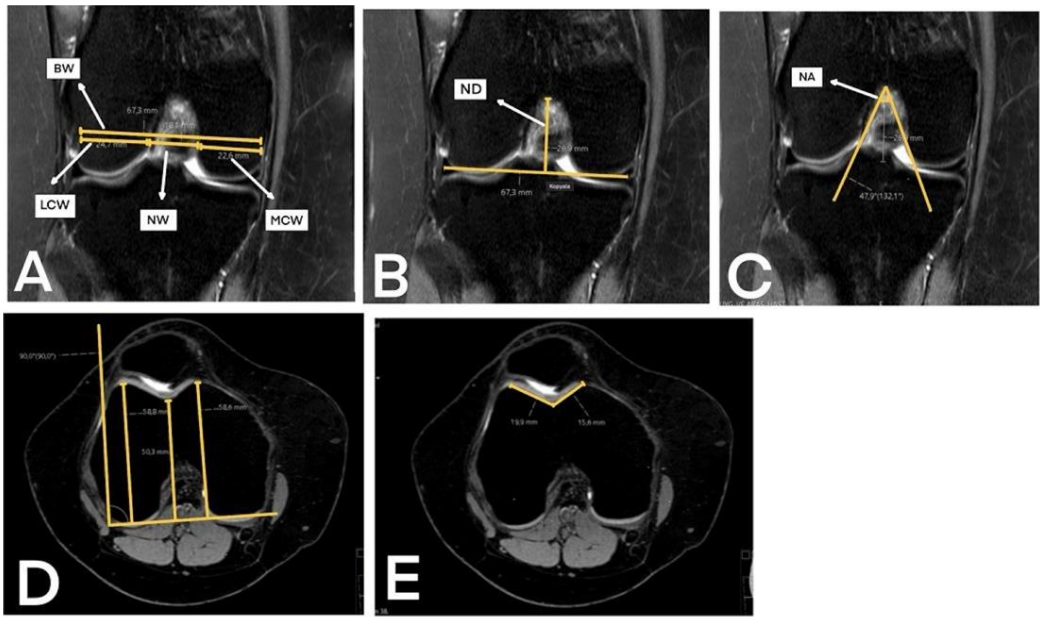

Figure 2. A: MCW, LCW, BW, NW measurements in the coronal section of the right knee **B:** ND in the coronal section of the right knee **C:** NA measurement in the coronal section of the right knee **D:** STD measurement in the axial section of the right knee **E:** TFA measurement in the axial section of the right knee

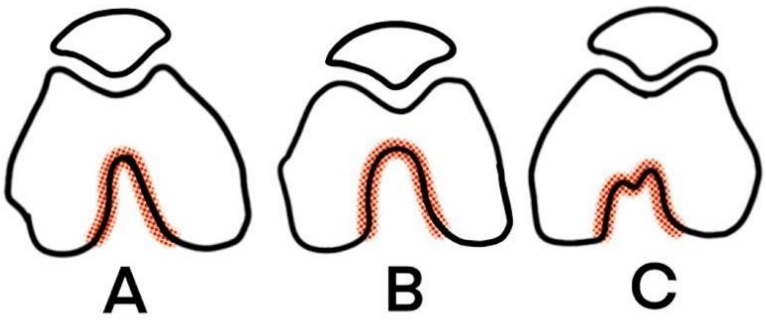

Figure 3. NMC. A-type fossa intercondylaris **(A)** (right knee), U-type fossa intercondylaris **(B)** (left knee), W-type intercondylaris **(C)**

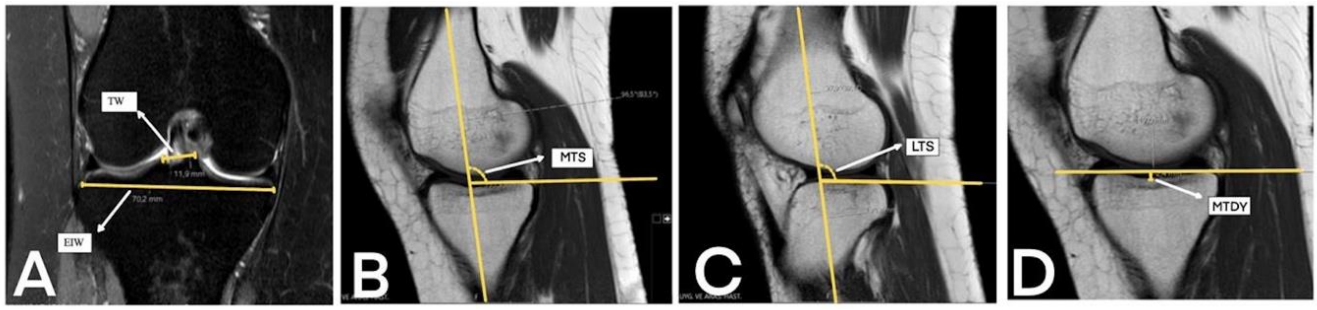

Figure 4. A: Measurement of EWI in the coronal section of the right knee **B:** Measurement of the MTS in the sagittal section of the right knee **C:** Measurement of the LTS in the sagittal section of the right knee **D:** MTD in the right knee

Measurements Used to Evaluate Patellofemoral Concordance

Tibial tuberosity and trochlear groove (sulcus trochlearis) distance (TT-TG) is measured in the 2 axial sections and calculated (5) Patellar tilt (PT), Lateral patellofemoral angle (LPFA), and Sulcus trochlearis angle (STA) were measured in the axial section (5). Congruence Angle (CA) was measured as the angle between the line dividing the sulcus trochlearis angle obtained in the axial section and the line extending from the deepest point of the sulcus trochlearis to the point of the articular surface of the patella that is closest to the femur (12) **(Figure 5)**.

Statistical Analysis

Research data were evaluated using SPSS 21.0 statistical program. Conformity of continuous variables to the normal distribution was investigated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). For the descriptive statistics of the study, the mean and standard deviation in data with normal distribution, median, minimum and maximum in data that do not fit normal distribution are shown. Chi-square test was used to show whether there is a difference between categorical variables in the study. Student-t Test or One Way ANOVA was used to compare continuous variables with parametric properties in independent groups, and Mann-Whitney U Test or Kruskal-Wallis Analysis of Variance was used to compare continuous variables with non-parametric properties in independent groups. ROC Analysis was used to show whether a variable recorded by numerical measurement was diagnostic or exclusionary. For statistical significance, the p-value was determined to be less than 0.05.

RESULTS

A total of 310 cases were included in the study, 110 of which were in the control group and 200 in the study group (cases with ACL injury). Out of 200 cases in the study group, 78 with isolated ACL injury and 122 with ACL and meniscal injury, and were divided into two separate study groups.

When the demographic characteristics of the cases were examined, 58.18% of the cases in the control group were female, 41.82% were male; 46.15% of the cases in the isolated ACL injury group were female, 53.85% were male, and combined ACL and meniscus injury. It was determined that 46.72% of the cases in the group were female and 53.28% were male. In addition, the median age of the cases was 31.00 (18.00-54.00) in

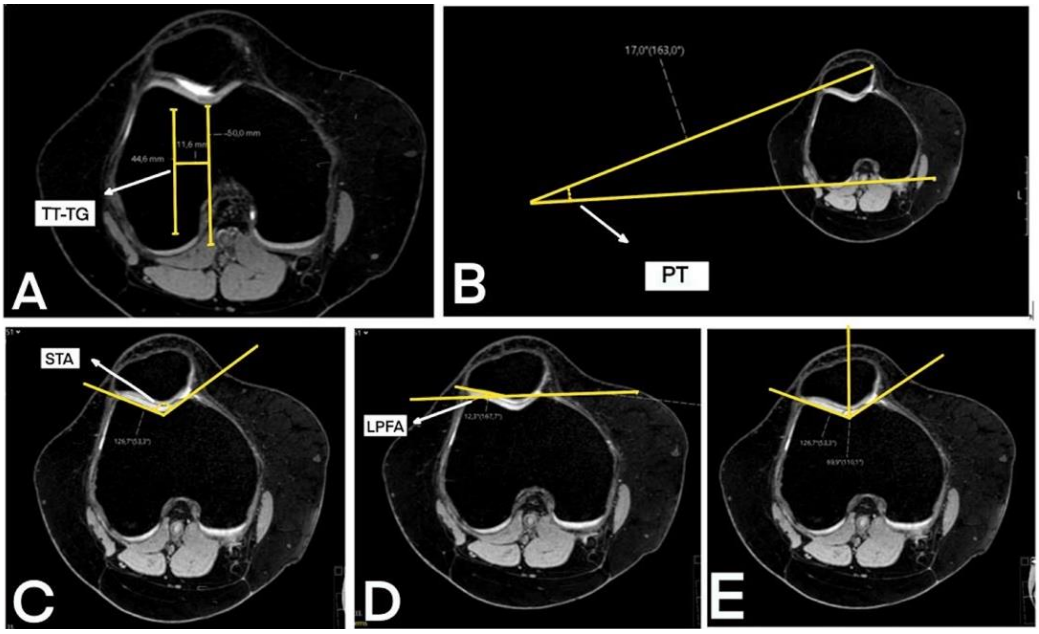

Figure 5. A: Measurement of TT-TG in the axial section of the right knee. **B:** PT measurement in the axial section of the right knee. **C:** Measurement of the STA in the axial section of the right knee **D:** LPFA measurement in the axial section of the right knee **E:** CA measurement in the axial section of the right knee

the control group, 38.00 (18.00-57.00) in the isolated ACL injury group, and 40.00 (18.00-57.00) in the ACL and meniscus combined injury group. When we examined the MRIs in our study, no statistically significant difference was found between the groups with fossa intercondylaris morphological classification.

In **Table 1**, the measurement values of the anatomical structures related to the knee joint were compared between the control group and the isolated ACL injury groups.

In **Table 2**, the measurement values of the anatomical structures related to the knee joint were compared between the control group and the ACL and meniscus combined injury groups.

When the measurement values of the anatomical structures related to the knee joint were evaluated by ROC analysis between the control and isolated ACL injury groups. Details are shown in **Table 3**.

When the measurement values of the anatomical structures related to the knee joint were evaluated by ROC analysis between the control and ACL and meniscus combined injury groups. Details can be seen in **Table 4**.

DISCUSSION

There are many studies investigating predisposing factors for ACL and meniscal injuries. Some of the factors are morphological factors in knee anatomy. Many morphological characteristics of bone structure have been associated with increased ACL injuries such as intercondylar notch stenosis, low intercondylar notch index, tibia eminentia stenosis (13,14).

Distal femur is an anatomical region that is frequently investigated in relation to ACL injuries due to its role in load transfer in the knee joint. In the study conducted by Kızılgöz et al., while the MCWvalue measured in the coronal plane was found to be associated with ACL injuries, they did not find a statistically significant relationship with CLW and BW values (6). Park *et al.* found the MCW value to be associated with ACL injury (15). In light of the data in our study, we think that the high MCW value may play a role as a predisposing factor for all isolated ACL and accompanying meniscal injuries.

Many measurements, such as NW, ND, NA, and NSI, have been reported in the literature in close association with ACL injuries (16-19). In a study, it was stated that the structure of the fossa intercondylaris (intercondylar notch) is the most important anatomical factor related to ACL injuries (16). Cha *et al.* combined arthroscopy and MRI in their study and showed that mucoid hypertrophy occurs due to compression of the ACL fibers during movement in people with a narrow intercondylar fossa, and therefore suggested that the narrow fossa plays a role as a predisposing factor in ACL injuries (17). In addition, Li *et al.* classified the NI and NSI values as risk factors for MM and ML injuries (19). In our study, no significant difference was found between

Table 1. Comparison of the measurement values of the anatomical structures of the knee joint between the control group and isolated ACL injury groups

	Groups		p
	Control Group (N=110)	Isolated ACL injury group (N=78)	
Medial Condyl width (MCW)	24,03 ± 2,25	25,82 ± 2,88	**0,000**
Lateral Condyl width (LCW)	25,50 (21,00-30,20)	26,20 (18,70-36,40)	**0,013**
Bicondylar width (BW)	69,10 (59,30-84,30)	73,10 (59,50-87,30)	**0,009**
Intercondylar notch width (NW)	18,87 ± 2,89	18,56±3,24	0,494
Intercondylar notch depth (ND)	23,60 ± 2,35	24,19 ± 2,47	0,102
Intercondylar notch angle (NA)	57,05 (38,70-79,00)	56,70 (41,30-73,90)	0,330
Intercondylar notch shape index (NSI)	0,80 ± 0,12	0,77 ± 0,11	**0,037**
Intercondylar notch index (NI)	0,27 ± 0,03	0,25 ± 0,004	**0,008**
Eminentia intercondylaris width (EIW)	12,60 (8,20-21,40)	13,50 (9,10-18,40)	**0,007**
Tibia width (TW)	71,00 (60,00-84,30)	74,75 (63,30-85,90)	**0,014**
Eminentia Intercondylaris width index (EWI)	0,18 (0,12-0,26)	0,18 (0,11-0,24)	0,168
Patellar length (PL)	40,53 ± 3,20	41,95 ± 3,81	**0,006**
Patellar ligament length(PLL)	43,76 ± 5,51	44,41 ± 5,59	0,425
Insall Salvati index (ISI)	1,08 ± 0,14	1,06 ± 0,14	0,346
Medial Tibial depth (MTD)	2,65 ± 0,87	2,73 ± 0,90	0,511
Medial tibial slope (MTS)	5,52 ± 2,56	5,34 ± 2,86	0,650
Lateral tibial slope (LTS)	5,59 ± 3,26	5,84 ± 3,11	0,592
Patella width (PW)	41,10 (34,10-53,40)	42,80 (28,50-50,60)	0,060
Patella facies articularis angle (WA)	126,60 (104,30-139,50)	129,45 (112,10-150,40)	**0,036**
Sulcus trochlearis angle (STA)	131,45 (115,40-144,30)	133,55 (122,60-162,40)	**0,011**
Sulcus trochlearis depth (STD)	7,39 ± 1,39	6,81 ± 1,54	**0,007**
Trochlear facet asymmetry (TFA)	0,79 (0,54-0,99)	0,75 (0,049-1,01)	**0,002**
Tibial tuberosity to trochlear groove distance (TT-TG)	9,60 (1,20-24,50)	8,10 (-7,70-19,00)	**0,023**
Patellar tilt (PT)	9,40 (1,80-34,90)	10,05 (1,80-28,20)	0,546
Lateral patellofemoral angle (LPFA)	9,92 ± 4,54	11,02 ± 4,94	0,117
Congruence angle(CA)	1,30 (-21,60-21,20)	-2,85 (-32,40-47,30)	0,711

Table 2. Comparison of the measurement values of the anatomical structures related to the knee joint between the control group and the ACL and meniscus combined injury groups

	Group		p
	Control Group (N=110)	**ACL and meniscus combined injury group (N=122)**	
MCW	23,65 (19,50-30,90)	25,80 (6,50-41,00)	**0,000**
LCW	25,72 ± 2,35	27,02 ± 3,52	**0,001**
BW	69,10 (59,30-84,30)	72,60 (59,70-89,90)	**0,003**
NW	18,87 ± 2,89	18,02 ± 3,30	**0,038**
ND	23,60 ± 2,35	24,09 ± 2,68	0,144
NA	57,14 ± 7,65	55,51 ± 8,25	0,121
NSI	0,80 ± 0,12	0,75 ± 0,12	**0,001**
NI	0,27 (0,19-0,35)	0,25 (0,13-0,36)	**0,000**
EIW	12,60 (8,20-21,40)	13,20 (9,10-19,10)	**0,044**
TW	71,00 (60,00-84,30)	73,80 (62,70-87,80)	**0,003**
EWI	0,18 (0,12-0,26)	0,18 (0,11-0,25)	0,384
PL	40,53 ± 3,20	41,79 ± 3,85	**0,007**
PLL	43,76 ± 5,51	45,53 ± 6,22	**0,023**
ISI	1,08 ± 0,14	1,10 ± 0,16	0,547
MTD	2,60 (0,70-5,40)	2,80 (0,80-22,00)	0,125
MTS	5,52 ± 2,56	4,64 ± 2,68	**0,011**
LTS	5,59 ± 3,26	6,04 ± 3,60	0,324
PW	41,10 (4,40-53,40)	43,05 (33,20-52,30)	**0,005**
WA	126,60 (104,30-139,50)	130,30 (106,60-157,40)	**0,000**
STA	131,45 (115,40-144,30)	134,05 (117,50-160,50)	**0,001**
STD	7,39 ± 1,39	6,82 ± 1,56	**0,003**
TFA	0,79 (0,54-0,99)	0,74 (0,39-1,72)	**0,000**
TT-TG	9,60 (1,20-24,50)	7,30 (-6,90-23,60)	**0,000**
PT	9,40 (1,80-34,90)	8,15 (1,20-24,40)	**0,016**
LPFA	9,92 ± 4,54	10,71 ± 5,14	0,216
CA	1,30 (-21,60-21,20)	1,95 (-31,40-38,70)	0,319

Table 3. Evaluation of the measurement values of the anatomical structures related to the knee joint between the control group and isolated ACL injury groups by ROC analysis

	AUC	AUC% %95 CI		p	Cut Point	Sensitivity	Specificity
		Lower Limit	Upper Limit				
MCW	0,687	0,611	0,763	**0,000**	24,45	0,692	0,591
LCW	0,606	0,524	0,688	**0,013**	26,05	0,590	0,582
BW	0,612	0,530	0,694	**0,009**	70,10	0,641	0,545
NI	0,599	0,516	0,681	**0,021**	0,2618	0,577	0,573
EIW	0,615	0,532	0,698	**0,007**	13,05	0,564	0,627
TW	0,606	0,524	0,687	**0,014**	74,05	0,564	0,600
PL	0,604	0,521	0,687	**0,015**	41,45	0,526	0,627
WA	0,590	0,508	0,672	**0,036**	128,25	0,577	0,555
STA	0,609	0,528	0,691	**0,011**	132,25	0,551	0,573
STD	0,613	0,530	0,696	**0,008**	7,35	0,628	0,564
TFA	0,636	0,554	0,718	**0,002**	0,7605	0,603	0,618
TT-TG	0,597	0,514	0,681	**0,023**	8,70	0,590	0,582

AUC, area under the curve CI, confidence interval

Table 4. Evaluation of the measurement values of the anatomical structures related to the knee joint between the control and ACL and meniscus combined injury groups by ROC analysis

	AUC	AUC %95 CI		p	Cut Point	Sensitivity	Specificity
		Lower Limit	Upper Limit				
MCW	0,708	0,642	0,773	**0,000**	24,85	0,631	0,627
LCW	0,597	0,524	0,669	**0,011**	26,10	0,566	0,582
BW	0,612	0,540	0,684	**0,003**	70,70	0,607	0,573
NW	0,575	0,501	0,648	**0,049**	18,35	0,557	0,555
NSI	0,610	0,538	0,682	**0,004**	0,7730	0,549	0,545
NI	0,648	0,578	0,719	**0,000**	0,2584	0,623	0,618
EIW	0,577	0,503	0,650	**0,044**	12,65	0,590	0,555
TW	0,612	0,540	0,685	**0,003**	72,35	0,598	0,573
PL	0,596	0,523	0,669	**0,012**	40,95	0,549	0,545
PLL	0,575	0,502	0,649	**0,047**	43,95	0,582	0,564
MTS	0,598	0,526	0,671	**0,010**	4,95	0,566	0,564
PW	0,607	0,534	0,679	**0,005**	41,85	0,582	0,582
PFAA	0,657	0,588	0,727	**0,000**	129,75	0,590	0,609
STA	0,624	0,552	0,695	**0,001**	132,50	0,623	0,582
STD	0,609	0,536	0,681	**0,004**	7,15	0,590	0,582
TFA	0,638	0,567	0,710	**0,000**	1,315	0,607	0,618
TT-TG	0,678	0,609	0,747	**0,000**	8,15	0,648	0,636
PT	0,591	0,518	0,664	**0,016**	9,15	0,574	0,564

AUC, area under the curve CI, confidence interval

the isolated ACL injury group and the control group in NW, ND, and NA measurements. However, NSI was found to be significantly lower in the isolated ACL injury group ($p<0.05$). When groups were compared, NW measurements were significantly lower in groups with ACL injury ($p<0.05$). According to the ROC analysis results for these measurements, Breakpoints were determined for NW, NI, and NSI measurements (Tables III, IV). In light of this information, while low NSI and NI values can be considered as a predisposing factor for ACL injuries, we think that low NW values, together with other factors, may pose a risk for meniscal injuries. These results of the morphological features of the fossa intercondylaris obtained in our study support the literature.

The morphological classification of the fossa intercondylaris (NMC) was made by evaluating the shape of the fossa intercondylaris in three types. There are studies in the literature concluding that type A fossa structure is a predisposing factor for ACL injury (18). At the same time, some studies do not find NMC differences statistically significant in terms of risk of ACL injury (19). In our study, there was no statistically significant difference in FIMS rates between the groups. The fact that the NMC is a visual scale and not based on an objective and metric value may have caused this classification to have a lower correlation between scientific studies compared to measurements such as NW, NSI, and NI.

It has been reported that patellofemoral kinematics, contact area, contact pressure and stability are significantly affected by trochlear dysplasia (TD,20). Işıklar et al. suggested that the strength of the extensor mechanism in knees with TD may cause ACL injuries by causing a change in the normal position of the patella (21). Some of the measurements used to define TD are; sulcus trochlearis angle (STA), sulcus trochlearis depth (STD) and trochlear facet asymmetry (TFA) in sulcus trochlearis. In many studies, higher values of STA are determined to be an indicator for TD (22). In our study, it was found to be 133.55° (min: 122.60°; max: 162.40) in the isolated ACL injury group and 134.05° (min: 117.50°; max: 160.50°) in the ACL and meniscus combined injury group. STA degrees were statistically significantly higher than the control group ($p<0.05$).

Pfirrmann et al. reported that in cases with suspected TD, the specificity and sensitivity of STD measurement are also high, as is the case with STA measurement (8). In our study, STD values were found to be statistically significantly lower in the isolated ACL injuries and ACL and meniscus combined injury group compared to the control group ($p=0.007$, $p=0.003$). In our study, the fact that the STD value was significantly lower in the groups with ACL injury compared to the control group, although it was not at the limit of trochlear hypoplasia and dysplasia in the groups with ACL injury, indicates the relationship between STD and ACL injuries.

The number of studies examining the relationship between TFA and ACL or meniscal injuries is very few. Kwak et al. found no statistically significant relationship between TFA and ACL injuries in their study (3). In the study by Chen et al., the rate of TFA was found to be statistically significantly lower in the group with ACL injury (23). In our study, we found the TFA value to be statistically significantly lower in the isolated ACL injuries group and in the ACL and meniscus combined injury group compared to the control group ($p=0.002$, $p=0.000$). Considering that lower values in TFA are associated with TD, the findings of our study support the close relationship between TD and ACL injuries. According to the results of the ROC analysis, since the area under the curve (AUC) value was above 0.6 in both groups, TFA measurement with a cutoff value of 76% can be recommended to clinicians for ACL risk assessment as a qualified clinical assessment tool.

Increased tibial inclination (slope) values can be considered as a predisposing factor in ACL injuries by causing an increase in anterior translation load during knee movements (14). When we look at the literature, it can be seen that many studies associate the increase in tibial medial inclination and tibial lateral inclination with ACL injuries (14,24). When we examined all the data in our study, we saw that the MTS and LTS values were distributed in a wide range. There was no statistically significant difference in the MTS value in the isolated ACL injury group compared to the control group. In the ACL and meniscus combined injury group, the MTS value was found to be significantly lower than in the control group ($p=0.011$). There was no statistically significant difference between the groups in LTS value. While high MTS and LTS values cause a biomechanical problem that may cause pathological conditions by increasing anterior translation, there is no data that low values within the normal range cause a pathology in knee joint biomechanics.

In a study conducted on cadavers, it was reported that there was a correlation between the ACL volume and the EIW value; however, female individuals were more prone to ACL injuries due to low EIW and thus low ACL volume (25). In our study, when the study groups were compared with the control group, it was observed that the EIW value was significantly higher in the groups with ACL injury ($p<0.05$). It was observed

that the EWI value was not significantly different between the groups.

There are not many studies in the literature examining the width of the coronal tibial plateau as a risk factor. Mısır et al. in their study found the relationship between TW and ACL injuries significant (26). In our study, we found that the TW value for the isolated ACL injury group and the ACL and meniscus combined injury group was statistically significantly higher than the control group (p=0.014, p=0.003). We think that it is possible to evaluate it as a risk factor. To support our theory, larger studies examining the relationship between ACL injuries and TW value are required.

Misir et al. suggested that the high MTD value can be used to interpret the risk of ACL injury independently of other values (26). In our study, we did not find a statistically significant difference in terms of MTD between groups.

There are studies in the literature that associate the size of the TT-TG distance with ACL injuries (27,28). In our study, no significant difference was found in the TT-TG distances of the isolated ACL injury group. However, when the ACL and meniscus combined injury group was compared with the control group, the TT-TG distance was found to be significantly lower in patients with ACL injuries for the whole group (p=0.000). In the ROC analysis, the limit value was calculated as 8.15.

The patella plays a key role in load transmission in knee joint biomechanics. In the case of patella alta or patella baja can result in deterioration in knee biomechanics (29). In our study, we used the ISI, which is reported to be the most reliable method to interpret patella location. When all MRIs in our study were examined, no statistically significant difference was observed in the ISI value when looking at the combinations between the groups with ACL injury and the control groups.

Although there are very few studies in the literature that associate PL, PLL and PW values with ACL and meniscal injuries, Akgün et al. in their study, while they found the high ISI and PLL values to be statistically significant as a risk factor in ACL injuries, they reported that they could not find a statistically significant difference in the PL value (30) Vasconcelos et al. stated in their study that the PL value was significantly lower in cases with ACL injury (31). In our study, PL values in the isolated ACL injury group and ACL and meniscus combined injury group were statistically significantly higher than the control group (p=0.006, p=0.007). When the PLL values were examined in our study, in the ACL and meniscus combined injury group, it was found to be statistically significantly higher than the control group (p=0.023). When the PW values in our study were examined, there was no significant difference between the isolated ACL injuries group and the control group; PW value was found to be statistically significantly higher in the ACL and meniscus combined injury group than in the control group (p=0.005). The high PLL value only in the group accompanied by a meniscus showed that this value can be associated with meniscus injuries.

Other parameters used to evaluate patellar instability can be listed as the patellar facies articularis angle (Wiberg angle) (WA), patellar tilt (PT), lateral patellofemoral angle (LPFA), and congruence angle (CA). Vasconcelos et al. reported that they found CA values to be statistically significantly higher in the group with ACL injury in their study on X-ray images (31). There was no statistically significant difference between the groups in CA measurements in our study. In the study from Vasconcelos *et al.*, LPFA value was found to be statistically significantly lower in the group with ACL injury (31). There was no statistically significant difference between the groups in LPFA measurements in our study. Again, in the study of Vasconcelos et al., PT was evaluated, and it was found to be significantly lower in cases with ACL injury (31). In our study, there was no statistically significant difference between the group with isolated ACL injury and the control group in the evaluation made over the measured PE values, while PT in the group with ACL and meniscus combined injury group was found to be significantly lower than the control group (p=0.016). In light of this information, the low PT values in our study support the literature. Since the low PT value in groups accompanied by meniscal injury is a finding that has not been investigated before, it should be supported by larger studies.

Patellar facies articularis angle, or Wiberg angle (WA) is also a test used to evaluate patellar instability. WA measurement has not been previously investigated as a predisposing factor for ACL or meniscal injuries. In our study, the WA with isolated ACL injury was found to be statistically significantly higher (p=0.036). WA was also found to be significantly higher in the case group compared to the control group (p=0.000). In the ROC analysis, the threshold value was found to be 128.25° for isolated ACL injuries (p=0.036), while the threshold value was found to be 129.75° for combined ACL and meniscus injuries (p<0.001). Because it provides patellofemoral harmony in terms of anatomical relationship, sulcus trochlearis and patellar facies articularis structures show key-lock harmony as the opposite faces of the joint. WA measurement is evaluated by

many researchers in the literature in terms of ACL and meniscus injuries, and while its increase is associated with an increased risk of ACL injury, There is no data we found other than our current study regarding the relationship of WA value with ACL and meniscus injuries. In our study, we planned to reveal the risk factors that can be associated with ACL and meniscus injury.

The limitations of our study; that it is retrospective, the body mass index and height information of the individuals cannot be obtained, the dominant extremity of the individuals is unknown, the subclassification of meniscus injuries cannot be made, and the measurements are made by a single physician. Measured in our study, MCW, LCW, BW, EIW, TW, PL, PLL, WA, STA values were found to be statistically significantly different in both isolated ACL injury and ACL and meniscus combined injury groups. Again evaluated in our study, NSI, NI, MTS, STD, TFA, TT-TG, and PT values were found to be statistically significantly different in both isolated ACL injury and ACL and meniscus combined injury groups.

Conclusively, based on our findings, we think that it is possible that the high MTD value can be considered a risk factor for ACL injuries. To support our hypothesis, larger studies examining the relationship between ACL injuries and MTD value are required. To explain more clearly the relationship between the incidence of ACL and meniscus combined injuries, which we showed in our study, and the increase in WA and the PLL, and the decrease in the TT-TG distance and the PT, in the coming years; Large-scale case-control and knee biomechanics studies are needed to examine the risk formation mechanism between ACL and meniscal injuries and these measurements.

We think that by examining these findings in daily clinical practice, individuals can be evaluated to determine whether they are at risk for ACL and meniscus injuries.

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REFERENCES

1. Arıncı K, Elhan A. Anatomi. Vol 1. 6th ed. Güneş Tıp Kitabevleri; Ankara. 2014.
2. Washke J, Böckers TM, Paulsen F. Sobotta Anatomi Konu Anlatımı. In: Mustafa Fevzi Sargon (ed.). Elsevier GmbH; Ankara. 2016.
3. Hae Kwak Y, Nam JH, Koh YG, Park BK, Hong KB, Kang KT. Femoral trochlear morphology is associated with anterior cruciate ligament injury in skeletally immature patients. Knee Surgery, Sports Traumatology, Arthroscopy. 2020;28:3969-3977. doi:10.1007/s00167-020-06267-z
4. Leiprecht J, Mauch F, Huth J, Ambros LP, Best R. Weight-bearing MRI with a knee flexion angle of 20°: a study on additional MRI investigation modalities to support a more accurate understanding of patellofemoral instability. BMC Musculoskelet Disord. 2021;22(1). doi:10.1186/S12891-021-04733-4
5. Sebro R, Weintraub S. Knee morphometric and alignment measurements with MR imaging in young adults with central cartilage lesions of the patella and trochlea. Diagn Interv Imaging. 2017;98(5):429-440. doi:10.107/S00167-4052-Y
6. Kızılgöz V, Sivrioğlu AK, Ulusoy GR, Aydın H, Karayol SS, Menderes U. Analysis of the risk factors for anterior cruciate ligament injury: an investigation of structural tendencies. Clin Imaging. 2018;50:20-30. doi:10.1016/j.clinimag.2017.12.004
7. Stein V, Li L, Guermazi A, et al. The relation of femoral notch stenosis to ACL tears in persons with knee osteoarthritis. Osteoarthritis Cartilage. 2010;18(2):192-199. doi:10.1016/j.joca.2009.09.006
8. Pfirrmann CWA, Zanetti M, Romero J, Hodler J. Femoral trochlear dysplasia: MR findings. Radiology. 2000;216(3):858-864. doi:10.1148/RADIOLOGY.216.3.R00SE38858
9. Choi W, Lee SJ, Oh J, et al. Diagnostics Magnetic Resonance Imaging of Patellofemoral Morphometry Reveals Age and Gender Variations in the Knees of Children and Adolescents. Diagnostics. 2021;11(11):1985. doi:10.3390/diagnostics11111985
10. Chen C, Ma Y, Geng B, et al. Intercondylar Notch Stenosis of Knee Osteoarthritis and Relationship between Stenosis and Osteoarthritis Complicated with Anterior Cruciate Ligament Injury. Medicine (United States). 2016;95(17). doi:10.1097/MD.0000000000003439
11. Uhorchak JM, Scoville CR, Williams GN, Arciero RA, St Pierre P, Taylor DC. Risk Factors Associated with Noncontact Injury of the Anterior Cruciate Ligament A Prospective Four-Year Evaluation of 859 West Point Cadets, The American Journal of Sports Medicine. 2003;31(6):831-842. doi:10.1177/03635465030310061801
12. Dai Y, Yin H, Xu C, Zhang H, Guo A, Diao N. Association of patellofemoral morphology and alignment with the radiographic severity of patellofemoral osteoarthritis. Journal of orthopaedic surgery and research. 2021;16(1):548. doi:10.1186/s13018-021-02681-2
13. Rahnemai-Azar AA, Abebe ES, Johnson P, et al. Increased lateral tibial slope predicts high-grade rotatory knee laxity pre-operatively in ACL reconstruction. Knee Surg Sports Traumatol Arthrosc. 2017;25(4):1170-1176. doi:10.1007/S00167-016-4157-3
14. Suprasanna K, Chamala T, Kumar A. Comparison of anatomical risk factors for noncontact anterior cruciate ligament injury using magnetic resonance imaging. J Clin Orthop Trauma. 2019;10(1):143-148. doi:10.1016/J.JCOT.2017.08.002
15. Park JS, Nam DC, Kim DH, Kim HK, Hwang SC. Measurement of Knee Morphometrics Using MRI: A Comparative Study between ACL-Injured and Non-Injured Knees. Knee Surg Relat Res. 2012;24(3):180-185. doi:10.5792/KSRR.2012.24.3.180

16. Stijak L, Nikolić V, Blagojević Z, et al. [Influence of morphometric intercondylar notch parameters in ACL ruptures]. Acta Chir Iugosl. 2006;53(4):79-83. doi:10.2298/ACI0604079S
17. Cha JH, Lee SH, Shin MJ, Choi BK, Bin S Il. Relationship between mucoid hypertrophy of the anterior cruciate ligament (ACL) and morphologic change of the intercondylar notch: MRI and arthroscopy correlation. Skeletal Radiol. 2008;37(9):821-826. doi:10.1007/S00256-008-0527-3
18. Fahim SM, Dhawan T, Jagadeesh N, Ashwathnarayan YP. The relationship of anterior cruciate ligament injuries with MRI based calculation of femoral notch width, notch width index, notch shape - A randomized control study. J Clin Orthop Trauma. 2021;17:5-10. doi:10.1016/J.JCOT.2021.01.006
19. Li W, Liang J, Zeng F, et al. Anatomic characteristics of the knee influence the risk of suffering an isolated meniscal injury and the risk factors differ between women and men. Sports Traumatology, Arthroscopy. 2021;29:3751-3762. doi:10.1007/s00167-020-06396-5
20. Ireland ML, Ballantyne BT, Little K, McClay IS. A radiographic analysis of the relationship between the size and shape of the intercondylar notch and anterior cruciate ligament injury. Knee Surg Sports Traumatol Arthrosc. 2001;9(4):200-205. doi:10.1007/S001670100197
21. Isıklar S, Ozdemir ST, Gokalp G. An association between femoral trochlear morphology and non-contact anterior cruciate ligament total rupture: a retrospective MRI study. Skeletal radiology, 2021;50(7):1441–1454. doi:10.1007/s00256-020-03706-3/Published
22. Duran S, Cavusoglu M, Kocadal O, Sakman B. Association between trochlear morphology and chondromalacia patella: an MRI study. Clin Imaging. 2017;41:7-10. doi:10.1016/J.CLINIMAG.2016.09.008
23. Chen M, Qin L, Li M, Shen J. Correlation analysis between femoral trochlear dysplasia and anterior cruciate ligament injury based on CT measurement. Quant Imaging Med Surg. 2020;10(4). doi:10.21037/qims.2020.03.15
24. Imhoff FB, Comer B, Obopilwe E, Beitzel K, Arciero RA, Mehl JT. Effect of Slope and Varus Correction High Tibial Osteotomy in the ACL-Deficient and ACL-Reconstructed Knee on Kinematics and ACL Graft Force: A Biomechanical Analysis. Am J Sports Med. 2021;49(2):410-416. doi:10.1177/0363546520976147
25. Chandrashekar N, Slauterbeck J, Hashemi J. Sex-based differences in the anthropometric characteristics of the anterior cruciate ligament and its relation to intercondylar notch geometry: a cadaveric study. Am J Sports Med. 2005;33(10):1492-1498. doi:10.1177/0363546504274149
26. Misir A, Sayer G, Uzun E, Guney B, Guney A. Individual and Combined Anatomic Risk Factors for the Development of an Anterior Cruciate Ligament Rupture in Men A Multiple Factor Analysis Case-Control Study. The American journal of sports medicine. 2022;50(2), 433–440. doi:10.1177/03635465211062594
27. Shen X, Xiao J, Yang Y, et al. Multivariable analysis of anatomic risk factors for anterior cruciate ligament injury in active individuals. 2019;139:1277-1285. doi:10.1007/s00402-019-03210-x
28. Polat AE, Polat B, Gürpınar T, Sarı E, Çarkçı E, Erler K. Tibial tubercle-trochlear groove (TT-TG) distance is a reliable measurement of increased rotational laxity in the knee with an anterior cruciate ligament injury. Knee. 2020;27(5):1601-1607. doi:10.1016/J.KNEE.2020.08.014
29. Biedert RM, Tscholl PM. Patella Alta: A Comprehensive Review of Current Knowledge. Am J Orthop (Belle Mead NJ). 2017;46(6):290-300. Accessed May 4, 2022. https://pubmed.ncbi.nlm.nih.gov/29309446/
30. Akgün AS, Agirman M. Associations between Anterior Cruciate Ligament Injuries and Patella Alta and Trochlear Dysplasia in Adults Using Magnetic Resonance Imaging. The journal of knee surgery 2021;34(11):1220-1226. doi:10.1055/S-0040-1702198
31. Vasconcelos DP de, Mozella A de P, Filho PGT de S, Oliveira GC, Cobra HA de AB. Femoropatellar radiographic alterations in cases of anterior cruciate ligament failure. Revista brasileira de ortopedia (Sao Paulo). 2015;50(1):43-49. doi:10.1016/J.RBOE.2015.01.005

Research Article (Araştırma Makalesi)

Emesis Gravidarum Prevalence in Pregnant Women in Rize Region

Rize Bölgesindeki Gebelerde Emesis Gravidarum Prevalansı

Mehmet KAGITCI[1], Senol SENTURK[1], Deniz DERECI DELIBAS[1], Nalan KURUCA[1], Mehmet KIVRAK[2]

[1] Recep Tayyip Erdogan University, Faculty of Medicine, Department of Obstetrics and Gynecology, Rize, Turkiye
[2] Recep Tayyip Erdogan University, Faculty of Medicine, Department of Basic Medical Sciences, Biostatistics and Medical Informatics, Rize, Turkiye

Özet

Amaç: Gebelikte bulantı ve kusma (NVP) gebelikte sıklıkla karşılaşılan bir durumdur ve ihmal edilirse ciddi maternal ve fetal komplikasyonlara yol açabilir. Bu çalışmanın amacı Rize'de NVP sıklığını ve ilgili faktörleri belirlemektir.

Gereç ve Yöntemler: Bu prospektif çalışmada, NVP şiddeti ve sıklığı, 5-20 gebelik haftası arasındaki gebelerde, Pregnancy-Unique Quantification of Emesis and Nausea (PUQE) skorlama sistemi kullanılarak puanlanarak belirlendi. PUQUE skoru 7'nin altında olan gebeler hafif NVP grubu, 7 ve üzeri olan gebeler ise orta ve şiddetli NVP grubu olarak tanımlandı. Demografik veriler ve kan elektrolit seviyeleri her iki grup arasında karşılaştırıldı.

Bulgular: Toplam 221 gebe kadın çalışmaya dahil edildi. Orta-şiddetli NVP sıklığı %10 (n=22) olarak bulundu. Hiperemesis gravidarum sıklığı %2 (n=4) olarak bulundu. Orta-şiddetli NVP semptomları olan gebelerin ortalama vücut kitle indeksi, hafif semptomları olan gebelerden daha yüksek bulundu (p<0,001). Orta-şiddetli NVP semptomları olan gebelerin ortalama kan sodyum ve potasyum düzeyleri daha düşük bulundu (p=0,003 ve <0.001).

Sonuç: Rize ilinde NVP sıklığı literatürle benzerdir. Vücut kitle indeksinin artması NVP sıklığı ile ilişkili olabilir. Bu gebelerde kanda elektrolit dengesizlikleri görülebilir. Bu nedenle tüm gebeler NVP açısından dikkatlice değerlendirilmeli ve gerekli hastalarda elektrolit dengesizliklerini ortadan kaldırmaya yönelik tedaviler planlanmalıdır.

Anahtar kelimeler: Bulantı, Kusma, Gebelik, Hiperemesis Gravidarum, Prevalans

Abstract

Objective: Nausea and vomiting of pregnancy (NVP) are frequently encountered in pregnancy and can lead to serious maternal and fetal complications if neglected. This study aims to determine the frequency of NVP and related factors in Rize.

Material and Methods: In this prospective study, the severity and frequency of NVP were determined by scoring pregnant women between 5-20 weeks of gestation, using the Pregnancy-Unique Quantification of Emesis and Nausea (PUQE) scoring system. Pregnant women with a PUQUE score below 7 were defined as the mild NVP group, and a score of 7 and above was defined as the moderate and severe NVP group. Demographic data and blood electrolyte levels were compared between the two groups.

Results: A total of 221 pregnant women were included. The frequency of moderate-severe NVP was found to be 10% (n = 22). The frequency of hyperemesis gravidarum was 2% (n=4). The average body mass index of pregnant women with moderate-severe NVP symptoms was found to be higher than that of pregnant women with mild symptoms (p<0.001). The average blood sodium and potassium levels of pregnant women with moderate-severe NVP were found to be lower (p=0.003 and <0.001).

Conclusion: The frequency of NVP in Rize province is similar to the literature. Increased body mass index may be associated with the frequency of NVP. Electrolyte imbalances may occur in the blood of these pregnant women. For this reason, all pregnant women should be carefully evaluated in terms of NVP, and treatments should be planned to eliminate electrolyte imbalances in patients.

Keywords: Nausea, vomiting, pregnancy, hyperemesis gravidarum, prevalence

Correspondence: Mehmet KAGITCI, Recep Tayyip Erdoğan Üniversitesi Zihni Derin Yerleşkesi - Fener Mahallesi 53100 Merkez, Rize, Türkiye

Phone: +90 505 316 28 90 **e-mail:** mehmetkagitci1@hotmail.com

ORCID No (Respectively): 0000-0002-9141-1301, 0000-0001-7712-7278, 0000-0002-4585-4785, 0000-0002-8803-5819, 0000-0002-2405-8552

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INTRODUCTION

Emesis gravidarum or nausea and vomiting of pregnancy (NVP) is commonly seen among pregnant women (1). The symptoms occur 2-4 weeks after fertilization, reach their most severe form between weeks 9 and 16 of pregnancy, and usually decrease by week 20 of pregnancy. Symptoms may be observed in approximately 50% to 90% of all pregnant women (2). In one in 200 women, nausea and vomiting become more severe and may turn into hyperemesis gravidarum, accompanied by dehydration and weight loss (3).

Although NVP is considered normal during pregnancy and treated, for some women it is just an annoying symptom, while for others it can seriously affect the quality of life. In 10-35%, symptoms may increase depression and mood changes, which can negatively affect housework and social relationships (4). These pregnant women are also at risk for mood disorders and depression (5).

Having a history of NVP and hyperemesis gravidarum (HG) in previous pregnancies increases the risk of HG in the second pregnancy by 3 times. Additionally, NVP is more common in Asian countries compared to Western societies (6). Although the cause of NVP is unknown, it is thought that genetic, endocrine, and gastrointestinal factors may play a role.

This study aimed to determine the prevalence and risk factors of NVP and HG in pregnant women in Rize.

MATERIALS AND METHODS

This prospective study was conducted among patients who applied to the pregnancy outpatient clinic of Recep Tayyip Erdogan University Faculty of Medicine Training and Research Hospital from 01 January 2023 and 31 December 2023. The study included women between the ages of 17-45, 5-20 weeks of pregnancy. Age, body mass index (BMI), number of previous live births and stillbirths, and gestational age were recorded. The gestational age determination was based on the last menstrual period, obstetric examination, and ultrasonography findings.

A scoring system was developed in 2002, especially for use in research, to determine the severity of the disease in the clinic and to create certain standardization. According to the PUQE score index (Pregnancy-Unique Quantification of Emesis and Nausea, a pregnancy-specific measurement of nausea and vomiting), scores are assigned to the patient based on the number of hours with nausea and vomiting, as well as the frequency of involuntary retching. This was later modified in 2008 (7). In the current study, the Turkish validated form was used (8). Modified PUQE scoring Questions and scores in the Modified PUQE scoring system are as follows:

On average, how much nausea and stomach discomfort do you feel in a day?

None ≤ (1 point), 1h (2 points), 2-3h (3 points), 4-6h (4 points), >6h (5 points)

On average, how many times do you gag and vomit in a day?

No vomiting (1 point), 1-2 times (2 points), 3-4 times (3 points), 5-6 times (4 points), ≤7 times (5 points)

On average, how many times a day do you experience retching or dry vomiting without expelling anything?

None (1 point), 1-2 times (2 points), 3-4 times (3 points), 5-6 times (4 points), ≤7 times (5 points)

Modified PUQE scoring. According to the Modified PUQE scoring system, if the patient's total score is ≤ 6, mild; between 7 and 12, medium; and ≥ 13 will be considered as severe NVP. Data were collected by face-to-face interviews with pregnant women.

Pregnant women with a PUQUE score below 7 were defined as group 1 (mild nausea and vomiting), and those with a PUQUE score of 7 and above were defined as group 2 (moderate-severe nausea and vomiting).

The inclusion criteria of the patients in the study were: 17-45 years of age, 5-20 weeks of pregnancy.

Exclusion criteria for patients in the study: No systemic diseases such as gastritis, pyelitis, and hyperthyroidism that may cause complaints of nausea and vomiting, ectopic pregnancy, hydatidiform mole, and multiple pregnancies.

Statistical method: Statistical Package for Social Sciences (SPSS version 20.0) program was used for statistical analysis. The distribution of demographic data of the patients included in the study, mean, standard deviation, minimum, and maximum values, was recorded. The Mann-Whitney U test was used in the statistical evaluation of the data obtained. The statistical significance level was set as 5%.

The study was reviewed according to the "Declaration of Helsinki" and "Good Clinical Practice Guideline" and was prepared "duly" according to the guideline. Informed consent was obtained from all participants in the study.

Ethics Approval: Approval for the study was received from the ethics committee of Recep Tayyip Erdogan University (decision no: 2022/233).

RESULTS

A total of 221 pregnant women were included in the study. The demographic data of the pregnant women included in the study are shown in **Table 1**.

According to the PUQE scores, mild nausea and vomiting were detected in 199 (90%), while moderate and severe nausea and vomiting were detected in 22 (10%). It was observed that 4 (2%) of the patients in the moderately severe group were hospitalized for treatment. Statistically significant differences were observed in BMI, mean sodium, and potassium levels of the patients with mild and moderate-severe NVP groups. Comparison of PUQE scores according to demographic data is shown in **Table 2**.

DISCUSSION

Nausea and vomiting of pregnancy, which worsens the pregnancy experience and may lead to the need to terminate the pregnancy in some cases, is a very common condition in clinical practice. The fact that it is common and is a normal symptom in the natural course of pregnancy may cause treatment delays. In our study, it was determined that the frequency of NVP was mostly mild, while it was severe in 10 percent of cases and required hospital follow-up and treatment in two percent.

There are many studies on the pathophysiology of NVP. The theory that the placenta affects pregnancy nausea and vomiting. As evidence for this theory, the gene that codes the placental proteins such as GDF15 and IGFBP7 is associated with NVP and HG. Additionally, HG may occur in mol hydaditiforme despite the absence of the fetus (9).

Human chorionic gonadotropin (hCG) regulates some factors and interleukins that may cause emesis. In a study, high maternal serum hCG levels are found at the time period of nausea and vomiting simultaneously (10). High hCG level is accepted as a risk factor for NVP (11). Additionally, NVP symptoms are often more severe in conditions associated with high hCG levels (12).

Sex hormones (such as estrogen and progesterone) may also play a role in the mechanism of NVP. These hormones can alter gastric rhythm, increase gastrointestinal transit time, and slow gastric emptying in non-pregnant women. So these changes may cause an increase in nausea and vomiting (13). There are opinions that Helicobacter pylori may also affect pregnancy nausea and vomiting. It has been found that H. pylori is found more frequently in the stomachs of women with HG (14).

When looking at the epidemiological factors that determine the frequency and severity of NVP, it is seen

Table 1. Demographic data of pregnant women included in the study

	Mean	Std. Deviation	Minimum	Maximum
Age (year)	28,64	5,577	17	51
BMI (kg/m^2)	26,61041	5,135528	17,6	50,5
Gravida	2,84	1,21	0	8
Gestational weeks	11,83	4,84	5	20

BMI: Body mass index

Table 2. Comparison of the relationship between demographic data and PUQE score in pregnant women.

	Grup1 Mean±SD	Grup2 Mean±SD	p*
Age (year)	28,33±5,308	31,50±7,123	0,59
Gravida	2,84±1,15	2,82±1,65	0,407
BMI (kg/m^2)	25,27±3,56	28,9±2,7	0,001
Gestational weeks	11,86±4,990	11,55±3,2	0,992
Sodium	137,45±1,75	135,4±3,31	0,003
Potassium	4,1±0,26	3,83±0,25	0,001

* Mann-Whitney U test was used to compare groups. BMI: Body mass index

that African American women experience NVP and HG more frequently than European women. Risk factors include those experiencing their first pregnancy, adolescents, those with a history of nausea and vomiting in their previous pregnancy, high body mass index and multiple pregnancies (15). According to the data obtained in our study, pregnant women who experience moderate and severe nausea and vomiting appear to have a higher body mass index.

Imbalances in blood electrolyte levels may occur in pregnant women who have problems with nutrition and fluid intake due to severe nausea and vomiting. Patients in this situation can be hospitalized, and clinical improvement can be achieved within a few days with hydration therapy containing appropriate electrolytes (16). The data in our study also shows that there are imbalances in the sodium and potassium levels of pregnant women with moderate and severe nausea and vomiting.

Since the pathogenesis of NVP and HG is still unknown, their treatment is difficult. Treatment focuses on improving the symptoms. Treatment modalities depend on the severity of symptoms and can be administered on a broad spectrum, ranging from dietary modifications, intravenous fluid rehydration (including electrolytes, vitamins, and thiamine), pharmacological therapy, and hospitalization.

The frequency of nausea and vomiting in pregnant women in Rize is similar to the literature average. Elevated BMI is a risk factor for NVP. Sodium and potassium levels may be affected by nausea and vomiting. Taking this issue into consideration during pregnancy follow-ups, questioning patients' symptoms, and providing advanced examinations and treatments in necessary cases will contribute to improving the pregnancy experience.

Conflict of Interest and Financial Status: Our study has not been financed by an institution and institution. In this study, there is no conflict of interest among the authors on any subject.

Ethical approval: This study was approved by the Recep Tayyip Erdogan University Scientific Research Ethics Committee (date:22/12/2022; Decision no: 2022/233). The Helsinki declaration was followed in the study.

Authors' contribution: They declare equal contribution to the study.

REFERENCES

1. Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 189: Nausea And Vomiting Of Pregnancy. Obstet Gynecol. 2018; 131(1):e15-e30.
2. Joshi A, Chadha G, Narayanan P. From Discomfort to Distress: A Critical Analysis of Hyperemesis Gravidarum in the Emergency Room. Cureus. 2023; 15(8):e44004.
3. Festin M. Nausea and vomiting in early pregnancy. BMJ Clin Evid. 2014 Mar 19;2014:1405.
4. Liu C, Zhao G, Qiao D, Wang L, He Y, Zhao M, Fan Y, Jiang E. Emerging Progress in Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum: Challenges and Opportunities. Front Med (Lausanne). 2022 Jan 10;8:809270.
5. Nacar G, Derman G, Güzel İnal C. Hiperemezis Gravidarumlu Gebelerde Depresif Semptomlar ve Kişilik Özelliklerinin Bulantı Kusma Şiddeti ile İlişkisi. JSHS. 2023;8(2):323-338.
6. Verberg MF, Gillott DJ, Al-Fardan N, Grudzinskas JG. Hyperemesis gravidarum, a literature review [published correction appears in Hum Reprod Update. 2007 Mar-Apr; 13(2):207]. Hum Reprod Update. 2005;11(5):527-539.
7. Lacasse A, Rey E, Ferreira E, Morin C, Bérard A. Validity of a modified Pregnancy-Unique Quantification of Emesis and Nausea (PUQE) scoring index to assess severity of nausea and vomiting of pregnancy. Am J Obstet Gynecol. 2008 Jan;198(1):71.
8. Yilmaz T, Dinç Kaya H, Günaydin S, Güdücü N, Dişsiz M. Psychometric properties of the Pregnancy-Unique Quantification of Emesis (PUQE-24) Scale. J Obstet Gynaecol. 2022 Aug;42(6):1739-1745.
9. Fejzo MS, Trovik J, Grooten IJ, Sridharan K, Roseboom TJ, Vikanes Å, et al. Nausea and vomiting of pregnancy and hyperemesis gravidarum. Nature reviews. Disease primers. 2019;5(1):62.
10. Dekkers GW F, Broeren MAC, Truijens SEM, Kop WJ, Pop VJM. Hormonal and psychological factors in nausea and vomiting during pregnancy. Psychological Medicine. 2020; 50(2), 229-236.
11. Topçu H, Can İ, Oskovi A, Timur H, Dağlar K, Danışman N. Risk Factors of Prolonged Hospitalization in Patients With Hyperemesis Gravidarum. Cukurova Medical Journal, 2015;40(1):113-118.
12. Davis, Mitzi. "Nausea and vomiting of pregnancy: an evidence-based review." The Journal of perinatal & neonatal nursing 2004;18.4:312-328.
13. Body C, Christie JA. Gastrointestinal Diseases in Pregnancy: Nausea, Vomiting, Hyperemesis Gravidarum, Gastroesophageal Reflux Disease, Constipation, and Diarrhea. Gastroenterol Clin North Am. 2016;45(2):267-283.
14. Shaban MM, Kandil HO, Elshafei AH. Helicobacter pylori seropositivity in patients with hyperemesis gravidarum. Am J Med Sci. 2014 Feb;347(2):101-5.
15. Abramowitz A, Miller ES, Wisner KL. Treatment options for hyperemesis gravidarum. Arch Womens Ment Health. 2017 Jun; 20(3):363-372.
16. Summers A. Emergency management of hyperemesis gravidarum. Emerg Nurse. 2012 Jul; 20(4):24-28.

Research Article (Araştırma Makalesi)

The Effect of Robot-assisted Virtual Reality Therapy on Improving Upper Limb Functions, Pain, and Daily Living Activities in Stroke Patients

Robot Destekli Sanal Gerçeklik Terapisinin İnme Hastalarında Üst Ekstremite Fonksiyonları, Ağrı ve Günlük Yaşam Aktivitelerini İyileştirmedeki Etkisi

Canan AVCI[1] Kadriye ONES[1] Mustafa Aziz YILDIRIM[1]

[1] Istanbul Physical Medicine and Rehabilitation Training Research Hospital, Department of Physical Medicine and Rehabilitation, Istanbul, Türkiye

Özet

Amaç: Bu çalışmada amacımız inmeli hastalarda konvansiyonel tedaviye eklenen robot yardımlı sanal gerçeklik terapisinin (RYSGT) ağrı, fonksiyonel durum ve günlük yaşam aktiviteleri üzerine etkisini incelemektir.

Gereç ve Yöntemler: Çalışmaya 40 inmeli hasta dahil edildi. Hastalar iki gruba ayrıldı. Grup I konvansiyonel terapi (4 hafta boyunca haftada 5 gün, günde 1 saat) ve ek olarak 4 hafta boyunca haftada 5 gün, günde 30 dakika olmak üzere 20 seans üst ekstremite RYSGT'si aldı. Grup II ise sadece konvansiyonel terapi aldı. Tüm hastalar tedavi öncesi ve sonrası değerlendirildi. Hastaların ağrılarını değerlendirmek için Görsel Analog Skalası (VAS), günlük yaşam aktivitelerini belirlemek için Barthel İndeksi (BI) ve üst ekstremite motor fonksiyonlarını değerlendirmek için Fugl Meyer Üst Ekstremite Değerlendirmesi (FMA-UE) kullanıldı.

Bulgular: Hastaların ortalama yaşı 58,25 ± 14,7 yıl idi. Cinsiyet, eğitim durumu, inme sonrası geçen süre, lezyon tarafı ve lezyon tipi açısından iki grup arasında anlamlı bir fark yoktu (p>0,05). Grup I ve II'de tedavi sonrası (AT) tüm parametreler tedavi öncesine (BT) göre anlamlı (p<0,05) artış gösterdi. Ancak VAS, BI ve FMA-UE skorlarındaki BT/AT değişimi iki grup arasında anlamlı olarak farklı değildi (p>0,05).

Sonuç: Bu çalışma, RYSGT'nin kronik inmeli hastaların fonksiyonel durumunu, günlük yaşam aktivitelerini ve ağrı skorlarını iyileştirdiğini, ancak tedaviden sonra iki grup arasında fark olmadığını gösterdi. RYSGT yaklaşımıyla fonksiyonel iyileşmeler kaydedilmesine rağmen, tek başına geleneksel tedaviye üstün değildi.

Anahtar kelimeler: Robot Destekli Terapi, Rehabilitasyon, İnme, Üst Ekstremite, Sanal Gerçeklik

Abstract

Objective: In the present study, our aim is to examine the effect of robot-assisted virtual reality therapy (RAVRT) added to conventional treatment on pain, functional status, and daily living activities (DLA) in stroke patients.

Material and Methods: The study included 40 patients with stroke. The patients were divided into two groups. Group I received conventional therapy (5 days a week for 4 weeks, 1 hour a day) and additionally 20 sessions of upper extremity RAVRT for 4 weeks, 5 days a week, 30 minutes a day. Group II received only conventional therapy. All patients were evaluated before and after the treatment. The Visual Analogue Scale (VAS) was used to evaluate the patients' pain, the Barthel Index (BI) to determine DLA, and the Fugl Meyer Assessment Upper Extremity (FMA-UE) to evaluate the UE motor functions.

Results: The mean age of the patients was 58.25 ± 14.7 years. There was no significant difference between the two groups in terms of gender, educational status, time after stroke, lesion side, and lesion type (p>0.05). In groups I and II, after the treatment (AT), all parameters showed a significant (p<0.05) increase when compared to values before the treatment (BT). However, the BT / AT change in VAS, BI, and FMA-UE scores was not significantly different (p>0.05) between the two groups.

Conclusion: This study showed that RAVRT improved functional status, activities of daily living, and pain scores of chronic stroke patients, but there was no difference between the two groups after treatment. Although functional improvements were noted with the RAVRT approach, it was not superior to conventional therapy alone.

Keywords: Robot-Assisted Therapy, Rehabilitation, Stroke, Upper Extremity, Virtual Reality

Correspondence: Canan AVCI, İstanbul Fiziksel Tıp ve Rehabilitasyon Eğitim Araştırma Hastanesi, Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı. Bahçelievler Mahallesi, Adnan Kahveci Blv. No : 145, 34186 Bahçelievler /Istanbul, Türkiye

Phone: +90 2124965000 **e-mail:** cnndr@hotmail.com

ORCID No (Respectively): 0000-0003-4544-0133, 0000-0001-9438-4428, 0000-0001-6688-7626

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INTRODUCTION

Loss of motor function in the upper extremities (UE) is the most common and destructive consequence of disability due to stroke. The arm is more affected than the leg in stroke patients. One of the goals of stroke rehabilitation is to gain independence in DLA, so due importance should be given to UE rehabilitation (1). Various techniques are used for the UE rehabilitation. These are intensive, high-repetitive task-oriented therapies: constraint-induced movement therapy (CMIT), functional electrical stimulation (FES), virtual reality (VR), and robot-assisted therapy (RAT). Functional improvement of patients is associated with cortical reorganization, and active participation of patients increases this. This reorganization, called neuroplasticity (2). UE-RAT provides frequent repetition, intensive training, and interactive feedback (3). Robotic therapy has been shown to affect the results positively. These systems allow continuous and repetitive therapy to be performed with less effort and the less cost. In these systems, visual and auditory biofeedback can be provided with VR. Thus, motor learning is increased with neural plasticity (4). VR refers to the process of complete immersion of the person or patient in a virtual scenario as close as possible to the real world, using various devices. VR-based rehabilitation has been used with many neurological diseases, especially stroke patients, and there are many studies supporting its beneficial effects on patients (5,6).

RAT is an effective neurorehabilitation approach that has been widely used recently, enhances the effects of physical therapy, and facilitates motor recovery (7). Many studies on RAT treatment have been examined (8,9). Results vary according to the type of robot, study design, and characteristics of the patient. Many researchers showed that with a robot-assisted VR rehabilitation program, although the improvement in DLA was limited, the movement and muscle strength of the upper extremities increased. This can be explained by the limitation of UE-RAT in the proximal part of the UE. For functional improvement, coordination between the proximal and the distal parts is required (10-12).

The study aims to reveal how these new technologies affect the functional recovery of the UE, pain, and DLA.

MATERIALS AND METHODS

This is a prospective controlled study of patients with stroke inpatients in the Istanbul Physical Medicine and Rehabilitation Training Research Hospital, Department of Physical Medicine and Rehabilitation. Preliminary information was given to the participants about the study. Written informed consent was signed voluntarily by all participants or their immediate family members. 68 stroke patients who developed hemiplegia after cerebrovascular accident (CVA) and underwent inpatient rehabilitation were included in the study and were evaluated prospectively. 40 of these patients met the inclusion criteria **(Figure 1)**.

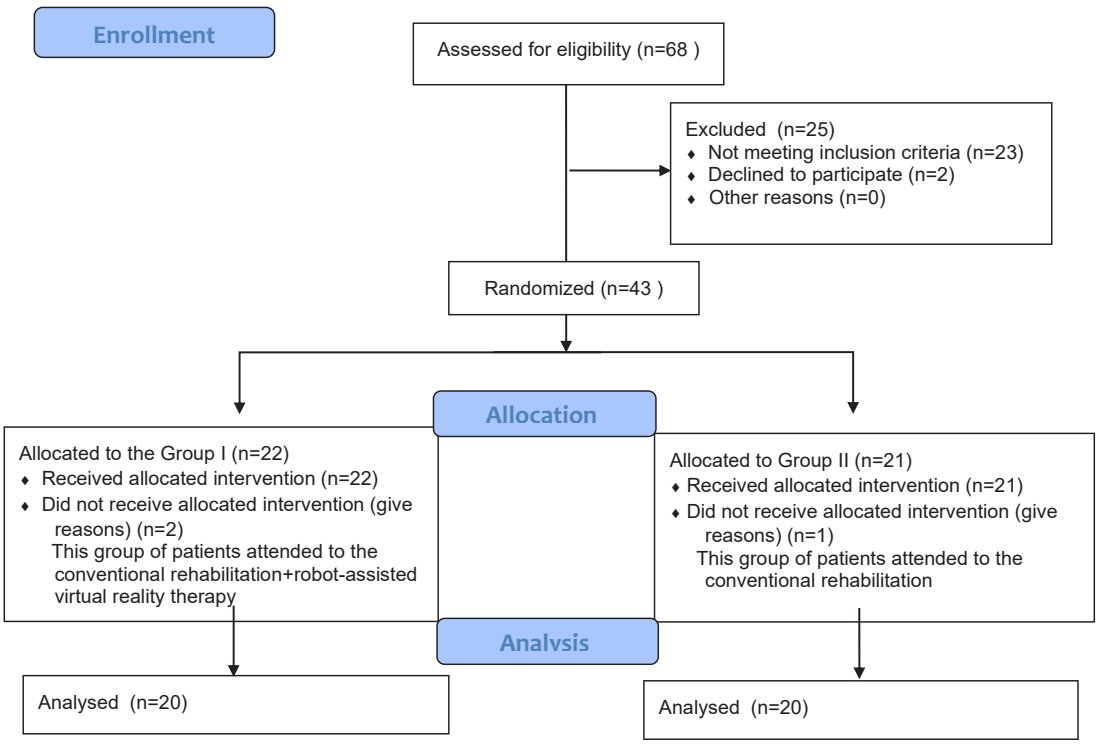

Figure 1. Flow diagram of Group I and Group II.

Participants were divided into two groups of 20 patients using the "Random Number Generator Program". Group I (n=20) received a total of 20 sessions of RAVRT (30 minutes per day) and conventional treatment (30 minutes per day). Group II (n = 20) received an equal number of sessions of conventional treatment (1 hour per day) only. The treatment program was conducted 5 times per week for one month. Conventional therapy consists of exercises that include passive or active range of motion exercises, muscle strengthening, gross motor training, grasping and releasing, and stretching for the affected side of the upper limb, as well as activities of daily living.

Inclusion criteria were as follows: ischemic or hemorrhagic CVA, 18-85 year old patients with a diagnosis of stroke, Brunnstrom UE motor stage ≥3, at least 3 months had passed after CVA, and modified Ashworth Score ≤2. The Brunnstrom stage ≥3 patients were included because patients must have at least level 3 motor movement to be able to perform the VR program on the Armeo Spring device. This is a prerequisite for the completion of the given tasks.

Exclusion criteria were as follows: aphasic patients, cognitive impairment, standardized mini-mental test score <24, contracture and/or deformity in the UE, and patients diagnosed with KBAS.

Armeo Spring device

The Armeo Spring device (http://www.hocoma.com/en/products/armeo/armeo-spring/; see also Figure 2) is an arm orthosis equipped with various components, including a pressure-sensitive grip. A spring-loaded mechanism provides adjustable weight support for the arm requiring therapy, thus facilitating functional arm movements.

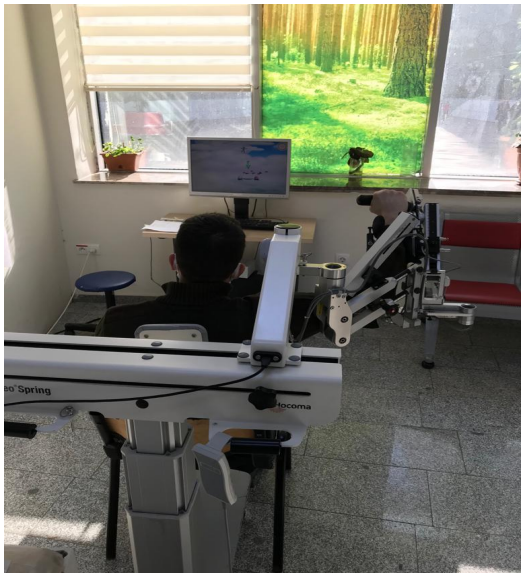

Figure 2. The Armeo Spring is an exoskeleton apparatus with an integrated spring mechanism allowing variable upper limb gravity support.

Adjustable ergonomic arm support functions as an exoskeleton equipped with integrated springs. It extends from the shoulder to the hand and enhances the full range of motion and neuromuscular control. This device assists in active movement over a wide 3-dimensional range and balances the weight of the arm with a consistent force. The pressure-sensitive handgrip is useful for exercises, connecting to computer software and games, and functional training for daily tasks. It also measures movement and functionality, allowing for intensive grip and release exercises in the early stages of rehabilitation. The device was attached to the hemiplegic upper extremities of the patients with upper and forearm cuffs. Adjusted for arm, forearm, and wrist lengths. Exercise programs suitable for the functional status of the patients were determined, and they were included in an exercise program in the form of a game (VR) with the monitor placed opposite them. The patients were enrolled in functional exercise programs that included activities such as collecting rain in a glass, grating vegetables, playing goalkeeper, cleaning the stove, watering flowers, cleaning windows, fishing, and exploring various landscapes **(Figure 2)**.

Evaluation Parameters

Before and following treatment, the patients were evaluated. Evaluations were performed by a single physician while the patient was in the inpatient clinic. During the evaluations, the following parameters were recorded.

Pain Inquiry

In this study, a 10 cm line called the VAS, which is among the visual methods, was used for pain questioning. On this line, "0" indicates painlessness and "10" indicates unbearable pain.

Daily Living Activities Evaluation

BI has been adapted for Turkish patients and includes 10 items that evaluate DLA and mobility. Feeding, washing, dressing, personal care, bowel and bladder care, sitting on the toilet, transferring from a wheelchair to a bed, walking on level ground, and climbing stairs are evaluated. A score is made based on whether or not the patient receives assistance while performing these tasks. A score between 0-20 indicates fully dependent, 21-61 points indicate highly dependent, 62-90 points indicate moderately dependent, 91-99 points indicate mildly dependent, 100 points indicate fully independent (13).

Fugl-Meyer Assessment -Upper Extremity (FMA-UE)

The FMA-UE evaluates the hemiparetic arm's mobility, including reflexes, the appearance of synergies, and each of the upper limb's isolated movements, including grasp. Items that assess patients' dysmetria, coordination, and velocity are also included in this measure. It is designed to evaluate reflex activities, movement control, and muscle strength after the stroke in the UE. It consists of 33 items, and each item takes a value between 0-2. No performance is indicated by a score of 0, partial performance is indicated by a score of 1, and complete performance is indicated by a score of 2. As a result of the total score, scores lower than 31 indicate weak capacity, scores between 32-47 indicate limited capacity, scores between 48-52 indicate remarkable capacity, and scores between 53-66 indicate full capacity (14).

Statistical analysis

The mean, standard deviation, median, minimum, maximum, frequency, and ratio values were employed in the data's descriptive statistics. The Kolmogorov-Smirnov test was used to measure the variables' distribution. The quantitative data were analyzed using the independent samples t-test and the Mann-Whitney U test. Repeated measurements were analyzed using the Wilcoxon and McNemar tests. Qualitative data were analyzed using the chi-square test, and when the chi-square test requirements were not satisfied, the Fisher test was employed. The analysis was conducted using the SPSS 22.0 program.

RESULTS

There was no notable difference between group I and group II regarding age, gender, marital status, dominant hand, event duration, standardized mini-mental score, cause, or hemiplegic side ($p < 0.05$) **(Table 1)**.

Table 1. Sociodemographic and clinical features of patients with conventional treatment +robot-assisted virtual reality therapy group and conventional treatment group

		Conventional treatment+ robot-assisted virtual reality therapy			Conventional treatment			p
		Mean.±SD/n-%		Med(Min-Max)	Mean.±SD/n-%		Med(Min-Max)	
Age		58,2 ± 14,1		60 (27 - 76)	58,3 ± 15,3		60 (18 - 77)	0,914
Gender	Female	14	70%		12	60%		0,507
	Male	6	30%		8	40%		
Marital Status	Married	17	85%		14	70%		0,256
	Single	1	5%		2	10%		
	Widow	2	10%		4	20%		
Dominant Hand	Right	18	90%		18	90%		1
	Left	2	10%		2	10%		
Event duration (month)		13,3 ± 15,6		8 (3 - 60)	13,1 ± 15,8		7 (3 - 60)	0,807
Standardized mini mental test		26,3 ± 2,2		26 (24 - 30)	25,3 ± 2,0		25 (24 - 30)	0,141
Etiology								
Ischemic CVA		15	75%		15	75%		1
Hemorrhagic CVA		5	25%		5	25%		
Hemiplegia Side	Right	8	40%		7	35%		0,744
	Left	12	60%		13	65%		
Brunnstorm Stage								
Upper extremity before treatment		4,0 ± 0,9		4 (2 - 5)	3,8 ± 0,8		4 (3 - 5)	0,491

Mann-whitney u test/Wilcoxon test
VAS: visual analog scaleMean.±SD : mean+ standard deviation Med(Min-Max): median (minimum-maximum)

VAS scores obtained before and after the treatment were not significantly different in group I and group II ($p > 0.05$). The VAS score for shoulder pain decreased significantly after treatment in both groups ($p < 0.05$) when compared to BT **(Table 2)**. The BT/AT change in VAS scores was not significantly different ($p > 0.05$) between the two groups.

BI calculated before and after the treatment was not significantly different in group I and group II ($p > 0.05$). BI increased significantly ($p < 0.05$) after the treatment in both group I and group II when compared to BT. The BT/AT change in BI was not significantly different ($p > 0.05$) between the two groups **(Table 3)**.

FMA-UE arm score, wrist score, hand score, coordination and speed score, and total score calculated before and after the treatment were not significantly different ($p > 0.05$) between group I and group II. FMA-UE scores increased significantly ($p < 0.05$) after the treatment in Groups I and II compared to pre-treatment. The BT/AT change in all FMA-UE scores was not significantly different ($p > 0.05$) between the two groups **(Table 4)**.

DISCUSSION

In this study, we investigated the effect of RAVRT on pain, motor and functional status, and DLA of patients with stroke. All patients completed the interventions without any major problems. The main findings of our study were that significant improvement was observed in VAS, Brunstromm, FMA-UE, and BI after the rehabilitation in both groups. On the other hand, there was no noticeable difference in DLA, motor and functional condition, or pain between the two groups. Pain is one of the important symptoms affecting the rehabilitation process. Shoulder pain masks the improvement in the patient's motor function. As a result, it affects the rehabilitation program of the patient and extends the rehabilitation duration (15). In the literature, the frequency of hemiplegic shoulder pain varies between 24-64% (16). Analysis of the patients' VAS pain scores

Table 2. Improvement of VAS values in patients with conventional treatment + +robot-assisted virtual reality therapy group and conventional treatment group

	Conventional treatment+ robot-assisted virtual reality therapy		Conventional treatment		p
	Mean.±SD/n-%	Med(Min-Max)	Mean.±SD/n-%	Med(Min-Max)	
Shoulder VAS					
Before Treatment (BT)	1,2 ± 1,7	0 (0 - 4)	1,1 ± 1,7	0 (0 - 5)	0,911
After Treatment (AT)	0,6 ± 1,2	0 (0 - 4)	0,5 ± 0,8	0 (0 - 2)	0,725
BT/AT Difference	0,6 ± 1,1	0 (0 - 4)	0,6 ± 1,1	0 (0 - 3)	0,986
p	***0,034***		***0,041***		

t test/Mann-whitney u test/Chi-Square test (Fischer test)

Mean.±SD: mean+ standard deviation Med(Min-Max): median (minimum-maximum) CVA: cerebrovascular accident

Table 3. Improvement of Barthel Index scores in patients with conventional treatment +robot-assisted virtual reality therapy group and conventional treatment group

	Conventional treatment+ robot-assisted virtual reality therapy		Conventional treatment		p
	Mean.±SD/n-%	Med(Min-Max)	Mean.±SD/n-%	Med(Min-Max)	
Barthel Index					
Before Treatment (BT)	69,0 ± 21,3	73 (15 - 100)	65,0 ± 24,1	65 (5 - 100)	0,615
After Treatment (AT)	80,0 ± 18,7	85 (25 - 100)	73,3 ± 21,7	78 (10 - 100)	0,248
BT/AT Difference	11,0 ± 10,3	10 (0 - 40)	3,8 ± 0,8	5 (0 - 35)	0,319
p	***0,000***		***0,001***		

Mann-whitney u test / Wilcoxon test

Mean.±SD : mean+ standard deviation Med(Min-Max): median (minimum-maximum)

Table 4. Improvement of VAS values in patients with conventional treatment + +robot-assisted virtual reality therapy group and conventional treatment group

		Conventional treatment+ robot-assisted virtual reality therapy		Conventional treatment		p
		Mean.±SD/n-%	Med(Min-Max)	Mean.±SD/n-%	Med(Min-Max)	
FMA-UE						
Arm	BT	21,6 ± 5,2	21 (11 - 29)	22,3 ± 5,9	23 (12 - 30)	0,664
	AT	26,3 ± 5,8	27 (14 - 34)	25,9 ± 7,0	28 (12 - 36)	0,839
BT/AT Difference		4,7 ± 2,9	5 (0 - 11)	3,6 ± 3,3	3 (0 - 10)	0,211
p		***0,000***		***0,001***		
Wrist	BT	2,6 ± 1,8	3 (0 - 6)	3,9 ± 2,3	5 (0 - 7)	0,051
	AT	4,0 ± 3,0	4 (0 - 10)	4,9 ± 3,0	5 (0 - 10)	0,268
BT/AT Difference		1,4 ± 1,6	1 (0 - 5)	1,0 ± 1,3	1 (0 - 4)	0,565
p		***0,003***		***0,005***		
Hand	BT	6,9 ± 4,1	7 (1 - 13)	7,1 ± 3,3	8 (0 - 12)	0,892
	AT	9,3 ± 3,9	10 (3 - 14)	8,8 ± 4,0	10 (0 - 14)	0,703
BT/AT Difference		2,4 ± 2,2	3 (0 - 6)	1,7 ± 1,7	2 (0 - 5)	0,337
p		***0,001***		***0,002***		
Coordination and speed	BT	2,7 ± 1,3	3 (0 - 5)	3,1 ± 1,2	3 (1 - 6)	0,512
	AT	3,5 ± 1,4	3 (1 - 6)	3,8 ± 1,5	4 (1 - 6)	0,415
BT/AT Difference		0,8 ± 1,0	0 (0 - 3)	0,7 ± 0,8	1 (0 - 2)	0,906
p		***0,006***		***0,004***		
Total	BT	34,3 ± 8,4	34 (19 - 49)	36,5 ± 10,8	38 (18 - 49)	0,357
	AT	43,0 ± 12,0	41 (20 - 63)	43,2 ± 14,0	45 (18 - 66)	0,903
BT/AT Difference		8,7 ± 5,4	8 (0 - 18)	6,8 ± 5,9	5 (0 - 18)	0,212
p		***0,000***		***0,000***		

Mann-whitney U test / Wilcoxon test
FMA-UE: Fugl Meyer Assessment Upper Extremity BT: Before treatment AT: After Treatment
Mean.±SD: mean+ standard deviation Med(Min-Max): median (minimum-maximum)

revealed a statistically significant reduction in pain in both groups and no significant variation in VAS difference scores between the groups. With these findings, we can comment that in the worst case, the robotic rehabilitation program applied to patients does not have a treatment side effect in terms of pain. The goal in stroke rehabilitation is to provide the highest level of independence in the DLA, despite existing motor impairments. It has been shown that the level of functional independence gained as a result of the rehabilitation program in patients with stroke is largely related to UE and hand motor deficiencies. To maintain the basic functions in daily life, the use of the UE is important, and UE paralysis causes problems in maintaining DLA. In stroke rehabilitation, it should be for the individual to attain the highest level of independence in activities of daily living, despite existing motor disabilities (17). In this study, DLA were evaluated with BI. Both groups ' post-treatment scores were statistically higher than the initial scores. While this increase was 11 points in group I patients who received UE-RAT, it was 8.3 points in group II. Although the increase was greater in group I, this was not statistically significant.

Ju-Hong Kim et al.'s study investigated the effect of the VR program on function in stroke patients. A total of 24 patients were included, and two groups were formed. Conventional treatment was applied to both groups, and the study group also applied a VR-based

video game exercise program. UE functional assessment was measured using the Fugl-Meyer Assessment and Manual Function Test, and DLA was measured with SIS (Stroke Impact Scale), unlike our study. Stroke patients who underwent extra training with VR games demonstrated significantly greater improvements in DLA than those who received only conventional rehabilitation therapy. Similar to our study, no significant difference was observed between the 2 groups in UE motor functions (18).

VR has become an advantageous treatment modality by providing many features that are important in neurological rehabilitation, such as task-oriented, functional, and repetitive training. Functional recovery, whether spontaneous or secondary to intensive rehabilitation, is maintained through neuroplasticity and the restructuring of neurons in the damaged brain in adults (19,20). Studies on the use of VR for rehabilitation purposes are increasing gradually. In the study conducted by Colomer et al., the effect of Armeo Spring in chronic stroke patients was evaluated. 23 patients with ischemic or hemorrhagic stroke were included in the study, 36 sessions of UE-RAT were applied 3 times a week, 1-hour sessions, and conventional treatments continued at the same time. Patients were followed up before and after the treatment and at the fourth month. The functional evaluation of the patients was investigated with FMA-UE, and the spasticity was evaluated with MAS. Statistical analysis showed a significant improvement in functional scales; however, there was no significant improvement in muscle tone (2). In the randomized controlled study of Lum et al., RAT and conventional therapy were compared in UE rehabilitation in stroke patients. 27 patients were included in the study, 24 sessions of RAT were applied to the study group, and 24 sessions of UE neurodevelopmental therapy were applied to the control group. As a result of the study, a significant improvement was observed in FMA-UE in the 1st and 2nd months after the treatment in the study group compared to the control group, but no significant difference was found in the 6th month evaluation (21). The lack of long-term control is a limitation of our study.

The combination of RT and VR interventions shows potential to improve UE function; however, additional research is needed to confirm these findings, investigate the underlying mechanisms, and assess the consistency and applicability of the results (22).

Masiero et al conducted a study of 35 patients to evaluate the effect of robotic therapy on motor development and functional activities in patients after acute stroke who received robot-assisted rehabilitation in the UE. In addition to the conventional treatment program, robotic (NeReBot) rehabilitation was applied to 17 patients included in the robotic treatment group, two sessions a day, 4 hours a week, and a total of 5 weeks. The robotic rehabilitation program focuses on the patient's shoulder and elbow movement patterns. In the control group of 18 patients, exercise therapy and robotic therapy were applied twice a week for 30 minutes. The patients were evaluated with FMA, FIM, Modified Asworth Scale, trunk control test, and muscle strength before and after the treatment and at 8-month follow-up. When compared to the control group, in patients after acute stroke who received robot-assisted rehabilitation in the UE, the method provided significant improvement in motor impairment and functional abilities, FMA proximal upper arm and FIM parameters, and these gains continued at the third and eighth months after the treatment. In this study, the treatment program consisting of conventional treatment (65% of the exercise time) and robotic rehabilitation (35% of the exercise time) showed similar results with the conventional treatment group in terms of motor recovery, DLA, and functional recovery of the hand (23).

Some researchers contend that robotic therapy is at least as effective as conventional therapy, while others have demonstrated that robotic systems yield better outcomes than conventional therapy. In this study, we found significant improvement in FMA-UE in both groups. Unfortunately, patients were evaluated before and after the treatment; follow-up results were not examined. In this case, we do not have a chance to predict the permanence of treatment results and make a comment on the improvement among the groups. This is one of the limitations of our study. Another limitation is the small sample size of patients.

After a four-week treatment program of 20 sessions, pain, DLA, and functional status scores increased in patients who received only conventional treatment, as well as patients in the robotic treatment group. The improvement in both treatment groups is not surprising, because the functional gains of the patients, taking more care to use their hands during DLA, and being encouraged in this direction, may have increased the awareness of the extremity that they normally use less and brought motor development. However, RAVRT did not lead to better outcomes compared with conventional rehabilitation. Therefore, it needs to be improved with new solutions and in clinical practice guidelines, especially in terms of applicability.

Ethical Approval: The study was prepared in accordance with the Declaration of Helsinki. Medical ethics committee approval was obtained from Bakırköy Dr

Sadi Konuk Training Research Hospital (protocol no: 136, date: 2015/08/31). This clinical trial was registered at ClinicalTrials. gov (Registration no. NCT05815823).

Conflict of Interest and Financial Status: There is no conflict of interest. No funding was received for this manuscript.

Author Contribution: This study was produced from Canan Avcı's medical specialization thesis. All authors contributed equally to the study.

REFERENCES

1. El-Kafy EMA, Alshehri MA, El-Fiky AA, Guermazi MA. The Effect of Virtual Reality-Based Therapy on Improving Upper Limb Functions in Individuals With Stroke: A Randomized Control Trial. Front Aging Neurosci. 2021;13:731343.
2. Colomer C, Baldoví A, Torromé S, Navarro MD, Moliner B, Ferri J, et al. Efficacy of Armeo® Spring during the chronic phase of stroke. Study in mild to moderate cases of hemiparesis. Neurologia. 2013;28(5):261-7.
3. Yoo DH, Kim SY. Effects of upper limb robot-assisted therapy in the rehabilitation of stroke patients. J. Phys. Ther. Sci 2015;27:677-679
4. Blank AA, French JA, Pehlivan AU, O'Malley MK. Current Trends in Robot-Assisted Upper-Limb Stroke Rehabilitation: Promoting Patient Engagement in Therapy. Curr Phys Med Rehabil Rep. 2014;2(3):184-195.
5. Rutkowski S, Kiper P, Cacciante L, Cieślik B, Mazurek J, Turolla A, et al. Use of virtual reality-based training in different fields of rehabilitation: A systematic review and meta-analysis. J Rehabil Med. 2020 19;52(11):jrm00121.
6. Abd El-Kafy EM, Alshehri MA, El-Fiky AA, Guermazi MA, Mahmoud HM. The Effect of Robot-Mediated Virtual Reality Gaming on Upper Limb Spasticity Poststroke: A Randomized-Controlled Trial. Games Health J. 2022;11(2):93-103.
7. Balasubramanian S, Klein J, Burdet E. Robot-assisted rehabilitation of hand function. Curr Opin Neurol. 2010;23(6):661-70.
8. Volpe BT, Lynch D, Rykman-Berland A, Ferraro M, Galgano M, Hogan N, et al. Intensive sensorimotor arm training mediated by a therapist or robot improves hemiparesis in patients with chronic stroke. Neurorehabil Neural Repair. 2008;22(3):305-10.
9. Prange GB, Jannink MJ, Groothuis-Oudshoorn CG, Hermens HJ, Ijzerman MJ. Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke. J Rehabil Res Dev. 2006;43(2):171-84.
10. Tseng KC, Wang L, Hsieh C, Wong AM. Portable robots for upper-limb rehabilitation after stroke: a systematic review and meta-analysis. Ann Med. 2024;56(1):2337735.
11. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. Lancet Neurol. 2009;8(8):741–54.
12. Adomavičienė A, Daunoravičienė K, Kubilius R, Varžaitytė L, Raistenskis J. Influence of New Technologies on Post-Stroke Rehabilitation: A Comparison of Armeo Spring to the Kinect System. Medicina (Kaunas). 2019;55(4):98.
13. Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. J Clin Epidemiol. 1989;42(8):703-9.
14. Page SJ, Levine P, Hade E. Psychometric properties and administration of the wrist/hand subscales of the Fugl-Meyer Assessment in minimally impaired upper extremity hemiparesis in stroke. Arch Phys Med Rehabil. 2012;93:2373–2376.
15. Wanklyn P, Forster A, Young J. Hemiplegic shoulder pain (HSP): Natural history and investigation of associated features. Disabil Rehabil. 1996;18(10):497–501.
16. Sharma AK, Asthana SS, Deshmukh I. Impact of Ultrasound-Guided Suprascapular Nerve Block in Stroke Survivors With Hemiplegic Shoulder Pain Undergoing Neurorehabilitation: A Retrospective Case Series. Cureus. 2024;16(9):e69051.
17. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. Cochrane Database Syst Rev. 2017;11(11):CD008349.
18. Kim JH. Effects of a virtual reality video game exercise program on upper extremity function and daily living activities in stroke patients. J Phys Ther Sci. 2018;30(12):1408-1411.
19. Alashram AR. Combined robot-assisted therapy virtual reality for upper limb rehabilitation in stroke survivors: a systematic review of randomized controlled trials. Neurol Sci. 2024;45(11):5141-5155.
20. Taveggia G, Borboni A, Salvi L, Mule C, Fogliaresi S, Villafane JH, et al. Efficacy of robot-assisted rehabilitation for the functional recovery of the upper limb in post-stroke patients: a randomized controlled study. Eur J Phys Rehabil Med. 2016;52:767-73.
21. Lum PS, Burger CG, Shor PC, Majmundar M, Van der Loos M. Robot-assisted movement training compared with conventional therapy techniques fort he rehabilitation of upper-limb motor function after stroke. Arch Phys Med Rehabil. 2002;83:952-9.
22. Alashram AR. Combined robot-assisted therapy virtual reality for upper limb rehabilitation in stroke survivors: a systematic review of randomized controlled trials. Neurol Sci. 2024;45(11):5141-5155.
23. Masiero S, Celia A, Rosati G, Armani M. Robotic-assisted rehabilitation of the upper limb after acute stroke. Arch Phys Med Rehabil. 2007;88(2):142-9.

Case Report (Olgu Sunumu)

Adams Oliver Syndrome: Our One-Year Experience

Adams Oliver Sendromu: Bir Yıllık Deneyimimiz

Aydın BOZKAYA[1], Salih DAVUTOGLU[2]

[1] Sanliurfa Training and Research Hospital, Department of Pediatrics, Sanliurfa, Turkiye
[2] Sanliurfa Training and Research Hospital, Department of Pediatrics, Division of Neonatology, Sanliurfa, Turkiye

Özet

Adams-Oliver sendromu nadir olmasına rağmen sıklıkla aplaziya kutis konjenita ve terminal ekstremite defektleri ile karakterize konjenital bir hastalıktır. Küçük lezyonlar sıklıkla kendiliğinden iyileşirken, daha büyük lezyonlar gastrointestinal, kardiyopulmoner, genitoüriner ve merkezi sinir sistemindeki yaygın ölümcül anomalilerle ilişkili olabilir.

Bu yazıda birçok sistemi etkileyen bu sendromu hatırlatmayı ve tedavisinde multidisipliner yaklaşımın önemini vurgulamayı amaçladık. Adams-Oliver sendromunun kriterleri ders kitaplarına ve güncel literatüre göre üç olguda değerlendirildi.

Birinci olguda sağ üst ekstremitede aplaziya kutis, iki taraf ayak parmaklarında tırnak hipoplazisi, polidaktili ve kutis marmaratus, ikinci olguda aplaziya kutis, kutis marmaratus ve intrauterin bağırsak perforasyonu ve üçüncü olguda aplaziya kutis, kutis marmaratus ve Kranial MR'da kistik ensefalomalazik değişiklikler tespit edildi.

Adams-Oliver sendromu çeşitli klinik bulgularla seyreden nadir bir sendromdur. Bu nedenle dismorfik bulgular ve Adams-Oliver sendromu ile başvuran olgularda tüm sistemlerin incelenmesi gerekmektedir. Tanı konulduktan sonra takip ve tedavi ilgili branşlar tarafından multidisipliner yaklaşımla yapılmalıdır.

Anahtar kelimeler: Adams-Oliver sendromu, Aplasia kutis konjenita, Terminal ekstremite defektleri, Hipoplastik falanjlar, Ekstremite malformasyonları

Abstract

Adams-Oliver syndrome, although rare, is a congenital disease commonly characterized by aplasia cutis congenita and terminal limb defects. While small lesions often heal spontaneously, larger lesions may be associated with common fatal anomalies in the gastrointestinal, cardiopulmonary, genitourinary, and central nervous systems

In this paper, we aimed to remind readers of this syndrome, which affects many systems, and to emphasize the importance of the multidisciplinary approach in its treatment. The criteria for Adams-Oliver syndrome have been evaluated in three cases, as outlined in textbooks and the current literature.

In case one, aplasia cutis, nail hypoplasia in bilateral toes, polydactyly, and kutis marmaratus in the right upper extremity, in case two, aplasia cutis, kutis marmaratus, and intrauterine intestinal perforation, and in case three, aplasia cutis, kutis marmaratus, and cystic encephalomalasic changes on cranial MRI have been detected.

Adams-Oliver syndrome is a rare syndrome with various clinical presentations. Hence, in cases presenting with dysmorphic findings and Adams-Oliver syndrome, all systems should be examined. After diagnosis, follow-up and treatment should be performed by the relevant branches with a multidisciplinary approach.

Keywords: Adams-Oliver syndrome, Aplasia cutis congenita, Terminal limb defects, Hypoplastic phalanges, Extremity malformations

Correspondence: Aydin BOZKAYA, Şanlıurfa Eğitim ve Araştırma Hastanesi, Pediatri AD, Şanlıurfa, Türkiye

Phone: +90 543 688 20 61 **e-mail:** 63aydinbozkaya@gmail.com

ORCID No (Respectively): 0000-0001-8800-2753, 0000-0003-3615-7934

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INTRODUCTION

Adams-Oliver syndrome (AOS) is a rare congenital disorder first described by Adams and Oliver in 1945 (1). The incidence of AOS is approximately 1 to 3 per 10,000 births (2,3), and the case fatality rate is as high as 18-50 % (4,5). There is no gender or racial difference reported (5).

Adams-Oliver syndrome is a congenital anomaly complex characterized by the combination of aplasia cutis congenita (ACC) in the vertex region, terminal transverse limb defects (TTLD), and cutis marmorata telangiectatic congenita (CMTC) in the extremities (1,6). The etiology and pathophysiology of AOS are not fully known; genetic, environmental factors, and external causes have been blamed (7,8). Autosomal dominant, autosomal recessive, and sporadic cases have been reported (4-9). The most widely accepted model of pathophysiology is defined as tension that prevents the skin from properly developing during fetal development (5). This may be due to factors such as inadequate blood supply to the skin, fetal and placental ischemia, intrauterine infections, and failure of neural tube closure (5,10).

There is great variation in the severity of the disease among affected individuals. Most patients have ACC, typically characterized by localized loss of skin in the vertex region of the head. Although the membranous type of ACC is the most common, the defect may involve only the epidermis and dermis, cause mild scarring, or spread to the subcutaneous tissue or, rarely, to the periosteum, skull, and dura (5). ACC may also be associated with various genetic syndromes, including Bart syndrome, Setleis syndrome, and Patau syndrome (8). Extremity anomaly; typical findings include malformations of the hands, arms, feet, and/or legs, ranging from hypoplastic fingers and toes to the hands and/or lower legs (11,12). AOS may also be associated with various anomalies such as congenital cataracts, strabismus, microphthalmia, cleft lip and/or palate, short stature, immature intestinal vasculature, central nervous system malformations, mental retardation, congenital heart malformations, and hepatoportal sclerosis (13,14). It is estimated that 20 % of AOS patients are associated with congenital heart defects; reported malformations include ventricular septal defect, anomalies of the great arteries and their valves, and tetralogy of Fallot (15). In these patients, visceral abnormalities can be fatal and affect survival (16).

In this paper, we presented three cases with Adams-Oliver syndrome and tried to emphasize the importance of the multidisciplinary approach in its treatment since it affects many systems. Ethics Committee approval was obtained for the study from Harran University Clinical Research Ethics Committee (date: 13.11.2023, protocol number: 23/21/26). Verbal and written informed consents were obtained.

CASE 1

A 38-week-old baby girl was born by caesarean section, with Apgar scores of 5 and 8 at one and five minutes, respectively. The mother is 39 years old, healthy, and unrelated to her husband, the fifth living baby from her eighth pregnancy. It was reported that the mother did not have any disease and did not use any medication during pregnancy. Regular follow-ups were performed, and routine ultrasonographic imaging was normal. There was no family history of a similar disease. Her other siblings were completely healthy, and her physical examination revealed a birth weight of 2430 grams (<3p), height 43cm (<3p), and head circumference of 30.5cm (<3p). Body temperature was 36.4°C, pulse rate 135/min, and respiratory rate 37/min. Head examination revealed a 10x3 cm scalp defect extending from the anterior fontanelle to the posterior fontanelle **(Figure 1)**. Nail hypoplasia was found in the bilateral toes **(Figure 2)**. Polydactyly was present in the right upper extremity. Other system examinations were normal. Laboratory tests included whole blood count, blood biochemistry, blood gas, and C-reactive protein values, which were within the normal limits.

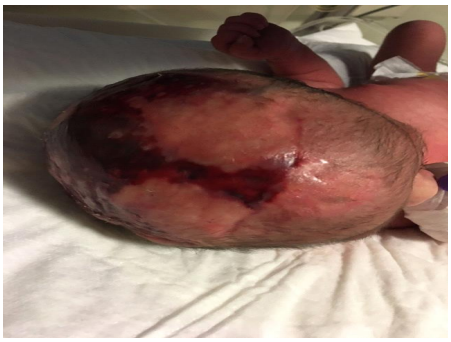


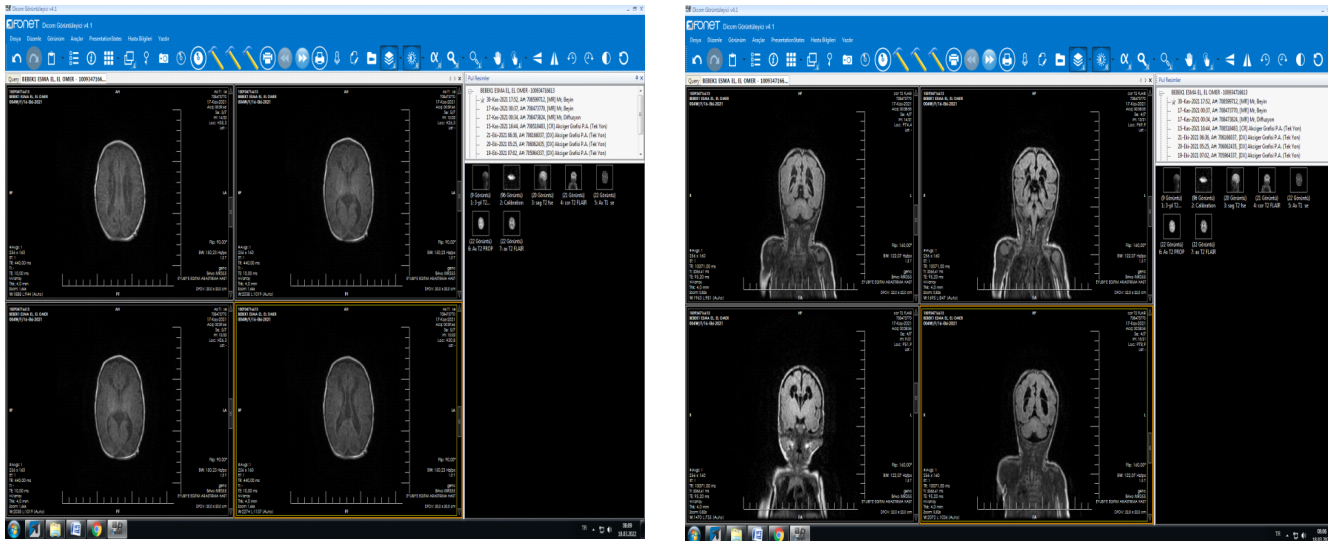
Figure 1. Scalp defect

Figure 2. Hypoplastic fingers and nails

There was no growth in blood and wound cultures. Breast milk feeding was initiated on the first postnatal day using an orogastric catheter, and on the fifth day, feeding was started by full enteral sucking without a catheter. Cranial and abdominal ultrasonography and transthoracic echocardiography were normal. Detailed ophthalmological, neurological, and audiometric evaluation was normal. Chromosome analysis was reported as 46 XX. TORCH analysis was negative. Molecular analysis could not be performed. In addition to routine neonatal care, local skin care was performed for the lesion on the scalp. The patient was discharged at 13 days of age for follow-up visits.

CASE 2

A 28-week-old baby girl was born by cesarean section. Apgar scores were 3 and 6 at the first and fifth minutes, respectively. The mother was 18 years old, healthy, and unrelated to her husband, the first living baby from her second pregnancy. It was reported that the mother did not have any disease during pregnancy, was followed up regularly, had normal routine ultrasonographic imaging, and did not use any medication during pregnancy. There was no family history of a similar disease. On physical examination, birth weight was 1400 grams (75-90p), height was 38 cm (25-50p), and head circumference was 25 cm (25-50p). Body temperature was 36.2ºC, pulse rate was 140/min, and respiratory rate was 45/min. On head examination, there was a 6x3 cm scalp defect extending from the anterior fontanelle to the posterior fontanelle and nail hypoplasia on the bilateral toes. The patient was intubated due to tachypnea, intercostal, and subcostal retractions. Surfactant treatment was given because of the reticulogranular appearance on the posterior chest X-ray and the oxygen requirement above 35%. Other system examinations were normal. In laboratory analysis, whole blood count, blood biochemistry, blood gas, and C-reactive protein values were within the normal ranges. Ampicillin and gentamicin were initiated as empirical antibiotic treatment. On the second postnatal day, minimal enteral feeding with breast milk was started using an orogastric catheter. Cranial, abdominal ultrasonography, and transthoracic echocardiography were normal. In cranial MRI, T1A and FLAIR showed hypointense, T2A marked hyperintense pathological signal changes were observed in bilateral periventricular and supraventricular white matter and the entire corpus callosum. Findings may be due to cystic encephalomalastic changes secondary to intrauterine damage or hereditary (such as cystic leukoencephalopathy). The posterior leg of the bilateral internal capsule was hyperintense in T2W compared to the thalamus, and myelination was reported to be retarded for the age of the patient **(Figure 3)**. Detailed ophthalmologic, neurologic, and audiometric evaluation was normal. Chromosome analysis was reported as 46 XX. TORCH analysis was negative. Molecular analysis could not be performed. In addition to routine neonatal care, local skin care was performed for the lesion on the scalp. She was switched to nasal CPAP on the third postnatal day and did not require oxygen on the eleventh day. Antibiotic treatment was discontinued on the fifth day as there was no growth in blood and wound cultures. On the postnatal 54th day, the patient, who reached a body weight of 2100 g, was discharged to come for the controls.



T1A T2A

Figure 3. T1A and FLAIR hypointense, T2A marked hyperintense pathological signal changes in bilateral periventricular and supraventricular white matter and entire corpus callosum on cranial MR

CASE 3

A 28-week-old baby boy was born by cesarean section. His Apgar scores are 8 and 9 at the first and fifth minutes, respectively. The mother is 28 years old, healthy, and unrelated to her husband, the third baby from her third pregnancy. It was reported that the mother had no disease during her pregnancy, was followed up regularly, had an intestinal anomaly in routine ultrasonographic imaging, and did not use any medication during pregnancy. There was no family history of a similar disease. In the physical examination of the patient whose other siblings were completely healthy, birth weight was 2600 grams (3-10p), height was 50 cm (75-90 p), and head circumference was 33 cm (25-50 p). Body temperature was 36.3oC, pulse rate was 45/min, and respiratory rate was 36/min. Head examination revealed an 11x3 cm scalp defect extending from the anterior fontanelle to the posterior fontanelle, cutis marmoratus telangiectasia, and a skin tag in the right ear **(Figure 4)**. In other system examinations, the abdomen was distended, and respiratory distress was present. In laboratory analysis, whole blood count, blood biochemistry, blood gas, and C-reactive protein values were within the normal ranges. The patient was intubated, and standing direct abdominal radiography was performed (ADBG). The radiograph was evaluated as free air in the abdomen **(Figure 5)**. The patient was referred to the pediatric surgery department and taken into the operating. It was learned that there was a perforation in the cecum, and direct repair was performed **(Figure 6)**. Ampicillin, gentamicin, and metronidazole combination was started as empirical antibiotic treatment. There was no growth in blood and wound cultures. Antibiotics were stopped on the fourteenth day. He was extubated on the 8th day of hospitalization. Breast milk feeding was initiated on postnatal day 10 using an orogastric catheter, and full enteral suction feeding was started on postnatal day 16 without a catheter. Cranial and abdominal ultrasonography and transthoracic echocardiography were normal. Detailed ophthalmologic, neurologic, and audiometric evaluation was normal. Chromosome analysis was reported as 46 XY. TORCH analysis was negative. Molecular analysis could not be performed. In addition to routine neonatal care, local skin care was performed for the lesion on the scalp. The patient was discharged at 18 days of age for follow-up.

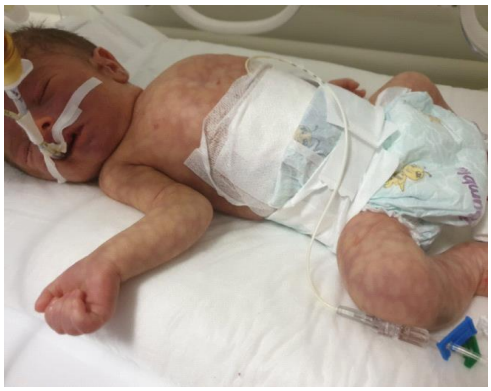


Figure 4. Diffuse cutis marmoratus

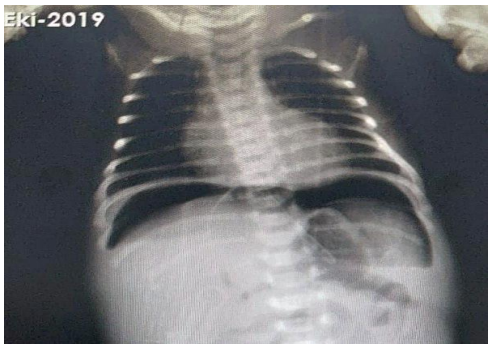


Figure 5. Bilateral sub-diaphragmatic air

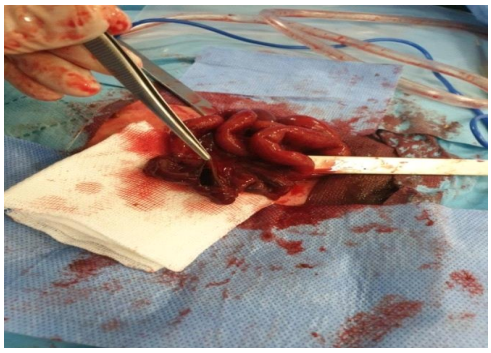


Figure 6. Intrauterine intestinal perforation

DISCUSSION

Adams-Oliver syndrome is a rare hereditary disease characterized by cutis aplasia, distal extremity anomalies, and cardiac malformations (1). Congenital scalp defects and extremity anomalies have been defined in the chromosome 3q13 region. Although it is mainly autosomal dominant, cases of autosomal recessive or sporadic occurrence with similar clinical presentation have been reported (17-19). Since our patients had no family history of scalp or limb anomalies, we defined them as three cases of sporadically inherited AOS. Major criteria for the diagnosis include transverse limb defects, cutis aplasia, and a family history of AOS. Minor criteria include cutis marmoratus, congenital heart defects, gastrointestinal, genitourinary, and vascular anomalies. The presence of two major criteria or a combination of one major and one minor criterion is sufficient for the diagnosis (20). We met the criteria for AOS in three

cases: case one with aplasia kutis, nail hypoplasia in bilateral toes, polydactyly, and kutis marmaratus in the right upper extremity, case two with aplasia kutis, kutis marmaratus, and intrauterine intestinal perforation, and case three with aplasia kutis, kutis marmaratus, and cystic encephalomalasic changes on cranial MRI.

Adams-Oliver syndrome is a complex disease with phenotypic variability and has been classified into nine types (21). Extremity defects are the most common phenotypic feature and are usually asymmetric. Short fingers, nail hypoplasia, and absence of the distal phalanx may be observed (22). Scalp defects are the second most common finding and may sometimes be accompanied by bone defects in the skull under the lesion (23). In the first of our cases, limb defects were present bilaterally; the other two cases were normal. Although all three cases had scalp defects, no bone defects were found under the lesions. Conservative treatment, wound cleansing, and antibiotics are sufficient for small, uncomplicated lesions. However, more complicated lesions may require emergency surgery due to the risk of infection and bleeding (24). All of our cases recovered with conservative treatment and did not require surgical intervention.

Congenital heart anomalies and conduction disorders accompany AOS in approximately 20 % of patients (25). Cardiopulmonary complications, including valvular defects, cardiomyopathy, heart block, pulmonary vascular malformations, and progressive pulmonary hypertension, have been reported (13,26,27). We did not detect any cardiopulmonary defect in the cases we followed.

Skin defects such as cutis marmoratus, hemangiomas, ablasia cutis congenita on the trunk and extremities, and hyperpigmented lesions may accompany AOS (28). Scalp defect and cutis marmoratus were present in all three of our cases.

Central nervous system findings, including microcephaly, encephalocele, pachygyria, cortical dysplasia, ventriculomegaly, middle cerebral artery hypoplasia, agenesis of the corpus callosum, and periventricular calcifications, are found in cases with AOS (17). In addition, microphthalmia, retinal detachment, and optic atrophy may be detected as ocular findings (29). While the transcranial ultrasonography of the first and third cases was reported as normal, in the brain MRI of the second case, T1A and FLAIR hypointense, T2A marked hyperintense pathological signal changes were reported in the bilateral periventricular and supraventricular white matter and the entire corpus callosum. Ophthalmological examinations were normal in three cases.

Rarely reported findings that are not necessarily associated with AOS include gastroschisis, umbilical hernia, diastasis recti, cryptorchidism (30), esophageal atresia, and duodenal stenosis with tracheoesophageal fistula (OA/TOF) (31). Furthermore, the relationship between intestinal obstructions and AOS has been associated with mutations in ITGP4 (32,33). In our third case, sub-diaphragmatic free air was detected on X-ray radiography taken due to abdominal distension immediately after birth. Emergency surgery was performed, and perforation was detected in the cecum. This is the first AOS study to come out with an incidental or as yet unrecognized association.

In the differential diagnosis, trisomy 13, scalp defects, amniotic band sequence, postaxial polydactyly syndrome, Johanson Blizzard syndrome, and Wolf-Hirschhorn syndrome should be considered (16).

Due to the normal karyotype structure of our cases and the absence of clinical findings of other syndromic diseases, differential diagnosis was made. The prognosis is determined by the associated cardiac and central system defects. Surgical intervention is decided according to the size and depth of the skin defect and whether the dura mater is intact or not. It has been reported that small and superficial scalp defects do not need to be treated, local care with antibacterial pomades should be applied to larger lesions, and that graft application may be required in extensive lesions and when the dura is affected (34,35). Local care was applied to our patients, and necessary graft application was planned in the follow-up.

Adams-Oliver syndrome is a rare syndrome with various clinical presentations. In cases presenting with dysmorphic findings and AOS, all systems should be examined, accompanying anomalies should be identified, and the relevant branches should perform follow-up and treatment with a multidisciplinary approach.

Ethical Approval: Ethics Committee approval was obtained for the study from Harran University Clinical Research Ethics Committee (date: 13.11.2023, protocol number: 23/21/26). An informed consent form was obtained from the family of the case.

Conflict of interest: None.

Author Contribution: Authors contribute equally to the article. They declare that they have contributed.

REFERENCES

1. Adams FH, Oliver CP. Hereditary deformities in man: due to arrested development. J Hered. 1945;36:3–7.
2. O'Neill J, Carter M, Warr RP. Aplasia cutis congenita: a case of scalp defect repair using two opposing bipedicled local flaps. J Plast Reconstr Aesthet Surg. 2010;63(3):e242–4.
3. Rogvi RE, Sommerlund M, Vestergaard ET. Aplasia cutis congenita is a rare and possibly overlooked congenital anomaly. Ugeskr Laeger. 2014;176(48):1–4.
4. Lei GF, Zhang J, Wang XB, You XL, Gao JY, Li XM, et al. Treating aplasia cutis congenita in a newborn with the combination of ionic silver dressing and moist exposed burn ointment: a case report. World J Clin Cases. 2019;7(17):2611–2616.
5. Mukhtar-Yola M, Mshelia L, Mairami AB, Otuneye AT, Yawe ET, Igoche P, et al. Aplasia cutis congenita: a report of two cases from National Hospital Abuja, Nigeria, and review of the literature. Pan Afr Med J. 2020;36:291
6. Rashid S, Azeem S, Riaz S. Adams–Oliver syndrome: a rare congenital disorder. Cureus. 2022;14(3):e23297.
7. Al Shehri A, Alfadil S, Alothri A, Alabdulkarim AO, Wani SA, Rabah SM. Aplasia cutis congenita of the scalp with a familial pattern: a case report. Case Rep Surg. 2016;2016:298302.
8. Burkhead A, Poindexter G, Morrell DS. A case of extensive aplasia cutis congenita with underlying skull defect and central nervous system malformation: discussion of large skin defects, complications, treatment, and outcome. J Perinatol. 2009;29(8):582–584.
9. Sybert VP. Aplasia cutis congenita: a report of 12 new families and review of the literature. Pediatr Dermatol. 1985;3(1):1–14.
10. Blionas A, Giakoumettis D, Antoniades E, Drosos E, Mitsios A, Plakas S, et al. Aplasia cutis congenita: two case reports and discussion of the literature. Surg Neurol Int. 2017;8:273.
11. Verdyck P, Holder-Espinasse M, Hul WV, Wuyts W. Clinical and molecular analysis of nine families with Adams–Oliver syndrome. Eur J Hum Genet. 2003;11:457–463.
12. Sankhyan N, Kaushal RK, Jaswal RS. Adams–Oliver syndrome: a case with complete expression. J Dermatol. 2006;33:435–436.
13. Zapata HH, Sletten LJ, Pierpont ME. Congenital cardiac malformations in Adams–Oliver syndrome. Clin Genet. 1995;47:80–84.
14. Kalina MA, Kalina-Faska B, Paprocka J, Jamroz E, Pyrkosz A, Marszal E, et al. Do children with Adams–Oliver syndrome require endocrine follow-up? New information on the phenotype and management. Clin Genet. 2010;78:227–235.
15. Adams–Oliver Syndrome Panel. Test code: MA1601. 8 gene panel includes assessment of non-coding variants. [Laboratory test description].
16. Küster W, Lenz W, Kääriäinen H, Majewski F. Congenital scalp defects with distal limb anomalies (Adams–Oliver syndrome): report of ten cases and review of the literature. Am J Med Genet. 1988;31:99–115.
17. McGoey RR, Lacassie Y. Adams–Oliver syndrome in siblings with central nervous system findings, epilepsy, and developmental delay: refining the features of a severe autosomal recessive variant. Am J Med Genet A. 2008;146A:488–491.
18. Temtamy SA, Aglan MS, Ashour AM, Zaki MS. Adams–Oliver syndrome: further evidence of an autosomal recessive variant. Clin Dysmorphol. 2007;16:141–149.
19. Mempel M, Abeck D, Lange I, Strom K, Caliebe A, Beham A, et al. The wide spectrum of clinical expression in Adams–Oliver syndrome: a report of two cases. Br J Dermatol. 1999;140:1157–1160.
20. Bonafede RP, Beighton P. Autosomal dominant inheritance of scalp defects with ectrodactyly. Am J Med Genet. 1979;3:354–361.
21. Brackenrich J, Brown A. Aplasia cutis congenita. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021. PMID: 30571024.
22. Whitley CB, Gorlin RJ. Adams–Oliver syndrome revisited. Am J Med Genet. 1991;40:319–326.
23. Narang T, Kanwar AJ, Dogra S. Adams–Oliver syndrome: a sporadic occurrence with minimal disease expression. Pediatr Dermatol. 2008;25:115–116.
24. Baroudi I, Alakhras O, Douri T, Alkhani N. Adams–Oliver syndrome, intestinal obstruction and heart defects: a case series of aplasia cutis congenita. Oxf Med Case Rep. 2022;2022(1):1–4.
25. Algaze C, Esplin ED, Lowenthal A, Hudgins L, Tacy TA, Selamet Tierney ES. Expanding the phenotype of cardiovascular malformations in Adams–Oliver syndrome. Am J Med Genet A. 2013;161A:1386–1389.
26. Atasoy HI, Tug E, Yavuz T, Cine N. Unique variant of Adams–Oliver syndrome with dilated cardiomyopathy and heart block. Pediatr Int. 2013;55:508–512.
27. Swartz EN, Sanatani S, Sandor GG, Schreiber RA. Vascular abnormalities in Adams–Oliver syndrome: cause or effect? Am J Med Genet. 1999;82:49–52.
28. Toriello HV, Graff RG, Florentine MF, Lacina S, Moore WD. Scalp and limb defects with cutis marmorata telangiectatica congenita: Adams–Oliver syndrome? Am J Med Genet. 1988;29:269–276.
29. Sukalo M, Tilsen F, Kayserili H, et al. DOCK6 mutations are responsible for a distinct autosomal recessive variant of Adams–Oliver syndrome associated with brain and eye anomalies. Hum Mutat. 2015;36:593–598.
30. Lehman A, Wuyts W, Patel MS. Adams–Oliver syndrome. GeneReviews®. Seattle (WA): University of Washington, Seattle; 2016 Apr 14.
31. Van Geyzel L, Gribbon C, Bradley S, Duffy D. Adams–Oliver syndrome associated with gastrointestinal malformations. Oxf Med Case Rep. 2016;2016(11):1–3.
32. Matyas M, Miclea D, Zaharie G. Uncommon association of ITGB and KRT10 gene mutation in a case of epidermolysis bullosa with pyloric atresia and aplasia cutis congenita: a case report. Front Genet. 2021;12:641977.
33. Baroudi I, Alakhras O, Douri T, Alkhani N. Adams–Oliver syndrome, intestinal obstruction and heart defects: a case series of aplasia cutis congenita. Oxf Med Case Rep. 2022;2022(1):1–4.
34. Zakanj Z, Bedek D, Kotrulja L, Ozanic Bulic S. Adams–Oliver syndrome in a newborn infant. Int J Dermatol. 2016;55:215–217.
35. Madan A, Sardana K, Garg VK. Adams–Oliver syndrome. Indian Pediatr. 2015;52:633–634.

Case Report (Olgu Sunumu)

Strangulated Inguinal Bladder Hernia: A Rare Case

Strangüle Inguinal Mesane Hernisi: Nadir Bir Olgu

Oğuzhan Fatih AY[1], Yurdakul Deniz FIRAT[2]

[1] Department of General Surgery, Kahramanmaraş Necip Fazıl City Hospital, Kahramanmaraş, Türkiye
[2] Department of General Surgery, Bursa Yuksek Ihtisas Research and Training Hospital, Bursa, Türkiye

Özet

Birçok organ inguinal herni ile ilişkili olabilir ancak mesane herniasyonu nadirdir ve vakaların sadece %1-4'ünde görülür. 48 yaşında erkek hasta gün içerisinde başlayan sol inguinal bölgede ağrılı şişlik şikayeti ile acil servise başvurdu. Vitalleri stabil olan hastada sol alt kadranda belirgin hassasiyet görülmesi ve Bilgisayarlı Tomografide intestinal strangülasyon şüphesi nedeniyle tanısal laparoskopi kararı alındı. İncelemede intestinal anslar salim olup direkt herni görüldü devamında herni onarımı için açık operasyona geçildiğinde herniye olan yapının kanlanmasının bozulmuş mesane dokusu olduğu izlendi. İskemik doku wedge rezeke edildi ve primer onarıldı. Operasyon bölgesine mesh serildi. Postoperatif üroloji kliniği ile birlikte takip edilen hasta postoperatif 3. gün sorunsuz taburcu edildi. Tekrarlayan stangüle herniasyon ile başvuran hastalarda, fıtık kesesi içinde mesane gibi retroperitoneal organlarla karşılaşma olasılığının dikkate alınması önemlidir. Ayrıca laparoskopik incelemede intraperitoneal organ herniasyonu bulunmazsa mesane herniasyonu akılda tutulmalıdır.

Anahtar Kelimeler: Mesane Hernisi, Mesane Rezeksiyonu, Strangüle Herni, İnguinal, Femoral

Abstract

Many organs can be associated with inguinal herniation, but bladder herniation is rare and occurs in only 1-4% of cases. A 48-year-old male patient attended to the emergency department with a complaint of painful swelling in the left inguinal region that started during the day. In the patient whose vitals were stable, a decision was made for diagnostic laparoscopy due to significant tenderness in the left lower quadrant and suspicion of intestinal strangulation on Computed Tomography. On examination, the intestinal loops were intact and a direct hernia was observed, and then open surgery was performed for hernia repair. Upon examination, it was observed that the blood supply to the herniated structure was impaired bladder tissue. Ischemic tissue wedge was resected and primary repaired. Mesh was utilized on the operation area. The patient, who was followed up with the postoperative urology clinic, was discharged on the 3rd postoperative day uneventfully. In patients presenting with strangulated recurrent herniation, it is crucial to consider the possibility of encountering retroperitoneal organs such as the bladder within the hernia sac. Additionally, in laparoscopic examination, if no intraperitoneal organ herniation is found, bladder herniation should be kept in mind.

Keywords: Bladder Hernia, Bladder Resection, Strangulated Hernia, İnguinal, Femoral

Correspondence: Oğuzhan Fatih AY Kahramanmaraş Necip Fazıl Sehir Hastanesi, Genel Cerrahi Bölümü, Kahramanmaraş, Türkiye

Phone: +90 344 228 28 00 **e-mail:** droguzhanf.ay@gmail.com

ORCID No (Respectively): 0000-0002-0726-3968, 0000-0002-1854-4765

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INTRODUCTION

Multiple organs may be involved with inguinal hernias, however bladder involvement is rare, occurring in 1-4% of instances (1). Femoral hernias, although more prevalent in females, are less common than inguinal hernias and are typically worsened by incarcerated or strangling of the organ that they contain.(2).

Male gender, advanced age, persistent urinary blockage, weak pelvic muscle, and obesity are risk factors for Inguinal Bladder Herniation (IBH). Significantly, only 7% of inguinal bladder hernias are identified before to surgery, with the great majority diagnosed intraoperatively and 16% diagnosed postoperatively as a result of complications such as bladder damage and leaking (3).

The literature classifies bladder hernia patients into intraperitoneal, paraperitoneal, and extraperitoneal subtypes. In the intra- and paraperitoneal but not the extraperitoneal subtypes, the peritoneum prolapsed **(Figure 1)** (4). Due to the retroperitoneal placement of the bladder, it was clinically significant that the prolapsed bladder could not be recognized intraperitoneally, and the hernial orifice could not be observed from inside the intraperitoneal cavity in instances of the extraperitoneal type (4).

In this case report, we will discuss a patient with recurrent inguinofemoral hernia on the left side.

CASE REPORT

A 48-year-old male patient attended the emergency room complaining of severe swelling in his left groin. The patient had undergone open surgery for bilateral inguinal hernias five years ago and was free of any known chronic diseases. The patient did not experience nausea or vomiting, burning while peeing, or urinating by pressing with his hands on the suprapubic region.

The patient's BMI was 26.2. During the patient's emergency room evaluation abdominal exam revealed no tenderness or rebound. The left inguinal area was quite sensitive.

The laboratory test revealed no leukocytosis, and renal function was normal. In the urine sample, there was no evidence of blood or infection.

Due to the patient's assessment being conducted during the night shift, an ultrasound examination was not feasible. By computed tomography (CT) with IV contrast, a left inguinal herniation was diagnosed radiologically. A hernia has been documented to contain intestinal loops or extraperitoneal tissue **(Figure 2)**.

The decision to perform a diagnostic laparoscopy was based on the patient's examination findings and radiographic evaluation. Laparoscopy was initially preferred because there was a need to check the bowel loops due to radiological guidance. Before the procedure, a Foley catheter was inserted into the patient. A transabdominal investigation demonstrates that the hernia sac contained no ans. However, because the hernia was not classified as transabdominal, a left inguinal incision was attempted. During the evaluation, it was observed that the strangulated, blood-supply-impaired bladder diverticular tissue was herniated **(Figure 3)**. Tissue with restricted blood supply was excised; the bladder mucosa was confirmed following resection; no extravasation of the urine was seen. The incision was closed with Vicryl 3.0 that was continuously locked, including the mucosa. The inguinal hernia was then repaired with a mesh.

It was explained by the presence of a narrow-necked bladder diverticulum herniation, as determined by the post-repair evaluation; the herniated area on the preoperative CT image is the bladder, but it lacks contrast.

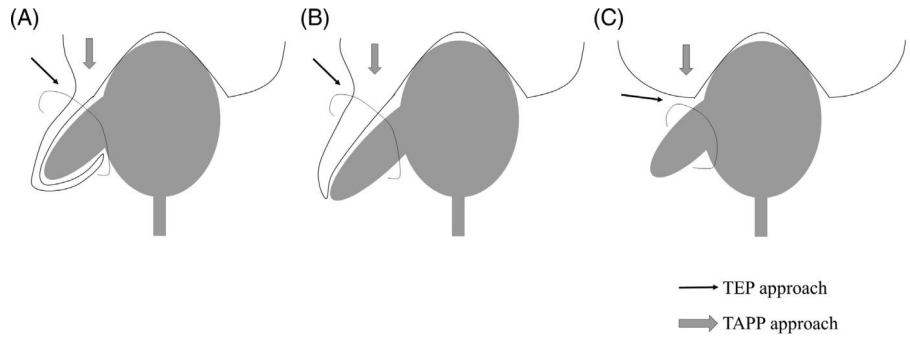

Figure 1. Subtypes of bladder herniation (the transabdominal preperitoneal [TAPP] surgery, the totally extraperitoneal [TEP] surgery) (4) *(Written permission was obtained from the author and the journal that published the cited article to utilize their images).*

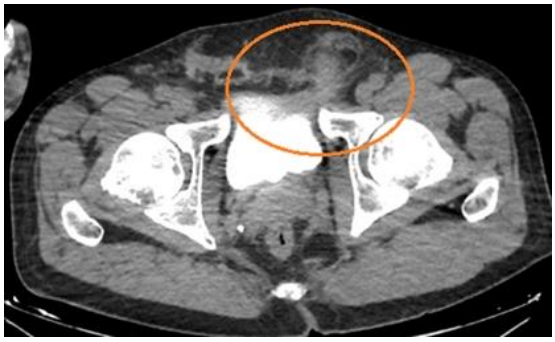

Figure 2. The marked area shows the herniated area on CT

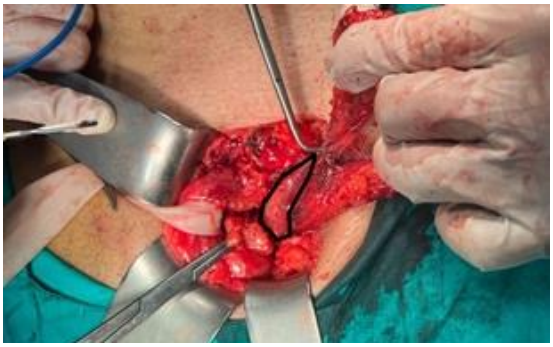

Figure 3. The marked area describes a herniated bladder

During the postoperative phase, the patient was followed by the general surgery and urology clinics. Irrigation was applied to control the hematuria that developed on the first postoperative day. Postoperative cystography revealed that the bladder's integrity was intact. The PSA test result was normal.

The patient was discharged uneventfully on the 3rd postoperative day. Foley catheter was removed at postoperative 3rd week as a result of urology and general surgery outpatient follow-ups.

The bladder was confirmed to be intact during a diagnostic cystoscopy conducted by the urology clinic two months after surgery. There was no evidence of bladder outlet obstruction (benign prostate hyperplasia, urethral stricture, etc.) or urological cancer.

The patient provided written consent for the use of his clinical data to be utilized for academic objectives.

DISCUSSION

Although minor bladder hernias are asymptomatic, patients with large bladder hernias typically complain of scrotal edema, decreased force of stream on urination, dysuria, double micturition due to manual compression of the hernia, and reduction of scrotal edema after urination, known as Mery's sign (5). Both the Mery sign and urine symptoms were absent in our patient.

The pathogenesis of an inguinal bladder herniation involves the pushing of the bladder and a peritoneal sheath that forms its sac via a weak spot in the abdominal fascia

Multiple factors may lead to the formation of an inguinal bladder hernia, such as bladder outlet obstruction, pelvic muscle weakness, decreased bladder tone, and obesity. Among the risk variables are male gender, advanced age, and benign prostatic hypertrophy (3). Our patient was not obese, and the previously suggested urological mechanical restriction to explain the bladder herniation was not observed during the postoperative urological follow-up.

Most bladder hernias are identified during surgery (77%), while only 7% are found before surgery and 16% are found after surgery due to complications (4). We confirmed a bladder hernia during the procedure after analyzing the differential diagnosis by radiology.

According to the data by Hasegawa *et al.,* the incidence of inguinal bladder hernia was 2.8%, and it was twice as common on the right side (4). According to the classification of inguinal bladder hernia presented in this paper, our patient had a paraperitoneal type C hernia. As highlighted in the same article, it was clinically significant that the prolapsed bladder could not be recognized intraperitoneally due to its retroperitoneal placement and that the hernial orifice could not be identified from within the intraperitoneal cavity in cases of the extraperitoneal variety (4). Therefore, we conclude that the transabdominal diagnostic laparoscopic examination failed to reveal the herniated structure.

Indications for partial bladder resection include a hernia neck with a diameter of less than 5 mm, bladder wall necrosis, perforation, and the presence of a diverticulum or bladder tumor. There is no consensus on the optimal repair strategy; the surgical approach is based on the surgeon's preference and the state of the patient (5). Because the herniated tissue's blood supply was compromised, we decided on resection.

As a result, inguinal bladder hernia is a rare condition requiring a high level of clinical suspicion for diagnosis. Preoperative imaging is crucial to avoid iatrogenic damage.

REFERENCES

1. Mejri R, Chaker K, Mokhtar B, Rhouma SB, Nouira Y. Inguinal bladder hernia: a case report. J Surg Case Rep. 2021;2021(9):rjab386. doi:10.1093/jscr/rjab386
2. Biswas S, Morel EM, Petersen K, McCrae A. Incarcerated Bladder Diverticulum in a Femoral Hernia Presenting as Recurrent Hematuria. Cureus. 2020;12(8):e9681. doi:10.7759/cureus.9681
3. Elkbuli A, Narvel RI, McKenney M, Boneva D. Inguinal bladder hernia: A case report and literature review. Int J Surg Case Rep. 2019;58:208-11. doi:10.1016/j.ijscr.2019.04.040
4. Hasegawa S, Ogino N, Kanemura T, Sakao J, Fujii H, Kikkawa et. al. Clinical characteristics of inguinal bladder hernias and total extraperitoneal repair. Asian Journal of Endoscopic Surgery. 2021;14(3):394–400. doi: 10.1111/ases.12878
5. Karanikas M, Kofina K, Foutzitzi S, Deftereos S, Effraemidou E, Lyratzopoulos et. al. Urinary bladder-containing incarcerated inguinoscrotal hernia: a case report. J Surg Case Rep. 2020;(11): rjaa092. doi: 10.1093/jscr/rjaa092

Review (Review)

A Detailed Look At Autonomic Involvement in Multiple Sclerosis: Clinical and Diagnostic Approach

Multipl Skleroziste Otonomik Tutuluma Detaylı Bir Bakış: Klinik ve Tanısal Yaklaşım

Buket TUGAN YILDIZ[1]

[1] Sütçü İmam University, Faculty of Medicine, Department of Neurology, Kahramanmaraş, Türkiye

Özet

Multipl skleroz, merkezi sinir sisteminin otoimmün bir hastalığıdır ve gençlerde engelliliğin en yaygın nedenlerinden biridir. Somatik sinir sisteminde olduğu gibi otonom sinir sistemini de çok çeşitli semptom ve bulgularla etkiler. Hastaların %85'inde otonom sinir sistemi tutulumunun klinik bulguları saptanmıştır. Mesane ve bağırsak sorunları, cinsel, kardiyovasküler, termoregülatuar disfonksiyon, ortostatik hipotansiyon ve yorgunluk otonom sinir sistemi tutulumunun bulguları arasındadır. Otonomik semptomlar en az motor semptomlar kadar özürlülüğe ve yaşam kalitesinde azalmaya neden olur. Hastalar otonomik semptomlar açısından sorgulanmalı ve gerekirse tedavi başlanmalıdır.

Anahtar Kelimeler: Multipl sklerozis, otonomik tutulum, otonom sinir sistemi

Abstract

Multiple sclerosis is an autoimmune disease of the central nervous system and one of the most common causes of disability in young people. It affects the autonomic nervous system, presenting a wide range of symptoms and signs similar to those of the somatic nervous system. Clinical signs of autonomic nervous system involvement were found in 85% of patients. Bladder and bowel problems, sexual dysfunction, cardiovascular dysfunction, thermoregulatory dysfunction, orthostatic hypotension, and fatigue are among the findings of autonomic nervous system involvement. Autonomic symptoms cause disability and decreased quality of life at least as much as motor symptoms. Patients should be questioned regarding autonomic symptoms, and treatment should be initiated if necessary.

Keywords: Multiple Sclerosis, Autonomic involvement, Autonomic nervous system

Correspondence: Buket TUGAN YILDIZ Kahramanmaraş Sütçü İmam Üniversitesi, Kahramanmaraş, Türkiye

Phone: +90 533 489 06 19 **e-mail:** bukettugan@yahoo.com

ORCID No: 0000-0001-6783-2336

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INTRODUCTION

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system characterized by inflammation, demyelination, and axonal loss and is one of the most common causes of neurological disability in young people (1). It affects more than 2 million people worldwide (2).

MS affects the somatic and autonomic nervous system with a wide range of symptoms and signs. Autonomic dysfunction may occur in various stages of multiple sclerosis (3). Clinical signs of autonomic nervous system involvement were found in 85% of patients, and laboratory findings in 56% (4). Bladder and bowel problems, sexual, cardiovascular, thermoregulatory dysfunction, orthostatic hypotension, and fatigue are among the findings of autonomic nervous system involvement.

In Which Systems And With Which Clinical Findings Does Autonomic Involvement Occur?

The most common site of autonomic dysfunction in multiple sclerosis is the urinary system (4). Both sympathetic and parasympathetic systems influence the urinary system. While the sympathetic system provides urine storage, activation of the parasympathetic system allows the bladder to empty by contracting the bladder muscles (5). Frequent urination, sudden feeling of urgency, nocturia, intermittent urination, and difficulty at the onset of urination are clinical findings related to autonomic involvement of the urinary system (6). The location of the MS plaque is important in the pathophysiology of urinary system symptoms. The results obtained from studies suggest that disruption of the connections between the sacral and pontine micturition centers causes urinary symptoms. MS plaques are most commonly located on the cervical spinal cord, and the lateral corticospinal (pyramidal) and reticulospinal tracts are frequently affected. Since these two pathways are responsible for the innervation of the bladder detrusor muscle and external urethral sphincter, urinary system dysfunction is frequently encountered in MS (6-8).

The gastrointestinal system is one of the systems in which autonomic dysfunction is seen in MS and affects morbidity. Symptoms of gastrointestinal involvement include diarrhea, constipation, fecal incontinence, nausea, vomiting, and gastroesophageal reflux. Diarrhea and constipation are symptoms highly influenced by autonomic mechanisms, then sympathetic changes triggered by peripheral inflammatory processes may be responsible for the severe diarrhea and constipation found in the early stages of MS (5).

Various clinical findings may occur because of both sympathetic and parasympathetic involvement in the cardiovascular system. Cardiovascular complaints are one of the most common complaints of MS patients, and blood pressure and heart rate fluctuations can be seen frequently. Although it is thought to be caused by lesions in the midbrain, limbic lobe, insula, and parietal lobe, the exact pathophysiology is unknown. The triggering of catecholamine release by inflammatory lesions in the central nervous system may be considered as another mechanism (9).

Another form of autonomic involvement thought to be related to the severity and type of the disease is sexual dysfunction (10). 70% of MS patients complain about this issue (11). The most common symptom is erectile dysfunction (5). Other symptoms include ejaculation disorder, anorgasmia, decreased lubrication, and decreased libido. The parasympathetic system is responsible for erection, and the sympathetic system for ejaculation. Studies have shown that sexual dysfunction is related to total lesion area on magnetic resonance imaging, hypointense lesion area, atrophy on T1-weighted images, and lesion load in the pons (12-14).

Fatigue is a common symptom seen in 90% of MS patients. Studies suggest that autonomic involvement, vagal and sympathetic activity disorders, may be the cause of fatigue. Patients complain of fatigue from the early stages of their disease (15). In previous studies, no correlation was found between fatigue and disease duration and severity (16). This perception of fatigue is thought to be caused by inflammation in the amygdala, hypothalamus, insular cortex, and anterior cingulate cortex (15).

What Tests Are Performed To Detect Autonomic Involvement?

Since urinary system involvement is common in patients with MS, detailed urinary system evaluation should be performed (4). Urinary ultrasonography can be used to investigate urinary retention; urodynamic examination can be used to measure bladder function, urine flow, bladder internal pressure, and pediatric muscle activity; and somatosensory evoked potential can be used for pudendal nerve analysis (3).

Patients should be investigated in the presence of diarrhea, constipation, nausea, vomiting, and gastrointestinal reflux. Anal manometer, colon transit time, external anal electromyography, radionuclide gastric emptying time can be used for gastrointestinal system (5).

Electromyography, heart rate variability measurement, blood pressure measurement, tilt test, handgrip

test, corrected QT distance, and sympathetic skin response can be used to detect autonomic abnormality of the cardiovascular system (3,17).

Sympathetic skin response in the genital area and somatosensory evoked potentials of the pudendal nerve can be used to test sexual dysfunctions in terms of autonomic involvement (3).

Fatigue is a subjective complaint in MS patients. The fatigue severity scale can be used for screening purposes in patients without complaints (18).

Which Treatments Can Be Used in Which System Involvement?

While the sympathetic system provides urine storage, activation of the parasympathetic system allows the bladder to empty by contracting the bladder muscles. In urinary system treatment, bladder emptying is tried to be prevented, and the sphincter is tried to be relaxed, and treatment is decided according to the patient's condition. In overactive bladder, treatments such as oxybutynin and local botulinum toxin injection are used to prevent detrusor hyperactivity. Tricyclic antidepressants may be useful in mild urge incontinence (3).

Pelvic floor muscle training should be recommended in addition to medical treatment. Intermittent and permanent urinary catheterization is recommended in patients who do not respond to medical treatment (3).

Topical estrogen in women and phosphodiesterase 5 inhibitors in men may be used in sexual dysfunctions related to autonomic involvement in MS patients (3).

Patient education is primarily important in autonomic hypotension and postural orthostatic tachycardia syndrome. Volume expanders, vasoconstrictors, and adrenergic antagonists can be used in pharmacotherapy (19).

In addition to non-pharmacologic methods such as sleep hygiene and physical exercise, pharmacologic treatment methods such as Amantadine and Modafinil can also be used to reduce the perception of fatigue (3).

CONCLUSION

Autonomic symptoms seen in MS patients may not be questioned and may be ignored in busy outpatient clinics, but autonomic symptoms cause disability and decreased quality of life at least as much as motor symptoms. Patients should be questioned in terms of autonomic symptoms, and treatment should be initiated if necessary.

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REFERENCES

1. Oh J, Vidal-Jordana A, Montalban X. Multiple sclerosis: clinical aspects. Curr Opin Neurol. 2018 Dec;31(6):752-759. doi: 10.1097/WCO.0000000000000622. PMID: 30300239.
2. Reich DS, Lucchinetti CF, Calabresi PA. Multiple Sclerosis. N Engl J Med. 2018 Jan 11;378(2):169-180. doi: 10.1056/NEJMra1401483. PMID: 29320652; PMCID: PMC6942519.
3. Sirbu CA, Mezei RM, Falup-Pecurariu C, Bratu OG, Sirbu AM, Ghinescu MC, et al. Autonomic dysfunctions in multiple sclerosis: Challenges of clinical practice (Review). Exp Ther Med. 2020 Dec;20(6):196. doi: 10.3892/etm.2020.9326. Epub 2020 Oct 14. PMID: 33123226; PMCID: PMC7588778.
4. de Seze J, Stojkovic T, Gauvrit JY, Devos D, Ayachi M, Cassim F, et al. Autonomic dysfunction in multiple sclerosis: cervical spinal cord atrophy correlates. J Neurol. 2001 Apr;248(4):297-303. doi: 10.1007/s004150170204. Erratum in: J Neurol 2001 Dec;248(12):1111. PMID: 11374094.
5. Racosta JM, Kimpinski K, Morrow SA, Kremenchutzky M. Autonomic dysfunction in multiple sclerosis. Auton Neurosci. 2015 Dec;193:1-6. doi: 10.1016/j.autneu.2015.06.001. Epub 2015 Jun 7. PMID: 26070809.
6. Nakipoglu GF, Kaya AZ, Orhan G, Tezen O, Tunc H, Ozgirgin N, et al. Urinary dysfunction in multiple sclerosis. J Clin Neurosci. 2009 Oct;16(10):1321-4. doi: 10.1016/j.jocn.2008.12.012. Epub 2009 Jun 27. PMID: 19560927.
7. Aharony SM, Lam O, Corcos J. Evaluation of lower urinary tract symptoms in multiple sclerosis patients: Review of the literature and current guidelines. Can Urol Assoc J. 2017 Jan-Feb;11(1-2):61-64. doi: 10.5489/cuaj.4058. PMID: 28443147; PMCID: PMC5403674.
8. Litwiller SE, Frohman EM, Zimmern PE. Multiple sclerosis and the urologist. J Urol 1999 Mar;161(3):743-57. Erratum in: J Urol 1999 Jul;162(1):172. PMID: 10022678.
9. Sörös P, Hachinski V. Cardiovascular and neurological causes of sudden death after ischaemic stroke. Lancet Neurol. 2012 Feb;11(2):179-88. doi: 10.1016/S1474-4422(11)70291-5. PMID: 22265213.
10. Lensch E, Jost WH. Autonomic disorders in multiple sclerosis. Autoimmune Dis. 2011;2011:803841. doi: 10.4061/2011/803841. Epub 2011 Apr 17. PMID: 21603189; PMCID: PMC3096149.
11. Zorzon M, Zivadinov R, Monti Bragadin L, Moretti R, De Masi R, Nasuelli D, et al. Sexual dysfunction in multiple sclerosis: a 2-year follow-up study. J Neurol Sci. 2001 Jun 15;187(1-2):1-5. doi: 10.1016/s0022-510x(01)00493-2. PMID: 11440738.
12. Barak Y, Achiron A, Elizur A, Gabbay U, Noy S, Sarova-Pinhas I. Sexual dysfunction in relapsing-remitting multiple sclerosis: magnetic resonance imaging, clinical, and psychological correlates. J Psychiatry Neurosci. 1996 Jul;21(4):255-8. PMID: 8754594; PMCID: PMC1188782.
13. Janardhan V, Bakshi R. Quality of life and its relationship to brain lesions and atrophy on magnetic resonance images in 60 patients with multiple sclerosis. Arch Neurol. 2000 Oct;57(10):1485-91. doi: 10.1001/archneur.57.10.1485. PMID: 11030802.

14. Zivadinov R, Zorzon M, Locatelli L, Stival B, Monti F, Nasuelli D, et al. Sexual dysfunction in multiple sclerosis: a MRI, neurophysiological and urodynamic study. J Neurol Sci. 2003 Jun 15;210(1-2):73-6. doi: 10.1016/s0022-510x(03)00025-x. PMID: 12736092.
15. Hanken K, Eling P, Hildebrandt H. The representation of inflammatory signals in the brain - a model for subjective fatigue in multiple sclerosis. Front Neurol. 2014 Dec 11;5:264. doi: 10.3389/fneur.2014.00264. PMID: 25566171; PMCID: PMC4263099.
16. Sander C, Hildebrandt H, Schlake HP, Eling P, Hanken K. Subjective Cognitive Fatigue and Autonomic Abnormalities in Multiple Sclerosis Patients. Front Neurol. 2017 Sep 13;8:475. doi: 10.3389/fneur.2017.00475. PMID: 28955298; PMCID: PMC5601401.
17. Kodounis A, Stamboulis E, Constantinidis TS, Liolios A. Measurement of autonomic dysregulation in multiple sclerosis. Acta Neurol Scand. 2005 Dec;112(6):403-8. doi: 10.1111/j.1600-0404.2005.00446.x. PMID: 16281924.
18. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol. 1989 Oct;46(10):1121-3. doi: 10.1001/archneur.1989.00520460115022. PMID: 2803071.
19. Adamec I, Habek M. Autonomic dysfunction in multiple sclerosis. Clin Neurol Neurosurg. 2013 Dec;115 Suppl 1:S73-8. doi: 10.1016/j.clineuro.2013.09.026. PMID: 24321161.

Derleme (Review)

Pediatrik Görüntülemede Radyasyon

Radiation In Pediatric Imaging

Adil DOĞAN[1]

[1] Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, Kahramanmaraş, Türkiye

Özet

Çocuklarda tanısal ve girişimsel görüntüleme yöntemlerinde kullanılan iyonlaştırıcı radyasyon direk radyografi, bilgisayarlı tomografi ve floroskopidir. Teknolojinin hızlı bir şekilde gelişmesi ile birlikte hastaların tanı ve tedavisinde iyolaştırıcı radyasyon kullanımı teknolojik gelişmelere paralel olarak artış göstermiştir. Bireysel taramalarla ilişkili radyasyon dozundaki kayda değer düşüşlere rağmen, tıbbi görüntülemenin artan kullanımı radyasyona maruz kalmaya önemli bir katkıda bulunmaktadır. Çocuklarda bilgisayarlı tomografi kullanımları son yıllarda hızlı bir artış göstermiştir. İyonlaştırıcı radyasyon içeren her prosedür için radyolojik prosedürlerin titiz bir şekilde gerekçelendirilmeli ve iyonlaştırıcı olmayan görüntüleme yöntemlerinin kullanımı her zaman düşünülmelidir. İyonize radyasyon ile tıbbı görüntüleme esnasında tanı konabilecek görüntü oluşturan en düşük doz ile görüntüleme yapılmalıdır. Görüntüleme işleminde çocuklarda ilk tercih noniyonizan radyolojik modaliteler kullanılmalıdır.

Anahtar Kelimeler: Çocuklar, Radyasyon, Radyoloji, Korunma

Abstract

Diagnostic and interventional imaging in children uses ionising radiation, including direct radiography, computed tomography, and fluoroscopy. Technological advances have led to wider use of ionising radiation in diagnosis and treatment. While radiation doses per scan have decreased, the rise in medical imaging has significantly increased overall radiation exposure. The use of computed tomography in children has risen rapidly. Radiological procedures involving ionising radiation must be clearly justified, and non-ionising imaging options should always be considered. Medical imaging using ionising radiation should apply the lowest effective dose for diagnostic quality. Non-ionising modalities should be the primary choice for imaging children.

Keywords: Children, Radiation, Radiology, Protection

Yazışma Adresi: Adil DOĞAN, Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, Kahramanmaraş, Türkiye

Telefon: +90 505 484 48 13 **e-mail:** dradildogan@hotmail.com

ORCID No: 0000-0002-2501-1852

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GİRİŞ

İyonlaştırıcı radyasyon bir yüzyıldan fazla süredir hastaların tanı ve tedavisinde kullanılmaktadır. Radyolojik görüntüleme yöntemleri insan organlarının fizyolojik (fonksiyonel) ve biyolojik sistemlerinin anatomik iç yapılarının görüntülerini üretir. Tarama, tanı, tedavi yanıtını değerlendirme ve prognozu tahmin etme gibi durumlarda hasta yönetimine önemli katkıda bulunur. Modern tanısal radyoloji daha hızlı ve kesin tanı sağlayarak hastalıkların büyük bir bölümünün izlenmesine imkan tanır. Tıbbi radyografi, vücudun iç kısımlarının röntgen teknikleri kullanılarak görüntülenmesini sağlayan çeşitli çalışma türlerini kapsayan geniş bir terimdir. Radyolojik görüntüleme yöntemleri direkt grafi (DR), bilgisayarlı tomografi (BT), floroskopi, ultrasonografi (USG) ve manyetik rezonans görüntülemedir (MRG). İyonlaştırıcı radyasyon pediatri hastalarında tanısal ve girişimsel görüntüleme yöntemlerinde kullanılan DR, BT ve floroskopidir. Teknolojinin hızlı bir şekilde gelişmesi ile birlikte hastaların tanı ve tedavisinde iyolaştırıcı radyasyon kullanımı teknolojik gelişmelere paralel olarak artış göstermiştir. Bireysel taramalarla ilişkili radyasyon dozundaki kayda değer düşüşlere rağmen, tıbbi görüntülemenin artan kullanımı radyasyona maruz kalmaya önemli bir katkıda bulunmaktadır (1-4). İyonlaştırıcı radyasyon kullanımının artması ile birlikte radyasyon maruziyeti hastalarda önemli problem olarak karşımıza çıkmaktadır.

Bu yayının amacı pediatrik hastalarda sık kullanılan radyolojik görüntüleme yöntemlerinin seçiminde öncelikle radyasyon içermeyen radyolojik modalitelerin tercih edilmesi ve radyasyon içeren modaliteleri kullanmak zorunda olduğumuz durumlarda hastanın almış olduğu radyasyon dozunu nasıl azaltabiliriz.

PATOFİZYOLOJİ

Radyasyon canlı organizmalar üzerindeki etkisini hücresel ve organizma düzeyinde göstermektedir. Hücresel düzeydeki etki dozdan bağımsız olup sitokastik etkidir. Sitokastik etki; karsinogenesis, genetik hasar, DNA moleküllerinde hasar (DNA tek ve çift sarmal kırılmaları), genetik kodda değişiklik ve mutasyonlara neden olmaktadır. Radyasyonun organizma düzeyindeki etkileri alınan radyasyonun dozuna ve süresine bağlıdır. Bu etki deterministik etkidir ve başlıca hücre ölümüne neden olur. Deterministik etki alınan radyasyon dozunun şiddetine bağlı olarak artar. Hızlı çoğalan ve bölünme dönemindeki hücreler radyasyonu çok duyarlıdır; kemik iliği ana hücreleri, lenfoid doku. Lenfositlerin düşük dozlarda bile sayılarında azalma görülür. Tanısal radyolojide deterministik etki görülmez (2,5).

EPİDEMİYOLOJİ

Çocuklarda bilgisayarlı tomografi kullanımları son yıllarda hızlı bir artış göstermiştir. BT kullanımın artması tanısal açıdan önemli bir katkı sağlarken yüksek doz radyasyon maruziyeti söz konusudur. Radyasyon maruziyetinde en önemli problem kanser riskinin artmasıdır. Kanserlerin %2 kadarı (ve yılda 15.000 ölüm) tek başına bilgisayarlı tomografiye maruz kalmayla ilişkilendirilebilir. Bebek ve çocukluk dönemindeki radyasyon maruziyeti erişkinlere oranla kanser gelişme riski daha yüksektir (6,7). Literatürde radyasyona bağlı kanser riski çocuklarda yetişkinlerden 2-10 kat daha fazla olduğu tespit edilmiş (8). Çocuklarda ve genç erişkinlerde en sık görülen radyojenik maligniteler lösemi ve beyin tümörleridir. En az bir kafa BT'si olan Tayvanlı çocuklarda yapılan çalışmada özellikle ilk kafa BT taramasından dört ila beş yıl sonra, eşleşen bir karşılaştırma grubuna göre istatistiksel olarak anlamlı derecede daha yüksek iyi huylu beyin tümörü riskine sahip olduğu tespit edilmiş. Literatürde son yıllarda yapılan çalışmada BT taraması yapılan çocuklarda genel kanser insidansı malign santral sinir sitemi tümörü (CNS) dahil olmak üzere beklenenden 1.5 kat daha yüksekti. Kolon, kemik, kalın bağırsak, yumuşak doku, tiroid kanserleri ve melanom dışı cilt kanseri için de istatistiksel olarak anlamlı fazlalıklar tespit edilmiştir (9,10).

Birleşik Krallık'ta yakın zamanda yapılan bir araştırma, çocukların BT'den 30 mGy veya daha yüksek bir aktif kemik iliği dozu alanların lösemi riskinin 3,2 kat daha fazla olduğu ve 50 mGy veya daha yüksek bir beyin dozu alan çocukların beyin kanseri riskinin 2,8 kat daha fazla olduğu tespit edilmiştir (11).

Aynı dozu alan yetişkinlere kıyasla, pediyatrik hastalarda kansere yakalanma riski daha yüksektir. Çocuklarda daha uzun yaşam beklentisi, radyasyonun zararlı etkilerinin ortaya çıkması ve gelişmesi için daha fazla zaman sağlar. Çocuklarda kanser riskinin yüksek olması bu nedenler ile açıklanabilir (12).

KLİNİK KULLANIM

Çocuklardaki tıbbi görüntülemenin çoğu radyasyon temelli görüntülemelerdir. Radyografi, floroskopi ve BT'dir (14). Amerika Birleşik Devletleri'nde Radyasyondan Korunma ve Ölçümler Ulusal Konseyi (NCRP), yakın tarihli yayınlanan bir raporunda 2006 yılından önceki 25-30 yıllık sürede tıbbı görüntüleme amaçlı kişi başı radyasyon miktarının 5-6 kat arttığını belirtmiştir. NRCP nin 2016 yılında raporunda çocukların yıllık radyasyon maruziyetlerinin %9 tıbbi görüntüleme % 91 doğal kaynaklardan olduğunu belirtilmiştir. Çocuklarda

radyasyon kullanan tıbbi görüntüleme modlitelerinin %86'sı radyografi oluştururken tıbbı görüntüleme ile maruz kalınan radyasyonun % 84 den BT sorumludur. Pediatrik görüntülemede kullanılan modalitelerde maruz kalınan radyasyonun % 84 BT, % 6 radyografi, % 4 girişimsel işlemler, %3 floroskopi ve %3 nükleer görüntülemeler sorumludur (13,14).

Avrupa pediatrik görüntüleme komitesinin (PIDRL) yayınladığı raporda radyasyon kullanılan tıbbı görüntüleme modalitelerinin %92 radyografi, %5 BT ve %3 floroskopi olduğunu söylemektedir. Radyografi işlemlerinin büyük çoğunluğunu ekstremite ve akciğer görüntüleme oluşturmaktadır. Floroskopik işlemlerinin çoğunu voiding sistoüretrografi (%34), üst ve alt gastrointestinal (%55) görüntülemeler oluşturmaktadır. BT görüntülemenin çoğunluğunu baş-boyun (%49) ve toraks (%25) oluşturmaktadır (15).

Çocuklarda tıbbi görüntüleme esnasında maruz kalınan radyasyon dozu hastanın yaşı, görüntüleme bölgesinin kalınlığı, hastanın ağırlığı ve görüntüleme bölgesinin uzunluğuna bağlıdır. Uluslararası radyolojik koruma komisyonu (ICRP) radyasyon dozunu belirlemek için ortak bir değer olan diagnostik referans düzeyi (DRL) kullanılmasını tavsiye etmişlerdir. DRL değeri tavsiye niteliğindedir ve uygulamada, değer düzenli olarak aşılırsa ilgili uygulamanın araştırılması gerektiği şekilde ayarlanır. Bu, mutlaka kabul edilemez bir uygulama olduğu anlamına gelmez (2).

ICRP normal bireylerde tüm vücut dozu 5 yıl için ortalama 1 mSv/yıl, herhangi bir yılda maksimum tüm vücut dozu 5 mSv, organlar ve deri için 50 mSv'dir. Radyolojik görüntüleme yöntemlerinin çocuklarda efektif doz değerleri **(Tablo 1)**. Örneğin lösemi 0.01 Gy ışınlama ile olabileceği gibi 1 Gy de gelişebilir. Radyasyona bağlı kanser gelişimini etkileyen en önemli faktörler; yaş, cinsiyet ve genetik faktördür (16,17).

Tablo 1. Çocuklarda sık kullanılan radyolojik görüntüleme yöntemlerinin 5 yaşındaki hastada efektif doz değerleri (9)

Görüntüleme tipi	Efektif doz (mSV)*
Akciğer direkt grafi	0.04
Kafa direkt grafi	0.06
Lomber direkt grafi	0.44
Abdomen direkt grafi	0.4
DMSA	1
MAG-3 renogram	0.7
Baryumlu floroskopi	1
Beyin BT	2
Gögüs BT	2.5
Abdomen/pelvis BT	5

*1mSv=1mGy

NON İYONİZAN MODALİTELER

USG, pediatrik hastalarda kullanılan non-iyonizan bir görüntüleme tekniğidir. Çocuklar tarafından iyi tolere edilen ultrason çok çeşitli pediatrik görüntüleme endikasyonları içinde birinci basamak radyolojik modalitedir. Hem acil hem de ayakta tedavi ortamlarında kolayca erişilebilen ultrason, radyologlara iyonlaştırıcı radyasyon veya sedasyon kullanmadan dinamik bir görüntüleme sağlar (18). USG, pediatrik hastalarda karın bölgesini değerlendirmek için genellikle ilk seçenek görüntüleme olmalıdır. Deneyimli ellerde USG çok fazla bilgi sağlayabilir ve BT'yi önleyebilir; örneğin, USG akut apandisit şüphesi olan çocuklarda ilk düşünülen tetkik olmalıdır (19).

MRG, güçlü ve çok yönlü bir tanı aracıdır. MR teknoloji uygulamaları yeni doğan yoğun bakım bebekler de dahil olmak üzere tüm hasta popülasyonları için hızla genişlemektedir (20). MRG radyo dalgalarının kullanıldığı non-iyonizan, pediatrik görüntülemeye uygun, çok kullanılışlı radyolojik modalitelerden biridir. Beyin, kas iskelet sistemi, abdomen ve omurga ile ilgili mükemmel ayrıntılar sunar. İnceleme süresinin uzun olması ve hasta kooperasyonu sağlanması için sedasyon ve anestezi dezavantajları olarak karşımıza çıkmaktadır (9).

KORUNMA

Yukarıda bahsedilen çalışmalarda çocuklarda radyasyonun kanser riskini artırdığı konusunda hem fikiriz. İyonlaştırıcı radyasyonu içeren her görüntülemenin gerekçesi, her hastada ve özellikle pediatrik hastalarda önemlidir (12).

İyonlaştırıcı radyasyon içeren her prosedür için radyolojik prosedürlerin titiz bir şekilde gerekçelendirilmesinin önemi vurgulanır ve iyonlaştırıcı olmayan görüntüleme yöntemlerinin kullanımı her zaman düşünülmelidir. Radyolojik korumanın optimizasyonunun temel amacı, görüntüleme parametrelerini ayarlamak ve gerekli görüntünün mümkün olan en düşük radyasyon dozu ile elde edilmesidir. Tanısal yorumlama için yeterli kaliteyi sürdürmek, net faydanın en üst düzeye çıkarılması için koruyucu önlemler almaktır; bu nedenle ekipman, teknik ve görüntüleme parametrelerinin optimizasyonu ve modifikasyonuna özel dikkat gösterilmesini gerektirir. İyi radyografik ve floroskopik teknik örnekleri arasında hasta konumlandırmaya, alan boyutuna ve yeterli kolimasyona

dikkat, koruyucu kalkan kullanımı, maruz kalma faktörlerinin optimizasyonu, darbeli floroskopi kullanımı, floroskopi süresinin sınırlandırılması vb. sayılabilir (3).

Literaturde pediatrik kafatası travması geçiren hastalara BT incelemesi için klinik yönlendirme uygulamalarında yapılan ayarlamalar ile BT kullanımında sekiz kat azalma tespit edilmiştir (21). BT için, hastanın ağırlığına veya yaşına göre tarama parametrelerinin (mA, kVp ve pitch) ayarlanmasıyla doz azaltımı optimize edilmelidir. Diğer doz azaltma stratejileri arasında çok fazlı inceleme protokollerinin kısıtlanması, tarama bölgelerinin çakışmasından kaçınılması ve yalnızca söz konusu alanın taranması yer alır (12).

Spina bifida occulta yaygın bir varyasyon olduğu için herhangi bir görüntüleme gerek yoktur. Nörolojik semptomlar veya belirtiler varsa USG veya MRG endikedir.

Ekstremite yaralanmasında karşı tarafın direkt grafisine gerek yoktur. İrritabl kalçası veya topallaması olan çocuklarda, eklem efüzyonunu dışlamak-doğrulamak veya tanı ve tedaviyi yönlendirmek için USG endikedir. X-ışınları veya nükleer tıp muayeneleri sadece negatif USG durumunda endikedir.

Yabancı cisim aspirasyon şüphesinde radyografi gösterebilir, floroskopi ve BT sonra tercih edilmelidir. Göğüs röntgeni, hırıltılı solunum, akut stridor ve kalp üfürümleri için için rutin olarak endike değildir.

Yutulan yabancı cisimlerde boyunu içine alacak şekilde göğüs röntgeni çekilmelidir. Karın röntgeni yalnızca keskin yabancı cisimlerin veya zehirli maddelerin (örneğin piller) yutulduğundan şüphelenildiği durumlarda tercih edilmelidir.

BT, künt karın travmasında ilk tercih edilen görüntüleme olup USG bilinen organ yaralanmalarının takibinde faydalı olabilir. Basit kusmalar ve gastroözefagial reflülerde kontrastlı floroskopik incelemeye gerek yoktur. Batında kitle şüphesi olan hastalarda ilk modalite USG'dir. Klinik gereklilik halinde MRG tercih edilebilir. Ürogenital sistem patolojilerinde, invajinasyon tanısında, şüpheli invajinasyon durumlarında USG tercih edilmelidir (2).

SONUÇ

Radyasyona dayalı görüntüleme her yaşta son derece yararlıdır. Çocuklarda tıbbi görüntülemede iyonlaştırıcı radyasyon tetkiklerini isteyen ekip radyasyon yönetimi ve pediatrik uzman olmalıdır. İyonize radyasyon ile tıbbı görüntüleme esnasında tanı konabilecek görüntü oluşturan en düşük doz ile görüntüleme yapılmalıdır. Görüntüleme işleminde çocuklarda ilk tercih noniyonizan radyolojik modaliteler kullanılmalıdır. İlk tercih USG sonra MRG tercih edilmelidir.

KAYNAKLAR

1. International Commission on Radiological Protection (2020) Full membership list. ICRP website. http://www.icrp.org/icrp_membership.asp. Accessed 5 Aug 2019
2. ICRP Publication 121 Radiological Protection in Paediatric Diagnostic and Interventional Radiology. Ann ICRP 2013:42(2).
3. ICRP Publication 105 Radiological Protection in Medicine. Ann. ICRP 2007:37(6).
4. ICRP Publication 135 Diagnostic Reference Levels in Medical Imaging. Ann. ICRP 2017;46(1).
5. Gilbert ES. Ionizing radiation and cancer risks: what have we learned from epidemiology? Int J Radiat Biol. 2009;85(6):467–82.
6. Smith A, Gruskin K , Monuteaux M.C , Stack A.M, Sundberg M , Yim R et all. Reducing the Cranial CT Rate for Pediatric Minor Head Trauma at Three Community Hospitals. Pediatr Qual Saf 2019 ;4(2):e147
7. Mastrangelo M, Midulla F. Minor Head Trauma in the Pediatric Emergency Department: Decision Making Nodes. Curr Pediatr Rev. 2017;13(2):92-99.
8. Medina SL, Applegate KE, Blackmore CC. Evidence-based imaging in pediatrics. New York, NY: Springer; 2010
9. National Research Council. Health risks from exposure to low levels of ionizing radiation. BEIR VII Phase 2. Washington, DC: National Academies Press; 2006.
10. Huang WY, Muo CH, Lin CY, Jen YM , Yang MH, Lin JC et al. Paediatric head CT scan and subsequent risk of malignancy and benign brain tumour: A nation-wide populationbased cohort study. Br J Cancer. 2014;110(9):2354–2360
11. Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP et alL. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet. 2012;380(9840):499-505
12. Donald P. F,Erich Sorantin. Radiation use in diagnostic imaging in children: approaching the value of the pediatric radiology community. Pediatric Radiolog.2021;51:532–543.
13. Amis ES Jr, Butler PF, Applegate KE, Birnbaum SB, Brateman LF, Hevezi MJ et all.American College of Radiology white paper on radiation dose in medicine. J Am Coll Radiol 2007;4:272–284
14. Mettler FA, Mahesh M, Chatfield MB, Elee J, Vetter RJ. medical exposures of patients in the United States. National Council on Radiation Protection and Measurements (NCRP) website. https:// ncrponline.org/program-areas/sc-4-9/. Accessed 31 Aug 2020)
15. European Society of Radiology (2018) The ESR and EuroSafe Imaging are proud to announce the publication of the European guidelines on diagnostic reference levels for paediatric imaging in the European Commission's radiation protection series. ESR website. https://www.myesr.org/article/1869. Accessed 6 Aug 2019
16. Kaya T. Radyobiyoloji ,Rardyasyondan korunma ve yasal mevzuat. Gelal F. Radyoloji Fiziği.1.baskı,İstanbul, Nobel tıp kitabevleri, 2019;101-107
17. Öztürk E. Radyasyonun biyolojik etkileri. Sancak İ.T .Temel Radyoloji 1.baskı ,Ankara, Güneş tıp kitabevleri, 2015;48-57
18. Hryhorczuk AL, Restrepo R, Lee EY. Pediatric Musculoskeletal Ultrasound: Practical Imaging Approach . AJR Am J Roentgenol. 2016 May;206(5):W62-72
19. Alan J Quigley 1, Samuel Stafrace. Ultrasound assessment of acute appendicitis in paediatric patients: methodology and pictorial overview of findings seen. Insights Imaging. 2013 Dec;4(6):741-51.
20. Stokowski LA. Ensuring safety for infants undergoing magnetic resonance imaging. Adv Neonatal Care 2005;5:14 –27.
21. D M Macgregor , L McKie. CT or not CT--that is the question. Whether 'tis better to evaluate clinically and x ray than to undertake a CT head scan! Emerg Med J 2005 Aug;22(8):541-3.

Derleme (Review)

Pankreatik Nekroz ve Tedavisi

Pancreatic Necrosis and Treatment

Mesut KUŞ[1], Serhat AKPINAR[1], Bülent KANTARÇEKEN[1], Kadir GİŞİ[1]

[1] Sütçü İmam Üniversitesi, Tıp Fakültesi, Dahili Tıp Bilimleri Gastroenteroloji Bilim Dalı, Kahramanmaraş, Türkiye

Özet

Akut pankreatit temel olarak pankreas dokusunun inflamasyonudur ve hafif interstisyel (ödematöz) pankreatitten, önemli lokal veya sistemik komplikasyonlarla beraber ciddi oranda morbidite ve mortalitesi olan şiddetli hastalığa kadar ilerleyebilir. Vakaların %80'i hafif olup ciddi morbidite olmaksızın 5-7 günde gerilerken %20'sinde başvuruda veya ilk 72 saat içinde yaygın pankreatik nekroz ve organ yetmezliği ile birlikte seyreden şiddetli veya fulminant akut pankreatit tablosu ortaya çıkmaktadır. Bu durumda %25-30 mortal seyretmektedir. Bu derlemede pankreatik nekroz ve tedavisine güncel bilgiler ışığında pratik bir yaklaşım sunmak amaçlanmıştır.

Anahtar Kelimeler: Akut pankreatit, Pankreatik nekroz, Balthazar skorlaması

Abstract

Acute pancreatitis is essentially inflammation of pancreatic tissue and can progress from mild interstitial (edematous) pancreatitis to severe disease with significant local or systemic complications and significant morbidity and mortality. While 80% of cases are mild and resolve in 5-7 days without serious morbidity, 20% present with severe or fulminant acute pancreatitis with widespread pancreatic necrosis and organ failure on presentation or within the first 72 hours. In this case, 25-30% have a mortal course. In this review, we aimed to present a practical approach to pancreatic necrosis and its treatment in the light of current knowledge.

Keywords: Acute pancreatitis, Pancreatic necrosis, Balthazar scoring

Yazışma Adresi: Mesut KUŞ Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Gastroentereoloji Bilim Dalı, Kahramanmaraş, Türkiye

Telefon: +90 344 300 30 48 **e-mail:** mst.kus@gmail.com

ORCID No (Sırasıyla): 0009-0009-0709-7275, 0009-0002-3851-937X, 0000-0003-4214-817X, 0000-0003-4082-4832

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GİRİŞ

Akut pankreatit temel olarak pankreas dokusunun inflamasyonudur ve hafif interstisyel (ödematöz) pankreatitten, önemli lokal veya sistemik komplikasyonlarla beraber ciddi oranda morbidite ve mortalitesi olan şiddetli hastalığa kadar ilerleyebilir. Kadınlarda daha çok safra taşları etken iken erkeklerde ve genç erişkinlerde alkol, hiperlipidemi gibi nedenler daha sık etkendir (1). Son yıllarda toplumlarda obezite ve kolelitiazis insidansının artması, yaşam süresinin uzaması ve ilaç kullanımının artması ile birlikte sıklığı artmaktadır ve son 40 yılda neredeyse 10 kat arttığı bildirilmektedir. Hastalığın etiyolojisine bağlı olarak görülme sıklığı ülkeden ülkeye değişiklik göstermekle beraber 4.9 - 75 / 100.000 olarak bildirilmiş olup, pek çok diğer etiyolojik faktör de tanımlanmıştır (2-4). Bu faktörlerin etkisiyle, birtakım koruyucu mekanizmaların ortadan kalkması ve proenzimlerin pankreas dokusu içerisinde aktive olması ile inflamasyon başlamakta ve pankreatit ortaya çıkmaktadır (4). Vakaların %80'i hafif olup ciddi morbidite olmaksızın 5-7 günde gerilerken %20'sinde başvuruda veya ilk 72 saat içinde yaygın pankreatik nekroz ve organ yetmezliği ile birlikte seyreden şiddetli veya fulminant akut pankreatit tablosu ortaya çıkmaktadır. Bu durumda %25-30 mortal seyretmektedir (3,5). Buna rağmen tanı ve tedavi olanaklarındaki gelişmelere bağlı olarak 1988'den 2003'e akut pankreatitten mortalite oranının %12'den %2'ye düştüğü bildirilmiştir (6). Nekroz geliştiğinde hastalığın şiddetine bağlı olarak görülen mortalite oranı %2-47 arasında değişmektedir (3,7). Bir çalışmada 7 yıl süresince, akut pankreatit ile başvuran hastaların %4'ünün başvurudan 92 gün içinde öldüğü ve ölümlerin %50'sinin ilk 14 gün içinde görüldüğü bildirilmiştir (8). İlk 2 haftalık dönemde ölümler sistemik inflamatuar yanıt sendromu (SIRS) ve organ yetmezliğine bağlı iken, geç ölümlerin çoğu enfekte pankreas nekrozuna sekonder sepsis ve multiple organ disfonksiyonuna (MOD) bağlı olarak gelişmektedir (1,9). En yüksek ölüm oranları pankreatik nekroz ile birlikte MOD olduğunda görülür. Akut pankreatitte ölüm oranları tabloda gösterilmiştir **(Tablo 1)** (10).

Tablo 1. Akut pankreatitte ölüm oranları (10)

	Ortalama (%)	Aralık (%)
Tüm vakalar	5	2–9
İnterstisyel pankreatit	3	1–7
Steril nekroz	12	2–44
Nekrotizan pankreatit	17	8–39
Enfekte nekroz	30	14–62
Multisistem organ yetmezliği	47	28-69

SINIFLAMA

Günümüzde hem tanı hem de tedavi açısından daha basitleştirilmiş olan ve revize edilen Atlanta sınıflaması akut pankreatitleri temelde, İnterstisyel (Ödematöz) ve akut nekrotizan olarak iki genel gruba, erken ve geç olmak üzere iki faza, hafif, orta ve ciddi (şiddetli) olarak üç şiddet derecesine ayırmaktadır (11). Bu klinik durumların tanımlamaları tabloda gösterilmiştir **(Tablo 2)**.

İnterstisyel pankreatit, tipik olarak hafif seyreder, vakaların küçük bir oranında geçici MOD veya sıvı koleksiyonları ve psödokist gelişimi izlenebilir. Atlanta sınıflamasına göre; Nekroz (Steril veya enfekte, duvarlı veya duvarsız), apse, kanama ve psödokist varlığı da şiddetli pankreatit lehine olan lokal komplikasyonlar olarak kabul edilmiştir. Organ yetmezliği modifiye Marshall sınıflamasına göre >2 olarak tanımlanmıştır. Bu tabloyu genellikle sistemik bir cevap ve toksisite izler. Bu faktörler, öncelikle proinflamatuar faktörlerin uyarılmasını sağlayarak, SIRS, akut solunum sıkıntısı sendromu ve daha sonra MOD'a kadar gidebilen tablolara yol açabilir. Bu sınıflama, yapılacak tedavinin ve prognozun belirlenmesi açısından, büyük önem arz etmektedir. Hastalığın şiddetinin belirlenmesi, hastanın yoğun bakım ya da serviste mi tedavi edileceğine, acil müdahalenin (özellikle cerrahi) gerekli olup olmadığına karar vermede yardımcıdır. Lökositoz, c-reaktif protein (CRP) ve yüksek tripsinojen aktive

Tablo 2. Revize Atlanta sınıflamasına göre pankreatit sınıflaması (11)

Hafif akut pankreatit	En sık görülen tablo. Organ yetmezliği yok, lokal veya sistemik komplikasyonlar yok, genellikle 1 haftada düzelir.
Orta akut pankreatit	Geçici organ yetmezliği (<48 saat), lokal komplikasyonlar veya ko-morbid hastalıkta alevlenme
Ciddi akut pankreatit	(Bir veya birden fazla) Persistan organ yetmezliği (>48 saat)

edici peptid düzeyi şiddetli hastalık göstergelerindendir. Ranson kriterleri %80 doğrulukla hafif ve şiddetli hastalığı ayırabilir. Bunun dışında APACHE II, özellikle kontrastlı bilgisayarlı tomografi (BT) ile Balthazar skorlaması **(Tablo 3)** ve diğer pek çok skorlamalar hastalığın şiddetini ve prognozunu belirlemede yardımcıdır. Balthazar skorlamasında nekroz ve sıvı koleksiyonlarının varlığı, miktarı ve uzanımı değerlendirilerek hastaya bir skor verilir **(Tablo 3)** (12).

Balthazar skorlaması ile; Mortalite oranları sırası ile, nekroz yokluğunda ve herhangi derecede nekroz varlığında %0 ve %23 olarak bildirilmiş >%30 oranında nekroz varlığının morbidite ve mortalite ile güçlü ilişkisi gösterilmiştir (12). Balthazar skorlaması ile akut pankreatitli hastaların değerlendirildiği bir çalışmada, BT ciddiyet indeksi >5 olanların 8 kat daha fazla mortal seyrettiği, 17 kat daha fazla hastanede kalış sürelerinin olduğu ve 10 kat daha fazla nekrozektomiye gittiği bildirilmiştir (13). Retrospektif bir analizde, akut pankreatitin şiddetini belirlemede, Balthazar sınıflamasının, klinik parametreleri değerlendiren APACHE II veya BISAP skorlamasından istatistiki üstünlüğü olmadığı bildirilmiştir (14). Bununla beraber, BT'de nekrotizan pankreatitin varlığının (Hatta enfekte nekroz) organ yetmezliğini predikte etme açısından olmazsa olmaz olmadığı, nekrozun yaygınlığı ile organ yetmezliği ve/veya ölüm ile üniform bir korelasyon olmadığı da bildirilmiştir (15). Dolayısı ile sadece klinik parametre veya sadece BT skorlamalarının prognoz açısından yeterli olmayacağı aşikardır. Birlikte ve bireysel değerlendirme en uygunudur.

PANKREATİK NEKROZ

Pankreatik nekroz şiddetli pankreatitlerde görülür ve kötü prognoz bulgusudur. Akut pankreatit seyri sırasında pankreasta nekroz gelişme oranı % 4-47'dir. Makroskopik olarak pankreatik parankim ve peripankreatik yağ dokusunda fokal ya da diffüz nekroz vardır. Retroperitoneal bölgeler farklı derecelerde tutulabilir (10). Pankreatik nekroz, tipik olarak peripankreatik yağ nekrozu ile birlikte, fokal ya da diffüz olarak canlılığını kaybetmiş pankreas parankimi olarak tanımlanır. BT ile nekroz kriteri, fokal veya diffüz olarak iyi sınırlanmış, 3 cm'den fazla veya pankreasın %30'undan fazla kontrastlanmayan pankreas parankim alanlarının varlığıdır (16,17). Pankreatik nekroz, tipik olarak ilk 24-48 saat içinde gelişir. Pankreatik nekrozu, tedavi açısından belirgin farklılıklar olduğundan öncelikle steril ve enfekte olarak ayırmak gerekir. Steril nekrozda konservatif yaklaşım sıklıkla uygulanabilirken enfekte nekroz oluştuğunda tedavi hemen hemen tamamen cerrahiye dönmektedir. İnterstisyel pankreatitlerde %10 civarında organ yetmezliği görülürken, pankreas nekrozu olanlarda bu oran ortalama %54 (%29-78), steril nekrozda %45-73 enfekte nekroz durumunda ise %34-89'dur (10). Pankreatik nekrozlu hastaların %33'ünde (%16-47) enfekte nekroz vardır ve ilerleyen süreçte %40-70'inde enfeksiyon oluşabilir. Steril ve enfekte nekrozlarda ölüm oranı sırası ile %10 ve %25'dir. Başvuruda hemokonsantrasyonun olmamasının hastaların çoğunda pankreas nekroz varlığını dışladığı bildirilmiştir (18). CRP (rutin pratikte en değerli), sitokinler, fosfolipaz A2, antiproteazlar, tripsinojen aktivasyon

Tablo 3. Akut Pankreatitte Balthazar sınıflaması (12)

Grade	**Puan**
A: Normal pankreas	0
B: Pankreatik genişleme	1
C: Pankreas ve peripankreatik yağ dokusuyla sınırlı inflamasyon	2
D: Peripankreatik bir alanda sıvı koleksiyonu	3
E: 2 veya daha fazla alanda sıvı koleksiyonu	4
Nekroz Derecesi	
Nekroz yok	0
Pankreasın 1/3'ünde nekroz	2
Pankreasın 1/2'sinde nekroz	4
Pankreasın 1/2'sinden fazla alanda nekroz	6

peptidi (TAP), aniyonik tripsinojen 2 ve prokalsitoninin hastalığın ciddiyeti ile korele olduğu bildirilmiştir (19). Ciddi pankreatit atakları gastroenterolog, girişimsel radyolog, yoğun bakım uzmanları ve cerrahları da içeren bir ekip tarafından multidisipliner olarak takip edilmelidir. Bu hastalar öncelikle resüsitasyon ile yakînen monitörize edilmeli ve pankreatik nekrozun durumuna ve hastanın gidişatına göre tedavi edilmelidir. Bununla birlikte ciddi pankreatitin tedavisi merkezlerin deneyimine göre değişiyor görünmektedir (10, 20). Nekrozun yaygınlığı ve enfekte pankreatik nekroz akut nekrotizan pankreatitli hastalarda organ yetmezliği gelişimi ile ilişkilidir. Mortalite için en önemli prediktör ise enfekte pankreatik nekrozdur (21).

STERİL PANKREAS NEKROZU VE TEDAVİSİ

Genel İlkeler ve Beslenme

Hangi şekilde olursa olsun, akut pankreatitli hastaların başlangıç tedavisinde yeterli ve uygun destekleyici tedavi ile komplikasyonların önlenmesi ve tedavisi temel hususlardır. Orta ve şiddetli akut pankreatiti olan hastalar yoğun bakım ünitesinde takip edilmeli ve/veya bu alanda özelleşmiş merkezlere sevk edilmelidir. Her ne kadar steril nekrozların 1/3'ünde (10) enfeksiyon oluyor olsa da ilk 15 günde enfekte olma riski düşüktür ve ilk 2-3 hafta boyunca en iyi yaklaşım medikaldir. Agresif destek tedavisi özellikle sıvı ve oksijen desteği gerekir (22). Medikal tedavi pankreatik sekresyonları minimize etmek (Ocreotide ve/veya tekrarlayan drenaj prosedürleri), nazojejunal enteral veya tolere edemiyorsa total parenteral beslenme ile beslenmeyi içerir. Kan üre nitrojeninin (BUN) monitörize edilmesi özellikle önemlidir, çünkü başvurudaki BUN değerleri ile 24 saat boyunca izlenen değerler arasındaki değişiklikler mortaliteyi predikte etmektedir (23). Ringer laktat solüsyonunun normal salinden daha faydalı olduğuna dair bazı çalışmalar vardır (24). Ağrı kontrolü yapılmalıdır, çünkü kontrol edilemeyen ağrı hemodinamik instabiliteye katkıda bulunabilir. Ayrıca, ağrının 12 saatten uzun süre devam etmesi hastalığın ciddiyetini gösterebilmektedir (25). Erken enteral nütrisyona (24-48 saat) organ disfonksiyonu veya SIRS gelişen ve 48 saat boyunca süren ciddi akut pankreatitte yoğun bakım ünitesinde başlanmalıdır (26). Önceki meta-analizler ile tutarlı şekilde, erken enteral beslemenin MOD, sistemik enfeksiyon, cerrahi gereksinimini ve mortaliteyi parenteral beslenenlere göre anlamlı oranda düşürdüğü gösterilmiştir (27).

Antibiyotik Tedavisi

Profilaktik antibiyotik tedavisi genel olarak önerilmemektedir (10,28) ancak karbapenem türevlerinin mortaliteyi anlamlı düşürmese de enfeksiyon ve hatta nekroz gelişmesini anlamlı olarak düşürdüğü gösterilmiştir (29). Eğer şüphe var ise BT eşliğinde perkütan ince iğne aspirasyon biyopsisi (İİAB) yapılmalıdır (30). Pankreas nekrozunda enfeksiyon ajanları daha çok barsak kaynaklıdır ve sıklıkla etkenler Escherichia coli, Pseudomonas, Klebsiella ve Enterococcus'lardır. Enfeksiyonların yaklaşık %75'i monomikrobiyaldir. Fungal veya gram pozitif enfeksiyonlar nadir olmakla beraber 10-14 günden fazla profilaktik antibiyotik kullanımı sonucu daha fazla görülebilmektedir. Fungal enfeksiyonlar pankreas nekrozunda yaklaşık %9 oranında görülebilmektedir ve mortaliteye etkisi net değildir (10). Bu konu halen tartışmalı olmasına rağmen, pek çok merkez özellikle nekroz derecesi %30'un üzerinde ise 7-10 gün imipenem/meropenem tedavisi başlamaktadır. Aslında bu derecede bir nekrozun yüksek enfekte olma oranları nedeniyle mantıklı ve uygun görünmektedir. Enfeksiyon dökümante edilemezse kesilmelidir. Fungal enfeksiyon profilaksisi ise önerilmez (10,31). Bununla birlikte nekrotizan pankreatitlilerde, 3. hafta sonunda enfekte nekroz oranları %40-70'e ulaşabilmektedir (1). Bu nedenle halen kısmen tartışmalı olsa da, pankreatik nekroz oranı %30'dan fazla olanlarda başlangıçtan itibaren pankreasa penetrasyonu iyi olan geniş spektrumlu karbapenemler ile 14 günlük antibiyotik proflaksisi önerilmektedir (10,29).

Cerrahi Tedavi

Antibiyotik tedavisi sonrası karın ağrısı devam ediyor ve oral alımı engelliyor ise debridman düşünülmelidir ki buda, günümüzde perkütan, endoskopik, video assisted retroperitoneal debridman (VARD) gibi yaklaşımlar artmakla beraber, genellikle cerrahidir ve güvenli ve etkin olduğu bildirilmiştir (32). Ne var ki steril nekrozda ameliyat kriterleri objektif değildir. Ancak, perkütan veya endoskopik debridman uygun uzmanlık ile seçilmiş vakalarda kabul edilebilir bir yöntemdir. Nekrozlarda pankreatik kanal kaçakları ve fistüller sıktır ve bunlarda da endoskopik veya cerrahi tedavi gerekebilir (10). Organ yetmezliği steril nekrozların en az %48'inde oluşmasına (33) ve önceden bu durum nekrotik materyalin erkenden kaldırılması endikasyonu sayılmasına rağmen günümüzde ilk 2-3 haftalık dönemde medikal konservatif yaklaşımın daha az morbidite ve mortalite ile ilişkili olduğu görüşü artmaktadır (34). Ayrıca, steril nekroz özellikle ilk dört gün içinde cerrahi olarak debride edildiğinde, enfekte nekroz gelişimi ve tekrar cerrahi gereksinimi sık bir sekeldir (35). Aslında organ yetmezliğinin üstesinden gelmek için nekrotik dokunun, minimal invaziv şekilde kaldırılması halen geçerli bir tedavi yöntemidir. Örneğin minimal invaziv retroperitoneal cerrahi, enfekte nekrozda da olduğu gibi uygulanabilir (36). Esasen hangi minimal

invaziv yöntem olursa olsun güvenilir ve etkin olduğu bildirilmiştir (37). Ancak, ciddi steril nekrozlu hastalarda ilk 2-3 haftada minimal invaziv tedaviyi sadece konservatif tedavi ile karşılaştıran çalışmalar yoktur. Cerrahi 2-3 hafta geciktirildiğinde retroperitondaki diffüz inflamatuvar durum oldukça düzelmekte ve nekrotik pankreatik doku ve peripankreatik dokuyu saran enkapsüle bir yapı haline gelebilmektedir (Walled of necrosis) (38) ki bu da sıklıkla organize nekroz olarak adlandırılmaktadır. Bu durumda hastalık genellikle yatışmakta ve hastalar ek girişim gerektirmeyecek şekilde asemptomatik hale gelmektedir. Semptomatik olup ateşi devam eden, ciddi lökositozu olan hastalarda ise enfekte nekroz akla gelmelidir. Bir kısım organize nekrozlu hastalarda ise bulantı, kusma gibi kompresyon semptomları olmaktadır. Kültür pozitif nekroz olursa veya kompresyon durumlarında organize nekrozun perkütan, endoskopik veya cerrahi olarak dekompresyonu yapılmalıdır (10,31). Cerrahi tedavi; Nekrotik materyalin açık veya kapalı debridmanı, organize nekroz içindeki sıvının tahliyesi ve eğer uygun kapsül var ise midenin arka duvarına anastomozu veya jejunuma Roux – en Y gibi yöntemler ile uygulanabilir. Organize nekrozun perkütan drenajı bir veya birden fazla can sıkıcı dren yerleşimini, agresif lavajı (ki günümüzde önerilmemekte) gerektikçe de kateter yerlerinin düzeltilmesini gerektirir (39).

Endoskopik Tedavi

Endoskopik debridman organize nekroz mide veya duodenum duvarına sıkıca yapışık olduğunda ve endoskopik ultrasonografi arada damar yapısı olmadığını gösterdiğinde düşünülebilir (40). Bu teknikte duodenoskop veya endoskopik ultrasonografi (EUS) ile bir iğne duvardan geçirilerek nekroz içine girilir, nekrotik materyali ve sıvıyı rahat akıtmak için açıklığı genişletmek amacıyla balon dilatasyonu sonrası çoğunlukla kavite içine doğrudan endoskopik giriş gerekir. Katı içeriğin mekanik olarak çıkarılması sonrası drenajı sürdürmek için iki adet pigtail kateter yerleştirilerek işlem sonlandırılır. Tekrar endoskopik debridman veya uzun süreli drenaj genellikle gerekir. Sınırlı sayıda çalışmadan başarılı sonuçlar bildirilmiş olmasına rağmen vakaların %37'ye varanında enfeksiyon ve cerrahi gereksinimi, komplikasyonlar olarak bildirilmiştir ve terapötik endoskopi konusunda yeterli tecrübe ve uzmanlık sahibi kişilerce uygulanmalıdır (37). Aslında cerrahi dışı yöntemlerin tamamında ana endişe nekrotik materyalin yetersiz tahliyesi ve kalan nekrotik materyalin enfeksiyonudur. Steril pankreatik nekrozun, çok nadir olarak, hastalığın ilk birkaç haftasında, acil cerrahi yapılmasını gerektiren durumlar; Abdominal kompartman sendromu, perforasyon veya infarktüsü düşündüren ciddi karın ağrısı olması ve/veya bir pseudoanevrizmadan şiddetli kanamadır. Bu durumlarda laparotomi ile müdahale hayat kurtarıcı olabilir (41). Nekroz gelişen hastalarda spontan veya debridman girişimleri sonucu pankreatik kanal kaçakları veya pankreas kanal disconnection gelişebilir ve gidişatı kötüleştirebilir. Bunların üstesinden gelebilmek için endoskopist (gastroenterolog), cerrahi ve radyolojiye dayanışması gerekir (10, 31,39). Kanal kaçakları endoskopik retrograd kolanjiyopankreatografi (ERCP) veya manyetik rezonans kolanjiyopankreatografi ile tanınabilir. Ancak ERCP ve pankreatik kanala stent yerleştirilmesi ile oddi'den duodenuma akışın sağlanması bu konuda deneyimli kişilerce ve persistan ve/veya semptomatik kaçak var ise (Bakteri kolonizasyonu nedeniyle) yapılmalıdır (40, 42). Bu şekilde vakaların yaklaşık 2/3 – 3/4'ünde başarı sağlanmaktadır. Dirençli pankreatik fistüllerin endoskopik olarak injeksiyon veya perkütan olarak cyanoacrylate injeksiyonu ile kapatılabildiği bildirilmiştir (42). Disconnected duct sendromu ana pankreatik kanalda geniş bir gap varsa oluşur ve genellikle stent ile akım sağlanamaz. Bu vakalarda sonunda cerrahi sıklıkla gerekir (43).

ENFEKTE PANKREAS NEKROZU VE TEDAVİSİ

Genel İlkeler

Enfekte nekroz tüm pankreatit vakalarının %3-7'sinde görülür. Özellikle nekroz oranı %30 ve daha fazla olan hastalarda gelişir. Tipik olarak 2. veya 3. haftada, sepsis, ateş, lökositoz, organ yetmezliği genel durumda giderek bozulma ile kendini gösterir (1,10). Enfekte nekrozun tanınması ile ilgili spesifik bir labaratuvar belirteç yoktur ancak sepsis ve MOD bulguları ile birlikte biyokimyasal olarak yüksek CRP değerleri (Özellikle >125mg/L), lökositoz ve BT enfeksiyondan şüphelendirebilir, ancak enfeksiyonu belirlemede yetersizdir. Bundan dolayı nekrozun enfekte olduğu şüphesi varsa, altın standart olarak, BT veya EUS eşliğinde İİAB ile gram boyama ve kültür yapılmalıdır. Steril ve enfekte nekroz arasındaki ayırım sonraki tedavi için önemlidir. İlk İİAB genellikle akut atağın başlangıcından 10 gün sonra yapılmalıdır. Çünkü ilk haftada enfekte olma şansı %20'den düşüktür. Ancak, %50' den fazla nekroz varsa, yoğun konservatif tedaviye rağmen MOD bulguları şiddetleniyorsa, sepsis bulguları mevcutsa, APACHE II ve CRP yükselmelerinde vakit geçirmeden İİAB yapılmalıdır. Nekrozun 15. günden sonra enfekte olma şansının artacağı göz önünde bulundurularak birer hafta arayla İİAB tekrarlanmalıdır (10).

Antibiyotik Tedavisi

Tekrarlanan İİAB örneklerinde enfekte pankreas nekrozu saptanması durumunda, steril enfekte nekrozda bahsedilen tedavilere ek olarak antibiyotik başlanmalı ve 14 gün devam edilmelidir. Seçilecek antibiyotikler de pankreatik dokuya penetrasyonu iyi olan, özellikle

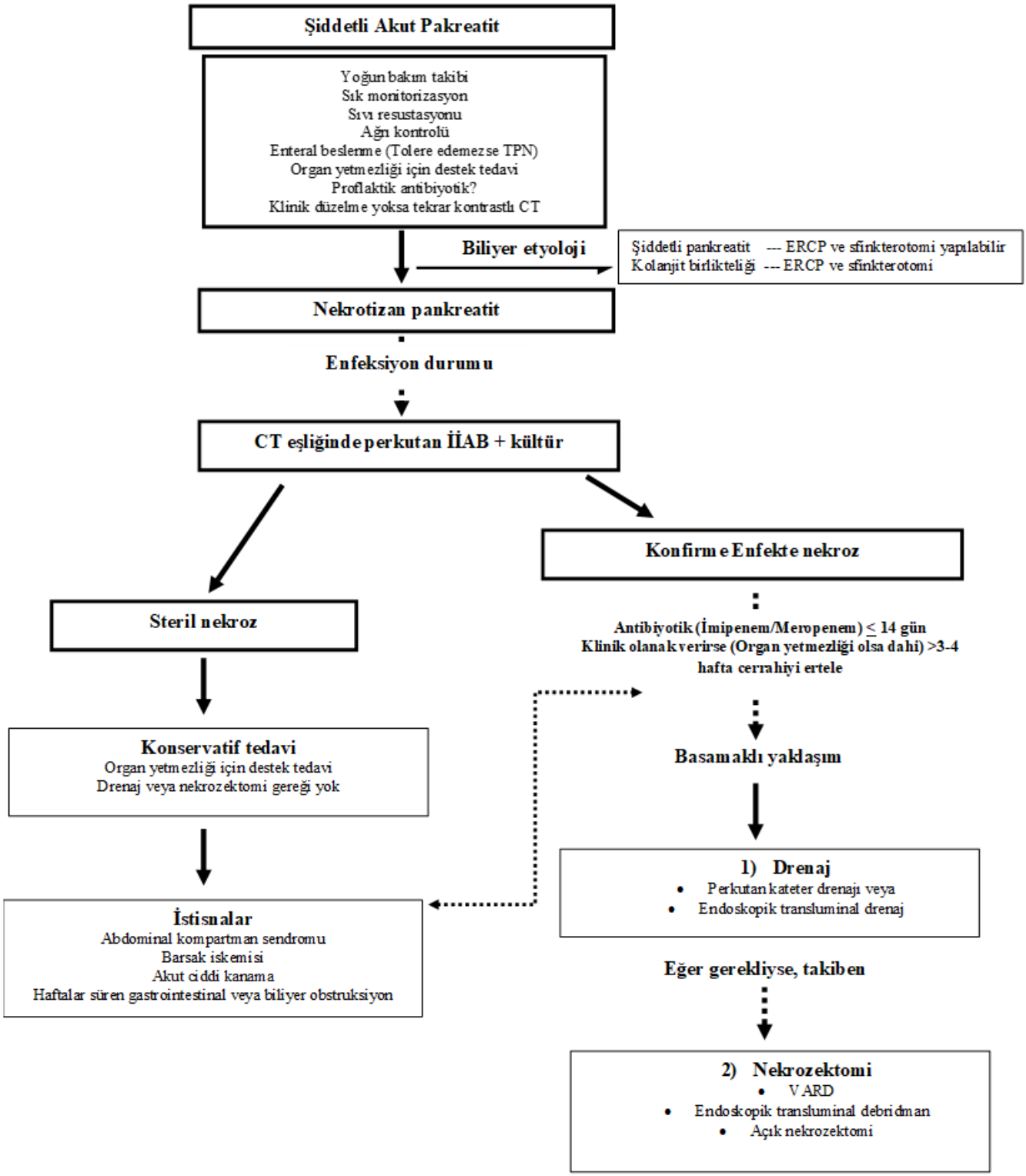
imipenem/meropenem ve/veya 3. kuşak sefalosporinler veya piperasilin grubundan olmalıdır (10,31). Eğer enfeksiyon konfirme edilmez ise sekonder fungal enfeksiyon gelişimini önlemek amacıyla hemen kesilmelidir. Tedavi 14 günü geçerse fungal infeksiyon riski artar. Enfeksiyon tanısı kesinleştirildikten sonra veya nekroz varlığında antibiyotiklerin etkisi sınırlı kalabilir ve enfekte dokuların drenajı sıklıkla gerekir (10,16,41).

Cerrahi Tedavi

Enfekte nekrozlarda klasik görüş cerrahi debridmandır (10,31). Perkütan drenajın etkili olduğunu bildiren yayınlar olmakla birlikte genelde tek başına yeterli olmamaktadır. Nekrozektomi sonrası kalan nekroz alanlarına ve gelişebilecek yeni nekroz alanlarına yönelik laparostomi (Açık abdomen) yapılarak tekrarlayan nekrozektomiler, pankreas lojunun pasif drenajı veya lojun sürekli lavajı gibi seçenekler mevcuttur. Son yıllarda retroperitoneal veya tomografi kılavuzluğunda loja ulaşıp nekrozektomi yapılması yöntemleri de uygulanmaktadır. Enfekte pankreatik nekrozlu hastaların cerrahi tedavisi mortalite oranlarını %20 azaltmıştır. Ancak yine de özellikle erken dönemde ki açık cerrahi ile oldukça yüksek komplikasyon (% 34–95) ve mortalite (% 11–58) oranları bildirilmiştir (35). Nekrozektominin zamanlaması daha çok bireysel olarak hastaya ve gelişen tabloya bağlı olmakla beraber eğer tablo beklemeye izin veriyor ise geç cerrahi daha düşük morbidite ve mortaliteye sahip olduğundan tercih edilir. Önce perkütan drenajlar, ardından geç nekrozektomi ile mortalitenin daha düşük olduğu bildirilmiştir (Step up – Basamaklı yaklaşım) (44). Genel durumu kötüye giden, MOD tablosu düzelmeyen veya nekroza bağlı lokal komplikasyon gelişen olgularda erken cerrahi girişim gereksinimi olabilir. Cerrahi ve diğer girişimsel işlemlerde debridman ve nekrozektomi gibi organ koruyucu yaklaşımlar tercih edilmeli ve retroperitoneal debris ve/veya nekrozun postoperatif boşaltılmasını içeren yöntemlerle kombine edilmelidir. Ancak, enfekte pankreas nekrozu tedavisinde henüz yayınlanmış bir meta-analiz minimal invaziv nekrozektomi ile açık nekrozektomiyi karşılaştırmış, MOD sıklığı, insizyonal herni, diyabet gelişimi ve pankreas enzim kullanım gereksinimi yönünden minimal invaziv nekrozektomiyi üstün bulurken, mortalite oranı, multiple sistemik komplikasyonlar, tekrar nekrozektomi için cerrahi girişim gereksinimi, intraabdominal kanama, enterokutanöz fistül veya visseral organ perforasyonu, pankreatik fistül, postoperatif komplikasyonlardan dolayı tekrar girişim yönünden farklılık bulamamıştır. Sonuç olarak da çalışmaların heterojenliğinden ve karşılaştırmalı çalışmaların yetersizliğinden dolayı tam bir yorum yapılamadığını bildirmiştir (45). Nekroz-canlı doku ayrımının güçlüğüne bağlı olarak yeterli nekrozektominin yapılamaması sonucu nekrozun nüksü, kanama veya canlı doku çıkarımı gibi komplikasyonların sıklığı erken cerrahinin sakıncalarıdır. Sadece, kanıtlanmış enfekte nekroz beraberinde MOD gibi durumlar veya masif kanama ve/veya barsak perforasyonu gibi komplikasyonlar varlığında erken dönemde cerrahi kaçınılmaz olarak yapılmalıdır. Çok yakın zamandaki bir sistematik derleme ve meta-analizden enfekte pankreas nekrozu olanlarda (perkütan drenaj ile birlikte veya değil) nekrozektomi yapmadan konservatif yaklaşım ile hastaların %64'ünde başarı sağlandığı bildirilmiştir (44). Bahsedilen endikasyonlar olmadıkça enfekte nekrozda da ilk 14 gün içinde erken cerrahi önerilmemektedir (35, 44). Nekrozda cerrahi girişim gerektiren en önemli durum enfeksiyon olmakla beraber MOD gelişmeye aday veya gelişen hastalarda enfeksiyon varlığından bağımsız olarak cerrahi girişim kararı verilmelidir. Steril nekrozlarda da nekroz oranının %50'nin üzerinde olmasının cerrahi gerektirecek kadar organ yetmezliğine neden olduğu bildirilmiştir. Dolayısı ile nekrozun sadece enfekte olması değil büyüklüğü de cerrahi girişim gereksinimini belirleyebilir. Cerrahi girişim sonrası en çok rastlanan komplikasyonlar ise pankreatik fistül, ince barsak ve kolon fistülleri, cerrahi yara yeri enfeksiyonu, herni ve karın içi kanamalarıdır. Pankreas yetmezliği de görülebilir. Son dönemde basamaklı tedavilere, minimal invaziv yaklaşımlara veya olabildiği kadar konservatif yaklaşıma, başarılı sonuçlarla birlikte, eğilim artmakta gibi görünmektedir (46).

SONUÇ

Hafif pankreatitin tedavisinin son yıllarda çok az değişmesine karşılık, ağır pankreatit tedavisindeki ilerlemeler, tedavi yaklaşımlarını cerrahi dışı yaklaşımlara da kaydırmış, morbidite ve mortalitede de belirgin bir azalma sağlanmıştır. Nekrotizan pankreatitin tanı ve tedavisindeki olumlu gelişmelerle ölüm oranı %10'un altına indirilmiştir. Günümüzde, steril pankreas nekrozunda en azından başlangıçta konservatif tedavi yaklaşımı uygun görünürken, enfekte pankreas nekrozunda cerrahi, olmazsa olmaz, görüşü yavaş yavaş değişmeye başlamıştır. Kaynaklardan modifiye edilmiş güncel tedavi yaklaşımları aşağıda şematize edilmiştir (Şekil 1). Merkezlerin uzmanlığına ve imkanlarına göre halen yaklaşımlar farklılık göstermekle beraber, unutulmaması gereken; Ne şekilde olursa olsun pankreatik nekrozda tedavinin multidisipliner yaklaşım gerektirdiğidir.



Şekil 1. Pankreas sekrozu tedavisinde algoritma (1,9,11,2031,44-46)

KAYNAKLAR

1. Frossard JL, Steer ML, Pastor CM. Acute pancreatitis. Lancet. 2008 Jan 12;371(9607):143-52.
2. Cappell MS. Acute pancreatitis: etiology, clinical presentation, diagnosis, and therapy. Med Clin North Am 2008; 92: 889-923.
3. Brown A, Young B, Morton J, Behrns K, Shaheen N. Are health-related outcomes in acute pancreatitis improving? An analysis of national trends in the U.S. from 1997 to 2003. JOP 2008;9(4):408-14.
4. Spanier BW, Dijkgraaf MG, Bruno MJ. Epidemiology, aetiology and outcome of acute and chronic pancreatitis: An update. Best Pract Res Clin Gastroenterol 2008; 22(1):45-63.
5. Mofidi R, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br J Surg. 2006;93(6):738.

6. Fagenholz PJ, Castillo CF, Harris NS, Pelletier AJ, Camargo CA Jr. Increasing United States hospital admissions for acute pancreatitis, 1988-2003. Ann Epidemiol. 2007;17(7):491.
7. Eland IA, Sturkenboom MJ, Wilson JH, Stricker BH. Incidence and mortality of acute pancreatitis between 1985 and 1995. Scand J Gastroenterol 2000;35(10):1110-6.
8. Frey CF, Zhou H, Harvey DJ, White RH. The incidence and case-fatality rates of acute biliary, alcoholic, and idiopathic pancreatitis in California, 1994–2001. Pancreas 2006; 33: 336–44.
9. Gloor B, Müller CA, Worni M, Martignoni ME, Uhl W, Büchler MW. Late mortality in patients with severe acute pancreatitis.Br J Surg. 2001;88(7):975.
10. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006;101(10):2379-400.
11. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus.Gut. 2013 Jan;62(1):102-11.
12. Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. Radiology. 1990;174(2):331.
13. Simchuk EJ, Traverso LW, Nukui Y, Kozarek RA. Computed tomography severity index is a predictor of outcomes for severe pancreatitis. Am J Surg. 2000;179(5):352.
14. Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, Mortele KJ. A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis. Am J Gastroenterol. 2012;107(4):612.
15. Tenner S, Sica G, Hughes M, Noordhoek E, Feng S, Zinner M, Banks PA. Relationship of necrosis to organ failure in severe acute pancreatitis. Gastroenterology. 1997;113(3):899.
16. Heinrich S, Schäfer M, Rousson V, Clavien PA. Evidence-based treatment of acute pancreatitis a look at established paradigms. Ann Surg 2006; 243: 154–68.
17. Kim DH, Pickhardt PJ.Radiologic assessment of acute and chronic pancreatitis. Surg Clin North Am 2007;87(6):1341-58.
18. Lankisch PG, Mahlke R, Blum T, et al. Hemoconcentration: an early marker of severe and/or necrotizing pancreatitis? A critical appraisal. Am J Gastroenterol 2001; 96: 2081–85.
19. Matull WR, Pereira SP, O'Donohue JW. Biochemical markers of acute pancreatitis. J Clin Pathol 2006; 59: 340–44.
20. UK working Party on acute pancreatitis. UK guidelines for the management of acute pancreatitis. Gut 2005;54:1–9.
21. Garg PK, Madan K, Pande GK, Khanna S, Sathyanarayan G, Bohidar NP, Tandon RK. Association of extent and infection of pancreatic necrosis with organ failure and death in acute necrotizing pancreatitis. Clin Gastroenterol Hepatol. 2005 Feb;3(2):159-66.
22. Haydock MD, Mittal A, Wilms HR, et al. Fluid Therapy in Acute Pancreatitis: Anybody's Guess. Ann Surg 2013; 257:182.
23. Wu BU, Johannes RS, Sun X, et al. Early changes in blood urea nitrogen predict mortality in acute pancreatitis. Gastroenterology 2009; 137:129.
24. Wu BU, Hwang JQ, Gardner TH, et al. Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. Clin Gastroenterol Hepatol 2011; 9:710.
25. Kapoor K, Repas K, Singh VK, Conwell DL, Mortele KJ, Wu BU, Banks PA. Does the duration of abdominal pain prior to admission influence the severity of acute pancreatitis? JOP. 2013 Mar 10;14(2):171-5. .
26. Wereszczynska-Siemiatkowska U, Swidnicka-Siergiejko A, Siemiatkowski A, Dabrowski A. Early Enteral Nutrition Is Superior to Delayed Enteral Nutrition for the Prevention of Infected Necrosis and Mortality in Acute Pancreatitis. Pancreas. 2013 May;42(4):640-646.
27. Al-Omran M, Albalawi ZH, Tashkandi MF, Al-Ansary LA. Enteral versus parenteral nutrition for acute pancreatitis. Cochrane Database Syst Rev 2010; :CD002837.
28. Jiang K, Huang W, Yang XN, Xia Q. Present and future of prophylactic antibiotics for severe acute pancreatitis. World J Gastroenterol. 2012 Jan 21;18(3):279-84.
29. Yao L, Huang X, Li Y, Shi R, Zhang G. Prophylactic antibiotics reduce pancreatic necrosis in acute necrotizing pancreatitis: a meta-analysis of randomized trials. Dig Surg. 2010;27(6):442-9.
30. Mortelé KJ, Girshman J, Szejnfeld D, et al. CT-guided percutaneous catheter drainage of acute necrotizing pancreatitis: clinical experience and observations in patients with sterile and infected necrosis. AJR Am J Roentgenol 2009; 192:110.
31. Forsmark CE, Baillie J; AGA Institute Clinical Practice and Economics Committee; AGA Institute Governing Board. AGA Institute technical review on acute pancreatitis. Gastroenterology 2007;132(5):2022-44.
32. Beck WC, Bhutani MS, Raju GS, Nealon WH. Surgical management of late sequelae in survivors of an episode of acute necrotizing pancreatitis. J Am Coll Surg. 2012 Apr;214(4):682-8.
33. Perez A, Whang EE, Brooks DC, et al. Is severity of necrotizing pancreatitis increased in extended necrosis and infected necrosis? Pancreas 2002;25:229–33.
34. Gotzinger P, Wamser P, Exner R, et al. Surgical treatment of severe acute pancreatitis: Timing of operation is crucial for survival. Surg Infect (Larchmt) 2003;4:205–11.
35. Mier J, Leon EL, Castillo A, et al. Early versus late necrosectomy in severe necrotizing pancreatitis. Am J Surg 1997;173:71–5.
36. Connor S, Alexakis N, Raraty MG, et al. Early and late complications after pancreatic necrosectomy. Surgery 2005;137:499–505.
37. Van Brunschot S, Bakker OJ, Besselink MG, Bollen TL, Fockens P, Gooszen HG, van Santvoort HC; Dutch Pancreatitis Study Group. Treatment of necrotizing pancreatitis. Clin Gastroenterol Hepatol. 2012 Nov;10(11):1190-201.
38. Baron TH, Harewood GC, Morgan DE, et al. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointest Endosc 2002;56:7–17.
39. Traverso LW, Kozarek RA. Pancreatic necrosectomy: Definitions and technique. J Gastrointest Surg 2005;9:436–9.
40. Sriram PV, Kaffes AJ, Rao GV, et al. Endoscopic ultrasound-guided drainage of pancreatic pseudocysts complicated by portal hypertension or by intervening vessels. Endoscopy 2005;37:231–5.
41. Werner J, Feuerbach S, Uhl W, et al. Management of acute pancreatitis: From surgery to interventional intensive care. Gut 2005;54:426–36.
42. Seewald S, Groth S, Omar S, et al. Aggressive endoscopic therapy for pancreatic necrosis and pancreatic abscess: A new safe and effective treatment algorithm. Gastrointest Endosc 2005;62:92–100.
43. Howard TJ, Rhodes GJ, Selzer DJ, et al. Roux-en-Y internal drainage is the best surgical option to treat patients with disconnected duct syndrome after severe acute pan- pancreatitis. Surgery 2001;130:714–9.
44. Mouli VP, Sreenivas V, Garg PK. Efficacy of Conservative Treatment, Without Necrosectomy, for Infected Pancreatic Necrosis: A Systematic Review and Meta-analysis. Gastroenterology. 2012 Oct 12. doi:pii: S0016-5085(12)01494-1.
45. Cirocchi R, Trastulli S, Desiderio J, Boselli C, Parisi A, Noya G, Falconi M. Minimally invasive necrosectomy versus conventional surgery in the treatment of infected pancreatic necrosis: a systematic review and a meta-analysis of comparative studies. Surg Laparosc Endosc Percutan Tech. 2013 Feb;23(1):8-20.
46. Angel García-Ureña M, López-Monclús J, Melero-Montes D, Blázquez-Hernando LA, Castellón-Pavón C, Calvo-Durán E, Gordo-Vidal F, Hoyo LF. Video-assisted Laparoscopic Débridement for Retroperitoneal Pancreatic Collections: A Reliable Step-up Approach. Am Surg. 2013 Apr;79(4):429-33.

Derleme (Review)

Özofagus Varislerinin Tedavisi: Primer Profilaksi, Akut Kanama ve Sekonder Profilaksi

Treatment of Esophageal Varices: Primary Prophylaxis, Acute Bleeding, and Secondary Prophylaxis

Mesut KUŞ[1], Serhat AKPINAR[1], Bülent KANTARÇEKEN[1], Kadir GİŞİ[1]

[1] Sütçü İmam Üniversitesi, Tıp Fakültesi, Dahili Tıp Bilimleri Gastroenteroloji Bilim Dalı, Kahramanmaraş, Türkiye

Özet

Siroz, karaciğerin ileri evre kronik hastalığı olup prognozu belirleyen en önemli komplikasyonlardan biri portal hipertansiyondur. Portal hipertansiyon sonucu gelişen özofagus varisleri ve bunlardan kaynaklanan gastrointestinal kanamalar, sirozun en ciddi ve yaşamı tehdit eden komplikasyonları arasında yer almaktadır. Sirotik hastaların yaklaşık %50'sinde özofagus varisleri bulunmakta olup, bu hastaların üçte birinde majör morbidite ve mortalite nedeni olan varis kanaması gelişmektedir. Özofagus varislerinin gelişimini önlemeye yönelik pre-primer profilaksi önerilmemektedir. Ancak varis saptanan hastalarda primer kanama profilaksisi, varisin boyutuna, karaciğer yetmezliğinin evresine ve hastanın tedaviye toleransına göre non-selektif β-blokerler ve/veya endoskopik band ligasyonu (EVL) ile yapılmaktadır. Akut varis kanamasında ise, acil kombine tedavi (EVL + vazoaktif ajanlar), yoğun bakım koşullarında dikkatli izlemle birlikte önerilmektedir. Sekonder profilakside, varislerin tamamen obliterasyonu sağlanmalı ve hepatik venöz basınç gradyenti (HVPG) 12 mmHg'nın altına düşürülmelidir; bu yaklaşım günümüzde standart kabul edilmektedir. Gelecekte, altta yatan karaciğer hastalığının tedavisinde sağlanacak ilerlemelerle portal basıncın daha etkin şekilde düşürülmesi mümkün olabilecek, hatta tek bir ilaç ile bu mortal komplikasyonun önlenmesi konusunda daha iyimser bir tablo ortaya çıkabilecektir.

Anahtar Kelimeler: Siroz, Özefagus varisi, Profilaksi, Endoskopik band ligasyonu, Endoskopik skleroterapi, Non-selektif beta bloker

Abstract

Cirrhosis is an advanced stage of chronic liver disease, and one of its most critical prognostic determinants is portal hypertension. Esophageal varices that develop as a consequence of portal hypertension, along with the gastrointestinal bleeding arising from them, represent among the most severe and life-threatening complications of cirrhosis. Approximately 50% of cirrhotic patients have esophageal varices, and one-third of these patients experience variceal bleeding, which is a major cause of morbidity and mortality. Pre-primary prophylaxis aimed at preventing the development of varices is not recommended. However, in patients with established varices, primary prophylaxis against bleeding is guided by the size of the varices, the stage of liver failure, and the patient's tolerance to treatment, and involves the use of non-selective β-blockers and/or endoscopic band ligation (EVL). In cases of acute variceal bleeding, emergency combination therapy (EVL combined with vasoactive agents), along with close monitoring in an intensive care setting, is recommended. In secondary prophylaxis, complete variceal obliteration should be achieved, and the hepatic venous pressure gradient (HVPG) should be reduced to below 12 mmHg; this approach is currently considered the standard of care. In the future, advances in the treatment of the underlying liver disease may allow for more effective reduction of portal pressure, and possibly, a single pharmacologic agent could emerge that significantly improves outcomes and offers a more optimistic perspective for managing this fatal complication.

Keywords: Cirrhosis, Esophageal varices, Prophylaxis, Endoscopic band ligation, Endoscopic sclerotherapy, Non-selective beta blocker

Yazışma Adresi: Mesut KUŞ Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Gastroentereoloji Bilim Dalı, Kahramanmaraş, Türkiye

Telefon: +90 344 300 30 48 **e-mail:** mst.kus@gmail.com

ORCID No (Sırasıyla): 0009-0009-0709-7275, 0009-0002-3851-937X, 0000-0003-4214-817X, 0000-0003-4082-4832

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GİRİŞ

Siroz, karaciğerin ileri evre kronik hastalığı olup, prognozu belirleyen en önemli komplikasyonlardan biri portal hipertansiyondur. Portal hipertansiyona bağlı olarak gelişen özofagus varisleri ve bu varislerden kaynaklanan gastrointestinal kanamalar, sirozun en ciddi ve yaşamı tehdit eden sonuçları arasında yer alır. Sirotik hastaların yaklaşık yarısında özofagus varisi vardır ve bunların 1/3'ünde ana morbidite ve mortalite nedenlerinden olan varis kanaması ortaya çıkar. Varisin boyutu, portal hipertansiyonun derecesi ve hepatik venöz basınç gradienti (HVPG) gibi birçok neden bu durum için risk oluştururken, temelde nedenin varisin büyüklüğü, görünümü ve hepatik yetmezliğin derecesi ile ilişkili olduğunu söyleyebiliriz (1). Tanı anında hastaların yaklaşık %50'sinde özofagus varisleri saptanırken, bu oran hastalığın ilerlemesiyle birlikte on yıl içerisinde %90'a kadar yükselmektedir. Bunların yaklaşık %20 - 40'ında varis kanaması gelişmektedir (2) ve varis kanaması gelişen hastaların % 40'ında kanama kendiliğinden durmasına rağmen kanama sonrası ilk altı haftada yaklaşık %20 mortalite riski vardır. Sirotik hastalardaki üst gastrointestinal sistem kanamalarının %50-90'ında neden varislerdir (3). 206 sirotik hastanın (Başlangıç değerlendirmesinde; 113'ünde varis yok, 93'ünde hafif derecede özofagus varisi mevcut) yıllık endoskopilerle ortalama 37 aylık takibinde; yeni varis gelişimi sırası ile 1 ve 3 yılda %5 ve %28 olarak saptanmıştır. Küçük varislerin 1 yılda %12'sinin, 3 yılda ise %31'inin büyüme gösterdiği gözlenmiştir. İlerleme özellikle Child C olanlarda, alkolik sirozlularda ve kırmızı kamçı izi şeklinde lekelenmeler olan varislerde daha belirgindir. 2 yıllık kanama riski başlangıçta küçük varisi olanlarda daha fazla saptanmıştır (%12 vs %2) (4). Sirotik hastalarda tanı sırasında gözlenen varis sıklığı sirozun evresine göre değişmektedir ve bu oranlar sırasıyla Child A'da yaklaşık %40, Child B'de %65 ve Child C'de %85 olarak belirtilmiştir (5). İlginç olan, bazı hastalarda siroz oluşmadan, erken hastalık döneminde de varis gelişebilmekte ve kanama ortaya çıkabilmektedir. Daha önce hiç varis saptanmamış hastalarda yılda %8 oranında varis gelişmektedir. Özofagus varislerinin gelişimini ve varis kanamasını öngörmede en önemli belirteç, HVPG'nin 10–12 mmHg'nin üzerine çıkmasıdır. Normal HVPG değeri 3–5 mmHg arasında olup, 5 mmHg'nin üzerindeki değerler portal hipertansiyon olarak kabul edilirken, 10 mmHg'yi aşan değerler klinik olarak anlamlı portal hipertansiyon olarak değerlendirilir. Sirotik hastalarda HVPG <10 mmHg olduğunda anlamlı olarak daha az varis gelişmektedir, HVPG >12 mmHg olduğunda ise varis kanama riski anlamlı olarak artmaktadır (6). Oniki çalışmanın sistematik olarak değerlendirildiği bir çalışmada HVPG < 12 mmHg olmasının varis kanaması ve mortalite riskinde anlamlı azalma ile ilişkili olduğu gösterilmiştir (7). Dolayısı ile hemoraji gelişimini önlemek için HVPG nin 12 mmHg altına çekilmesi veya bazal değerlerden % 20 azaltılması gereklidir (1,8,9).

Tanımlar — Terminolojideki karmaşıklığı gidermek için özofagus varis kanaması için iki çalışma gurubu tarafından tanımlamalar yapılmıştır **(Tablo 1)** (9).

SİROTİK HASTALARDA VARİS TARAMASI VE İZLEM

Tarama temel olarak üst endoskopi ile yapılır. Kapsül endoskopide kullanılmıştır ve ayrıca trombosit sayısının dalak büyüklüğüne oranı ve bazı klinik parametrelerin (Trombosit sayısı, dalak büyüklüğü ve albümin seviyeleri) çocuklarda varis için işaretçi olduğu gösterilmiştir (10). Son dönemde trombosit sayısının dalak çapına oranının (PC/SD) 909'un altında olmasının, bazı küçük modifikasyonlar ile ucuz, basit ve iyi bir

Tablo 1. Özofagus varis kanaması için terminoloji ve tanımları*

0 zamanı; Hastaneye kabul zamanı.	
Klinik olarak anlamlı kanama; 24 saatte ≥2 ünite kan transfüzyonu gereksinimi ile beraber sistolik kan basıncının <100 mmHg, kalp hızının >100/dk olması.	
Akut kanama epizodu; 0 zamanı – 120 saat arasındaki kanamalar.	
Tedavi başarısızlığı; Endoskopik veya spesifik tedaviye rağmen, 2 saat içinde taze hematemez veya nazogastrik tüpte >100 ml kan varlığı, hipovolemik şok gelişimi, 24 saatte Hgb değerinde ≥ 3 gr düşüş (Bu durumlardan herhangi biri)	
**Rebleeding; 5 gün – 6 hafta arasındaki kanamalar olarak kabul edilir.	Çok Erken rebleeding; 48 saat – 5 gün arasında
	Erken rebleeding; 6 gün – 6 hafta arasında
	Geç rebleeding; 6 hafta sonrasında

*Kaynak 9'dan modifiye edilmiştir, **Rebleeding; Yazının bundan sonraki kısmında rekürren kanama olarak kullanılacaktır.

non-invaziv varis belirteci olabileceği ileri sürülmektedir (11). Siroz tanısı konulan hastalarda varis taraması survey, proflaksi ve gidişatı öngörmek için önemlidir. Ancak konsensuslarda, Child A hastalarda taramanın gerekliliği konusunda çok ufak ayrılıklar olsada, hâkim görüş tüm sirotik hastalarda tanı anında bir varis değerlendirilmesi yapılması ve ayrıca tesbit edildiğinde büyüklük yönünden mutlaka sınıflandırılması yönündedir. Sınıflamada ise basit olarak küçük <5mm, büyük >5mm olarak önerenler olmakla beraber güncel olarak, küçük-orta-büyük (F1-F2-F3) şeklindeki sınıflama kabul görmektedir. Yüksek riskli hastalarda varislerin tanımlanması ve tedavisi klinik sonuçları iyileştirmektedir. Kompanse ve dekompanse sirozluların sırası ile %30 ve %60'ında tanı anında varisinin olduğu tahmin edilmektedir (12). Bu varislerinde yıllık kanama oranı %12'dir ve her kanama epizodu %15-20 mortalite riski taşımaktadır (13). Güncel kılavuzların tarama ve sonrası takip için önerileri tabloda gösterilmiştir **(Tablo 2)**.

VARİS KANAMASI İÇİN RİSK FAKTÖRLERİ

Özofagus varisi saptanan hastalarda riski belirlemek için pekçok çalışmadan varis kanamasını öngörebilecek önemli belirteçler ortaya konmuştur **(Tablo 3)**.

Varisin lokalizasyonu; Mid-özofagustaki varisler daha derinken distal özofagustakiler daha yüzeyeldir, özofago-gastrik bileşkedekiler ise en ince destek doku tabakasına sahiptirler ve dolayısı ile daha fazla rüptüre olur ve kanarlar.

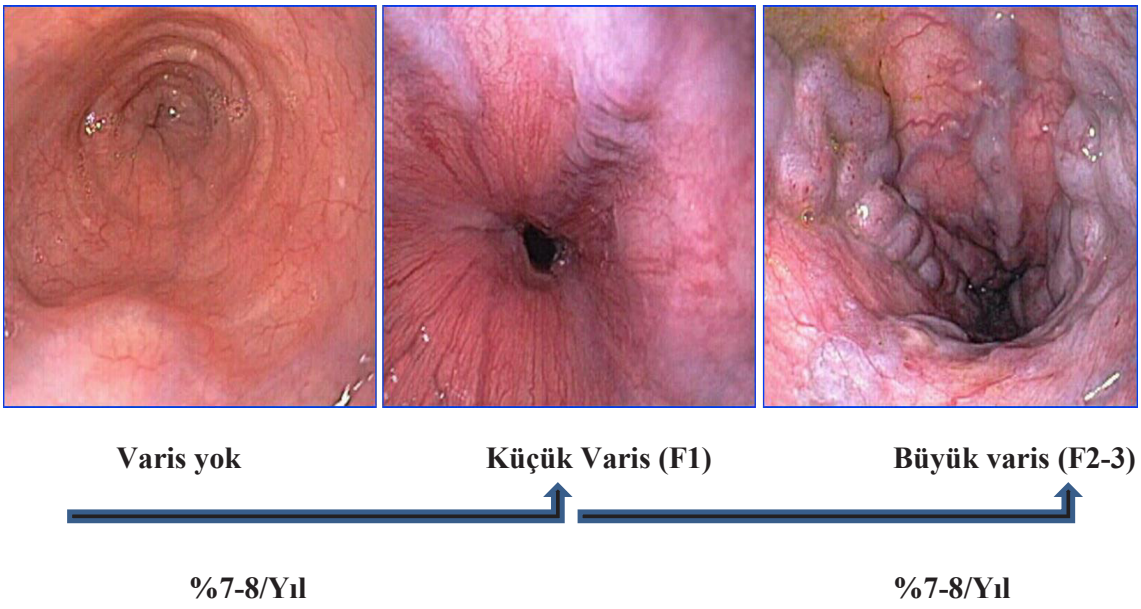
Varisin büyüklüğü; Varis kanaması riski varisin çapı (büyüklüğü) ile bağımsız olarak ilişkilidir. Çünkü varis çapındaki küçük bir artış duvar geriliminde büyük bir artışa neden olmaktadır. Özofagus varisleri çapına göre; F1 (Düz), F2 Lümenin üçte birinden azında tortuoze varisler, F3 (kangal şeklinde lümenin üçte birinden fazlasını kaplayan varisler) olarak sınıflandırılırlar **(Resim 1)**.

Tablo 2. Güncel kılavuzların tarama ve sonrası takip için önerileri (1,9,14)

KILAVUZ	TARAMA ÖNERİSİ	TAKİP	
ASGE 2005	Orta-şiddetli sirozu olan tüm hastalar (Child B/C) Portal hipertansiyon bulgusu olan Child A hastalar (Trombosit <140,000, Portal Ven çapı >13mm veya kollaterallerin varlığı)	Siroz var varis yok; 3 yıl sonra tekrar endoskopi	
		Siroz - Küçük varis; 1-2 yıl sonra tekrar endoskopi Alkolik, ciddi karaciğer yetmezliği, kamçı işareti; Yıllık endoskopi	
		Siroz – Büyük varis; Öneri yok	
AASLD - ACG 2007	Siroz tanısı konan tüm hastalar	Siroz var varis yok;	Kompanse; 3 yıl sonra endoskopi
			Dekompanse; Yıllık endoskopi
		Siroz - Küçük varis;	Beta bloker almıyor; 2 yılda bir endoskopi
			Dekompanzasyon: Yıllık endoskopi
			Beta bloker alıyor; Takip endoskopisi gerekmez
		Siroz – Büyük varis; EVL ve/veya Beta bloker ile primer proflaksi	
AASLD-EASL 2008 Single – topic konferansı	Siroz tanısı konan tüm hastalar	Endoskopik veya kapsül endoskopi ile Süre?	
WGO 2008	Siroz tanısı konan tüm hastalar	Kompanse siroz	Varis yok; 2-3 yılda bir endoskopi
			Küçük varis;1-2 yılda bir endoskopi
		Dekompanse siroz; Yıllık endoskopi	
BOVENO V 2010 Konsensus	Siroz tanısı konan tüm hastalar	*Öneri yok*	

Tablo 3. Varis Kanaması için önemli belirteçler	
Klinik Karaciğer hastalığının derecesi (Child-Pugh)	Child-Pugh A < B veya C Asit yok < Asit var
Endoskopik, Lokal faktörler	Varis boyutu Varis duvarının inceliği Kırmızı kamçı (red weal) işareti
Hemodinamik	HVPG > 10* - 12 mm Hg Kan volümü Kollateral kan akımı **İntraabdominal** basınç
Diğer	Alkol alımının sürdürülmesi-alkolik hastalarda Salisilat ve diğer NSAİİ kullanımı

*Hemen tüm çalışmalarda HVPG için 12 mmHg sınır alınmıştır ancak 2008'deki AASLD-EASL ortak single topic konferansında 10 mmHg sınır olarak bildirilmektedir (14).



Resim 1. Varislerin derecelendirilmesi (4)

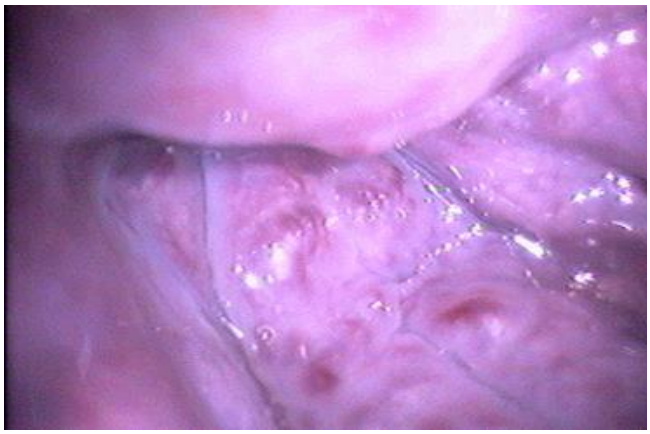
Varis Görünümü; Üzerinde kırmızı kamçı işareti olan (Resim 2) varisler her an kanayabilecek varislerdir (Özellikle sayıları arttıkça) **(Tablo 4)**.

Kırmızı kamçı işaretine göre varisin kanama ihtimali kırmızı kamçı işaretinin sayısı ve varisin büyüklüğü arttıkça katlanarak artmaktadır (15).

ÖZOFAGUS VARİSLERİNDE PROFİLAKTİK TEDAVİ

Pre-primer profilaksi

Pre-primer profilaksi, özofagus varislerinin gelişimini önlemeyi hedefler; ancak non-selektif beta-blokerlerle yapılan çalışmalar, bu tedavi yaklaşımının varis oluşumunu engellemede etkili olmadığını ortaya koymuştur. Ayrıca, bu ilaçların kullanımına bağlı olarak yan etki görülme sıklığının da yüksek olduğu bildirilmiştir. Gastroözofageal varisi olmayan hastalarda beta-bloker ile plasebonun varis gelişimini engellemede etkileri farklı değildir ve bu evrede spesifik tedavi yoktur. Esas amaç sirozun nedeninin saptanarak tedavi edilmesidir (portal hipertansiyon ve sonuçta klinik komplikasyon gelişiminin azaltılması). Dolayısı ile bugün için herhangi bir pre-primer profilaksi önerilmez. Sonrasındaki tarama endoskopisi için fikir birliği olmamakla beraber kompanse sirozlularda 2-3 yıl arayla, dekopmanse sirozlularda ise her yıl endoskopik değerlendirme uygun görünmektedir. Bir kısım araştırmacı HVPG'in izlenerek



Resim 2. Özofagus Varisinde "kırmızı kamçı" işareti

karar verilmesini önerse de klinik pratikte bunun izlenmesi güçtür ve rutine girmemiştir (1, 9).

Primer profilaksi

Primer profilakside amaç özofagus varisi olan ancak kanama öyküsü bulunmayan hastalarda varis kanamasının önlenmesidir. Günümüzdeki yaklaşımlar, portal hipertansiyonun azaltılmasını (Beta blokerler, cerrahi portal dekompresyon veya transjugular intrahepatik şantlar) ve/veya varislerin doğrudan tedavisini (EVL) hedeflemektedir. Varis kanamasında primer profilaksiden bahseden pek çok kılavuz yayınlanmıştır ve bunların farklı anlatımları olsa da önerileri hemen hemen ortaktır. Ancak, 2007 yılındaki AASLD ve 2010 yılındaki Boveno V kılavuzlarındaki hasta sınıflaması maliyet-etkinlik ve tedavinin olası yan etkilerinden kaçınma açısından daha akla yatkın görünmektedir (1,9). Sonraki kılavuzlarda da ufak farklılıklar olsa da hepsinde ortak olan primer proflakside hastanın risk durumuna göre non-selektif beta blokerler ve/veya EVL'nin kullanılmasıdır. Beta bloker – Nitrat/ EVL ve benzer kombinasyonlar henüz kabul görmemektedir. Boveno V konsensusunun kılavuzu, üzerinde kırmızı kamçı işareti olan küçük varislerde veya Child C sirozlularda non-selektif beta blokerler ile primer profilaksi önermektedir. Orta-büyük varislerde ise beta bloker ve/veya EVL önermektedir. AASLD kılavuzları ise benzer olarak, kompanse sirozu olup küçük varisi olan ve kırmızı kamçı işareti olanlarda non-selektif beta blokerler ile profilaksi önermektedir. Bu kılavuzlar yüksek riskli olmasalarda (Kırmızı kamçı işareti) küçük varisi olan sirotik hastalarda da beta-bloker proflaksisi yapılabileceğini de eklemektedirler. Çalışmalar seçilmiş hastalarda özellikle EVL veya non-selektif beta blokerler ile primer proflaksinin ilk kanamayı, dolayısı ile bununla ilişkili mortaliteyi azalttığını göstermiştir. Hem beta blokerler hemde EVL ilk varis kanamasının önlenmesinde tedavi almayanlara göre üstündür. Bazı raporlarda EVL'nin daha üstün olduğu ileri sürülsede genel kanaat belirgin bir fark olmadığı yönündedir (16). Aslında hastanın toleransı da göz önüne alınarak tercih yapılabilir, ancak orta-büyük varislerde EVL tercih edilmelidir. Primer proflakside beta bloker + EVL kombinasyonu, nitratlar, şant ve endoskopik skleroterapi (ES) önerilmez. Ancak yüksek riskli hastalarda, primer profilakside netleşmiş olmasa da beta-bloker + EVL kombinasyonu da uygun olabilir gibi görünmektedir. Nisbeten yeni ve potent bir beta bloker olan karvedilol da ümit vadetmektedir (1,9,16). Küçük varisi olup beta bloker kullanmayan hastalarda her iki yılda bir tekrar endoskopi yapılmalı ve kırmızı işaretler oluşmuş veya varis büyümüş ise tedavi başlanmalıdır (1,9). Eğer hastada hepatik dekompanzasyon işaretleri var ise endoskopi yapılmalı ve yıllık tekrarlanmalıdır. Beta bloker kullananlarda ise rutin endoskopi takibi önerilmemektedir, ancak küçük varisler tedaviye rağmen büyüme gösterebileceğinden 1-2 yılda bir endoskopik takibinin yapılması klinik pratiğe daha uygun görünmektedir. Takipte büyüdüğü görülen variste EVL'ye geçilebilir. Orta-büyük varisi olup medikal profilaksi alanlar içinde net belirlenmiş bir endoskopi takip önerisi yoktur ancak küçük varisler için ortaya çıkan durumlar bunlar içinde geçerlidir. Orta

Tablo 4. Endoskopik tedavilerin komplikasyonları

Lokal	Bölgesel	Sistemik
Ülser	Özofagus perforasyonu	Sepsis
Kanama	Mediastinit	Aspirasyon
Striktür	Plevral effüzyon	Spontan bakteriyal peritonit ve kandidemi
Özofagus motilitesinde bozulma	Akut gastrik dilatasyon	Ventilasyon-perfüzyon bozukluğu (hipoksi)
Ağrı		Adult respiratuar distress sendromu (ARDS)
Odinofaji		Portal ven trombozu
Laserasyon		

– büyük varisi olanlarda EVL yapıldığında 1-2 haftada bir varisler oblitere olana kadar EVL seansları yapılmalı (Band uygulanan kısımlardaki ülser ve diğer sakıncalar gözönüne alınarak, 2-4 haftalık aralara çıkılabilir), obliterasyon sonrasında ilk survelyans endoskopisi 1-3 ayda ve sonra her 6-12 ayda bir varis rekürrensi açısından yapılmalıdır (1,9).

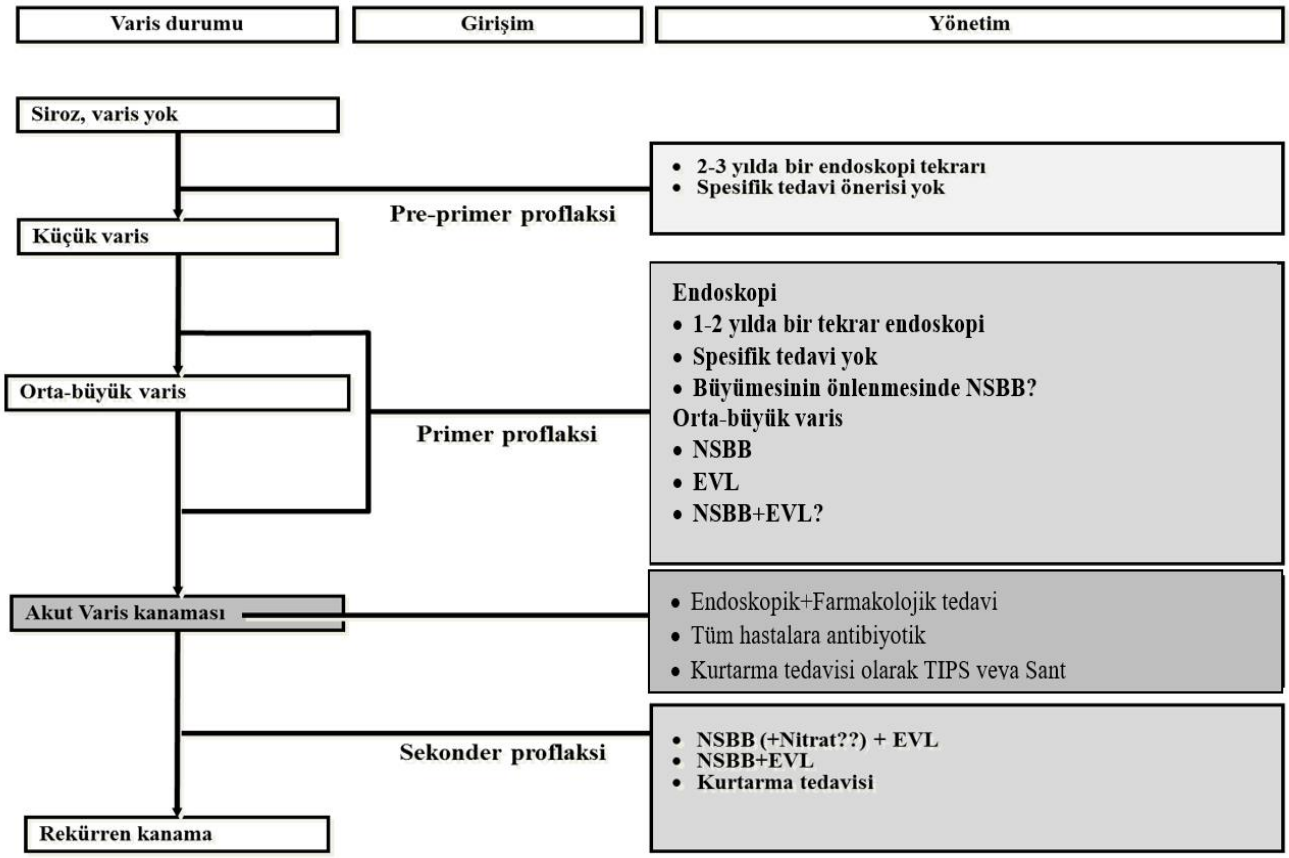
Non-selektif Beta blokerler; Günümüzde ensık kullanılan propranolol'dur (Nadolol, timolol son dönemde karvedilol). Propranolol 2x20 mg/gün peroral başlanır, istirahat nabzının 55-60/dk (Başlangıç nabızda bradikardiye yol açmayacak şekilde %25 azalma) hedeflenir. Tedavi hedefi sağlanana kadar 2-3 günde bir doz ayarlaması yapılarak maksimum tolere edilebilen doza çıkılır (Maksimum günlük doz 320mg). Büyük varise ilerleme ve ilk kanama riskini %50 azaltır. Bronkokonstrüksiyon, kalp yetmezliği, impotans, hipotansiyon, halsizlik güçsüzlük gibi yan etkileri ortaya çıkabilir, bu durumda uygun olanlarda EVL'ye geçilir.

EVL; İdeal EVL tekniğinde, bir mutiband ligatör kullanılmalı (4-10 band içerir) ve ligasyona gastroözofageal bileşkenin hemen üstünden (5-10 mm) başlanarak seri şekilde ve sıralı olarak 5 cm üzerine kadar çıkılmalıdır. Bir flush kateter ile görüş alanı temizlenmelidir. İlk seansta varislerin durumuna göre 6-10 banda kadar uygulanabilir (17). Sonraki seanslarda genellikle daha azı gerekir. Bununla birlikte randomize, prospektif bir çalışmadan, seans başına 6'dan fazla band yerleştirilmesinin hastanın akıbetini iyileştirmediğini ancak işlem süresini uzatıp hatalı band atımını artırdığı bildirilmiştir (18). Seanslar arasının (Normalde 1-2 hafta) banda bağlı ülserasyon gibi durumlarda 2-4 hafta olması uygundur. EVL, uygun olan tüm hastalarda primer profilakside (tek başına), en etkili yöntemdir (19). Şekilde özofagus varislerinde tüm profilaktik yönetimler gösterilmiştir **(Şekil 1)**.

AKUT VARİS KANAMASI

Genel yaklaşım

Akut varis kanaması hayatı ciddi şekilde tehdit eden ve acilen müdahele gerektiren bir durumdur. Kişinin genel vücut fonksiyonlarını da önemli derecede bozduğu için ilk yapılacaklar içinde mutlaka genel (ABC) destek yaklaşımları olmalıdır. Hastaya havayolu, solunum yönünden gerekli önlemler sonrası (Oksijen saturasyonunun %90 üzerinde tutulmasının güç olduğu hallerde, grade III-IV hepatik ensefalopatisi ve/veya aspirasyon pnömonisi olanlarda entübasyon düşünülebilir), mümkünse çift damar yolu açılmalı, aynı esnada



Şekil 1. Özofagus varis kanamasında proflaktik yönetim

CBC, PTZ, kan gurubu, temel biyokimyasal veriler ve cross için kan alınmalı, yoğun bakıma alınarak, volüm replasmanı dikkatli bir şekilde yapılmalı, kan transfüzyonu yapılırken, sistolik kan basıncı 90-100 mmHg civarında tutulacak ve kalp hızı 100'ün altında olacak şekilde, Hb; 8 g/dl'yi (Hematokrit % 21-24) mümkün olduğunca geçmemelidir, aşırı kan transfüzyonları kanamayı provake edebilir. Hastaların çoğunda hemostaz bozuk olduğundan, lüzumu halinde taze donmuş plazma ve trombosit desteği akılda tutulmalıdır. Bakteriyel enfeksiyonlar, gastrointestinal kanama nedeniyle hastaneye yatırılan hastaların %20'sinde başvuru sırasında mevcut olup, hastanede yatış süresince ek olarak %50 hastada daha gelişmektedir (20). Enfeksiyonlar tedavi başarısını düşürüp, sistemik komplikasyonları artıran bir durum olduğundan (En sık Gram (-) ler, özellikle E. Coli), optimal antibiyotik seçimi ve ne kadar kullanılması gerektiği kesin olarak belirlenmemiş olmakla birlikte kısa dönem (5-7 gün) profilaktik olarak seftriakson (1 gr/gün) veya kinolonlar (Norfloksasin 2x400 mg) gibi geniş spektrumlu antibiyotikler uygun görülmektedir (1,21). Bunlar enfeksiyon sıklığını azaltıp surviyi uzatmaktadır (22). Genel destek tedavisi de ara verilmeksizin dikkatli bir şekilde uygulanmalıdır. Özellikle yaşlı, kardiyovasküler komorbiditesi olanlarda, şok gelişmişlerde, böbrek yetmezliği olanlarda, tercihen juguler yoldan, CVP monitorizasyonu yapılmalıdır. Bazı hastalarda rekombinant faktör VIIa'nın kanama kontrolünde faydaları gösterilmiştir (23). Ancak kapsamlı olarak değerlendirildiğinde açık bir faydası gösterilememiştir (24).

Spesifik tedaviler

Varis kanaması için ideal başarılı tedavi, kanamayı kontrol etmeli, komplikasyonları önlemeli ve kanama-ilişkili mortaliteyi azaltmalıdır. Akut varis kanamasının kontrolü, tedaviden 24 saat sonra kanamanın kesilmesi ile birlikte hemodinamik stabilitenin sağlanmasıdır (8).

Farmakolojik tedavi

Temel olarak vazoaktif ilaçlar kullanılır (Somatostatin ve analogları (Octreotide/Vapreotide) Vasopressin (+nitratlar) ve analogları (Terlipressin), farklı mekanizmalarla splanknik alandaki damarlara etki ederek portal ven ve kollateral dolaşımda akım ve basınç azalmasına neden olurlar. Varis kanaması düşünüldüğü anda endoskopik işlem öncesinde başlanabilir ve tekrar kanama riskinin en yüksek olduğu 3-5 gün süreyle kullanılır. β-blokerler akut kanamada kullanılmaz.

Vazopressin; En potent splenik vazokonstriktördür, % 60-80 başlangıçta hemostazı sağlar. Yan etkileri klinik kullanımını sınırlar, nitratlarla kombinasyon yan etkilerini azaltır, etkinliğini ve güvenilirliğini artırır. Terlipressin ve somatostatine üstünlüğü yoktur, yan etkiler daha fazladır (Nitratla kombine edilse dahi). Dozu 0.4-0.8 ü/dk. infüzyon (+ 40 µg/dk Nitrat) şeklindedir. Güncel pratikte çok zorda kalınmadıkça tercih edilmez.

Terlipressin; Vazopressin sentetik analoğudur (daha yavaş ve kararlı salınır), Yan etki belirgin olarak daha azdır. Akut kanamayı kontrolde etkinliği somatostatin, oktreotid ve endoskopik tedavi ile yaklaşık aynıdır. Ancak kullanım öncesi bazal EKG çekilmelidir. Plasebo kontrollü çalışmalarda mortaliteyi azalttığı gösterilen tek ilaçdır. Oktreotide göre daha kararlı bir hemodinamik etki oluşturur. Her 4 saat arayla 2 mg bolus IV (kanama durunca 1 mg) 2-5 gün uygulanır.

Somatostatin ve Analogları; Somatostatin 250 mg IV bolus ve sonrasında 250-500 mg/saat infüzyon (6 gr/24 saat, 5 gün boyunca) Octreotid ise 50 mcg IV bolus sonrasında ise 50 mcg/saat infüzyon şeklinde uygulanır. Son meta-analizler tek başlarına yararlı etkilerinin sınırlı olduğunu göstermektedir ve terlipressine göre etkileri daha geçicidir. Endoskopik tedavi ile kombine edilmeleri daha yararlı gözükmektedir. Yine de terlipressin olmayan ülkelerde veya ulaşılamadığında klinik pratikte en sık kullanılan ve oldukça etkin görünen bir ilaçtır.

Çok yakın bir zamandaki bir meta-analiz akut varis kanamasında vazoaktif ilaç kullanımının akut mortaliteyi, transfüzyon gereksinimini, hastanede kalış süresini azalttığını ve kanama kontrolünü artırdığını bildirirken, farklı vazoaktif medikasyonları mukayese eden çalışmaların ise etkinlik farklılığı gösteremediğini bildirmektedir (25). Yakın dönemdeki bir başka sistematik değerlendirme raporunda endoskopik skleroterapinin tek başına vazoaktif ilaçlara üstün olmadığını ve hatta acilen ulaşılamasa da bu ilaçların yine de etkin ve güvenli olabileceği ileri sürülmüştür (26) ancak meta-analizler bu görüşü desteklememektedir ve endoskopik tedavi ile kombine kullanım önerilmektedir.

Endoskopik Tedavi

Tüm varis kanaması şüphesi olanlarda; tanısal ve teropatik endoskopi mümkün olan en erken zamanda yapılmalıdır. Varis kanaması düşünülüyor ise hızlı bir şekilde hazırlıklar yapılmalı ve müdahele edilmelidir. Endoskopi öncesi endoskopistin ve yardımcılarının kontrol etmesi gereken bazı durumlar vardır. Endoskopi öncesinde hasta hazırlığı kapsamlı bir şekilde yapılmalıdır. Bu süreçte hastanın vital bulguları sürekli olarak monitorize edilmeli, iki adet intravenöz kateter yerleştirilmiş olmalı ve sıvı replasmanının sürekliliği sağlanmalıdır. Ayrıca, hastaya destek oksijen tedavisi uygulanmalı, bilgilendirilmiş onam alınmalı ve olası

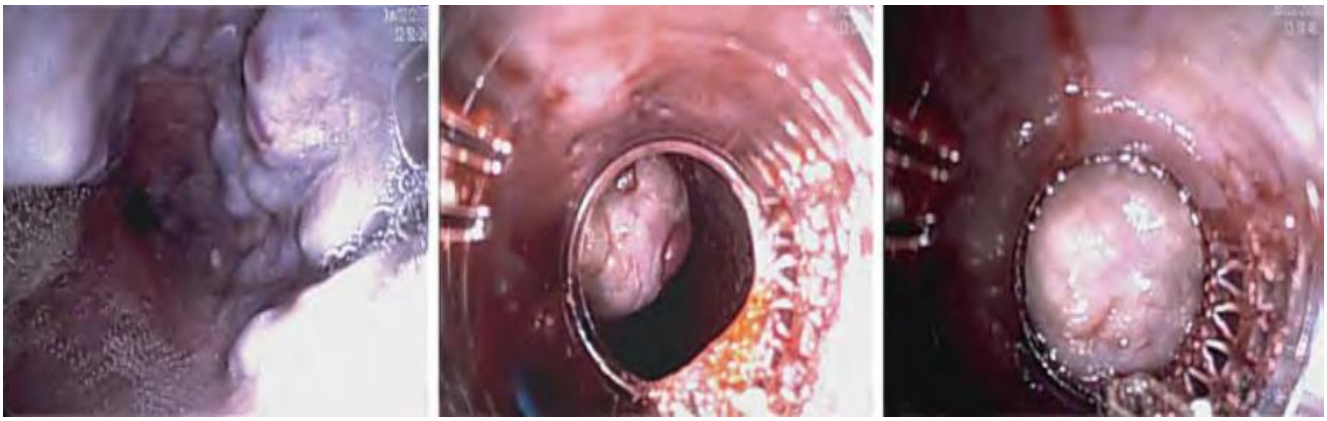
komplikasyonlara karşı acil resüsitasyon malzemeleri hazır bulundurulmalıdır. Endoskopi cihazının işlevselliği işlem öncesinde mutlaka kontrol edilmelidir. Bu kapsamda endoskopun hava-su kanalı, aspirasyon kanalı ve düğmeleri test edilmeli; cihazın sorunsuz çalıştığından emin olunmalıdır. İşlem sırasında gerekebilecek tüm malzemeler, özellikle EVL ve/veya ES için gerekli ekipmanlar hazır bulundurulmalıdır. Ayrıca, endoskopi sırasında yetersiz müdahale olasılığına karşı alternatif tedavi yöntemlerine yönelik önlemler de alınmalıdır. Bu bağlamda, Sengstaken-Blakemore tüpü hazır olmalı, transjuguler intrahepatik portosistemik şant (TIPS) işlemi için gerekli hazırlıklar yapılmalı ve gerektiğinde gastroenteroloji cerrahisi ile iş birliği sağlanmalıdır.

Akut varis kanamasında, EVL giderek artan şekilde kanama kontrolünde skleroterapinin yerini almaktadır, etkinliği benzer ancak yan etkileri daha düşüktür. Ancak görüş alanında yaşanabilecek sıkıntılardan dolayı yapılamadığında skleroterapi oldukça faydalı bir seçenektir. Endoskopi sırasında rutin sedasyon önerilmez ancak çok gerektiği durumlarda midazolam ve veya propofol kullanılabilir. Yakın dönemdeki bir meta-analizde, üst gastrointestinal sistem kanamalarında (Varis kanamalarını da içeren), endoskopik işlem öncesi hastaya düşük doz eritromisin verilmesinin midedeki kanı azaltıp, görüş alanını iyileştirip, ikinci endoskopi ihtiyacını ve hastanede kalış süresini azalttığı bildirilmiştir (27).

EVL: EVL ile akut kanama %80-100 kontrol edilebilmektedir ve ES'den hafif derecede daha etkin olduğu bildirilse de (%86 vs %77) (28) çok daha yakın bir zamandaki randomize prospektif bir tek merkez çalışmasında kanama kontrolü, komplikasyon ve mortalite yönünden anlamlı farklılık bulunamamıştır (6 hafta sonunda %80 vs %77) ve mortalite için en önemli parametrenin hastalığın evresi (Child ve MELD skorları) olduğu bildirilmiştir (29). İlk band kanayan varise atılmalı, kanayan noktasının veya hemen altının yakalanmasına çalışılmalıdır **(Resim 3)**. Multiband bir ligatör ile EVL akut varisiyel kanama için ilk tercihtir (Burada EVL-ES tercihi için endoskopistin deneyimi de önemlidir). İlk kanamanın kontrolü sonrası varislerin eradikasyonu için multiple seanslar gerekir.

Akut kanamada ilk band ligasyonu sonrası dönem — Tekrar kanama için yüksek riskli hastalarda eğer engel bir durum yoksa 7-10 gün içinde tekrar seanslarına başlanabilir. Ancak bu seansların ne zaman başlaması gerektiği konusu açık değildir ve klinik tecrübelere göre yön verilebilir. 2 ayda bir EVL seansları ile 2 haftada bir EVL seanslarını karşılaştıran bir Japon çalışmasında kanama kontrolü ve varislerin eradikasyonu açısından fark olmadığı bildirilmiştir (31). Ancak bunun ileri çalışmalarla desteklenmesi gerekmektedir ve akla yatkın görünen hastanın risk durumuna göre davranılmasıdır ki bunu destekleyen durum rekürren kanamaların çoğunun genellikle ilk müdahele ile varislerin obliterasyonu arasındaki zamanda oluşmasıdır. Aynı zamanda elektif yapılan EVL acil yapılan EVL'den anlamlı olarak daha başarılı olmaktadır (32). Rekürren kanama olmayıp varisler tamamen oblitere edildikten 1-3 ay sonra kontrolü ve sonrasında 6-12 aylık aralar ile kontrolü uygun görülmektedir (1,9). Sonuç olarak EVL akut kanamada (Eğer optimal yapılabilirse) ES'ye tercih edilebilir görülmektedir. Yan etkilerinin daha az olmasının yanı sıra, EVL'nin ES göre bir diğer üstünlüğü, varis obliterasyonu için daha az sayıda seans gerektirmesidir (3.7 vs 4.9). Önceki varis kanaması, özofajit, yüksek trombosit indeks skoru ve düşük protrombin indeksi post EVL ülserlerlerinden kanama için bağımsız risk faktörleridir (33).

ES: EVL'nin güç olduğu durumlarda veya EVL sonrasında rebleeding önlenmesinde, küçülmüş varislerde kullanılır. Polidokanol (Lauromakrogol) %1-3, absolut alkol, sodium tetradecyl sulfate %3, sodium morrhuate, ethanolamine oleate %5, fenol %3 kullanılabilir. Tercihen varis içine (Intravarisiyal) veya paravarisiyal uygulanabilir. En sık kullanılan sklerozan ajanlar polidokanol %1-3 veya ethanolamine oleate %5 (Avrupa-Asya), sodium



Resim 3. EVL uygulanışı(30)

morrhuate veya sodium tetradecyl sulfate (USA)'dır. Hiçbir ajanın standart dozu, birbirine üstünlüğü ve daha başarılı veya daha az ülserasyona neden olup olmadığı belirlenememiştir (34). ES için hangi sklerozan ajan kullanılırsa kullanılsın akut varis kanamasındaki delil seviyesi ES için Grade A'dır ve akut kanama hemostazı %70-100, rekürren kanama oranı %9-39 olarak bildirilmiştir. Paravarisiyal uygulamada daha fazla sklerozan maddenin komşu submukozaya injeksiyonu gerekir ki, ağrı ve diğer yan etkiler daha fazla gözlenir. İntravarisiyal uygulamanın akut kanama kontrolünde paravarisiyal uygulamaya göre çok daha üstün olduğu bildirilmiştir (%91 vs %18.7) (35). Özofagus varis skleroterapisinin yerini günümüzde geniş ölçüde bant ligasyonunun almasına ragmen aktif kanamaya bağlı, kanama yerinin iyi görülemedigi durumlarda veya teknik olarak güç olduğu durumlarda ES halen oldukça faydalı ve akut kanamada hayat kurtarıcı bir seçenektir. İntravarisiyel uygulamada kanama bölgesinin 1 cm altına injekte edilerek başlanır. Gastroözofagial bileşkede izlenen tüm varislere 1-2 mL injekte edilir. Proksimale doğru 2-5 cm aralarla bileşkenin 10 cm proksimaline kadar devam edilebilir (Tercihen distal 5 cm'lik bölgeye). Varislerin sayı ve boyutuna göre 10-20 mL (Ethanol hariç - en fazla 4 ml önerilir) her bir seansta enjekte edilir (36). Paravarisiyel kullanım daha yüksek miktarda sklerozan komşu submukozaya enjekte edilir. 23-25 gauge ve en fazla 5 mm ucu olan skleroterapi iğneleri tercih edilmelidir, çünkü iğne daha uzun olduğunda bakteriyemi ihtimali artmaktadır (37). ES'nin varis kanamalarında kanama kontrolünü anlamlı olarak artırdığı, kanama sayısı ve transfüzyon gereksinimini anlamlı şekilde azalttığı birçok çalışmada gösterilmiştir. Sklerozan madde veya işleme bağlı olmak üzere %20-40 oranında komplikasyon görülebilir. Hastanın durumuna ve endoskopistin tecrübesine göre değişmekle birlikte mortalite oranı %1-2 civarındadır. Bir çalışmada EUS kullanılarak özofagus venlerine doğrudan skleroterapi ile ümit vaadedici sonuçlar bildirilse de çalışmadaki hastalar akut kanayan değil, orta-büyük varisi olan elektif hastalardır (38).

Akut kanamada ilk ES sonrası dönem — Kan kaybı, pulmoner komplikasyonlar, ateş ve özofagus perforasyonu bulguları yönünden hasta takip edilir. Tedavi gerektirecek düzeyde ağrı olabilir. Tam varis obliterasyonu sağlanana kadar genellikle 3-6 seans gerekir (ortalama 4.9). Seans aralıklarının 1-3 hafta olması uygun görünmektedir. Daha sık intervaller daha az rekürren kanama fakat daha fazla ülserasyon ile ilişkilidir. Başarılı bir ES genellikle doku nekrozundan kaynaklanan yüzeyel varis ülserasyonları ile tanımlanır ki, bu ülserasyonlar birinci gün %90, bir hafta sonra ise %70 civarında hastada görülür. EVL ile benzer şekilde, en fazla tekrar kanama ilk kanamadan varisler tam olarak eradike edilene kadar ortaya çıkmakla beraber obliterasyon sonrası dönemde de % 20-50 tekrar kanama oluşabilmektedir, dolayısı ile survelyans ve gereğinde tekrar ES için 6-12 ayda bir endoskopik takip yapılmalıdır (39).

Endoskopik yöntemlerin akut kanama kontrolündeki başarı oranları yapılan çalışmalarda EVL için %71-100 iken ES'de %77-92 olarak saptanmıştır. ES EVL'ye göre daha fazla lokal veya sistemik komplikasyonla ilişkilidir (Göğüs ağrısı, plevral efüzyon, disfaji ve ateş gibi). EVL ve/veya ES ile ilişkili komplikasyonlar Tablo 4'te belirtilmiştir. Ayrıca yönteme göre komplikasyon oranları yapılan çalışmalarda EVL için %2-56 iken ES'de %10-60 olarak saptanmıştır. Komplikasyon oranının EVL de ES'e göre daha az görüldüğü yapılan çalışmalarda gösterilmiştir (40).

Kombinasyon tedavisi

Farmakolojik ve endoskopik tedavinin kombinasyonu akut kanama kontrolünde en etkili yaklaşımdır ve ilk basamak tedavisidir (1,8,9,14). Ancak endoskopik tedavi metodlarının gerek akut kanamada gerekse varis eradikasyonunda kombinasyonu bugün için kabul gören bir ilk basamak yaklaşımı değildir. Bazı çalışmalarda, argon plazma koagülasyonu ile EVL'nin ya da EVL ile skleroterapinin kombinasyonunun, komplikasyon oranlarında artış olmaksızın daha etkili varis eradikasyonu sağladığı (40) ve rekürren varis kanama oranlarını azalttığı (41) bildirilmiştir. Ancak bu yöntemler henüz rutin klinik uygulamada yer bulamamış olup, yüksek maliyetleri ve sınırlı erişilebilirlikleri nedeniyle yaygınlaşamamıştır. Rutin kullanımda yer almayan bir diğer kombinasyon tekniği ise, mikrodalga koterizasyon (termal tedavi yöntemi) ile EVL sonrasında uygulanan varis eradikasyonudur (42).

Balon Tamponadı

Farmakolojik ve endoskopik tedaviye rağmen kontrol edilemeyen kanamalarda geçici olarak, diğer tedavilere ulaşmada köprü olarak maksimum 12-24 saat kullanılabilir. En sık Sangstaken Blackmore tüpü kullanılmaktadır. Uygulamadan önce mide boş olmalıdır. Hasta sol lateral pozisyonda olmalıdır. Tüp burun ve ağızdan yutulduktan sonra önce mide balonu 100-300 ml hava ile şişirilerek hafifçe çekilir ve 0,5 kg ağırlıkla traksiyona alınır. Sonra özafagus balonu şişirilir. Özafagus balonundaki basınç saatlik kontrol edilmelidir. Son dönemde özel dizayn edilmiş self expandible metal stentlerin (SEMS) kurtarıcı tedavide balon tamponadının yerini alabileceği bildirilmiş olsa da ileri araştırma gerekmektedir (43).

TIPS

Farmakolojik ve endoskopik tedaviye rağmen kontrol edilemeyen kanamalarda hayat kurtarıcı olabilir ve

karaciğer transplantasyonu için köprü olabilir. Ancak deneyim gerektirir ve her merkezde ulaşılabilir değildir (1,8,9). Akut kanamada TIPS kombine farmakolojik ve endoskopik tedaviye rağmen kontrol edilemeyen kanamalarda uygulanır. Erken TIPS yerleştirimi (Kanamanın ilk 24 saati içinde) yüksek riskli hastalara (HVPG> 20) düşünülebilir. TİPS (ilk 72 saat içerisinde) standart tedavi başarısızlığında mortaliteyi oldukça azaltır. Fakat olası bir karaciğer transplantasyonu gereksiniminde operasyonda teknik güçlüklere neden olabilir (Hasta ve graft surveyini etkilemeden) Merkezin deneyimi önemlidir. TIPS disfonksiyonu kaplı stentler ile azaltılabilir (44).

Cerrahi

Cerrahi şantlar seçilmiş hastalarda oldukça etkindir, sık tekrar eden ciddi kanamaları olanlarda gastrorenal veya gastrocaval şantlar uygulanabilir. Özellikle yeterli deneyim sahibi merkezlerde Child A hastalarda düşünülebilir. Ancak ciddi mortaliteye sahiptir (%50). Cerrahi devaskülarizasyon başka seçenek kalmadığında, bir başka yaklaşımdır.

SEKONDER PROFLAKSİ; ÖZOFAGUS VARİSLERİNDE REKÜRREN KANAMANIN ÖNLENMESİ

Varis kanaması öyküsü olanlarda tekrar kanamanın önlenmesi sekonder proflaksinin amacıdır. İndeks kanama sonrası hastaların yaklaşık %70'inde (tedavisiz) rekürren varis kanaması ortaya çıkmaktadır ve %33 mortalite ile sonuçlanmaktadır (45). Rekürren kanama, indeks kanama kontrol altına alındıktan sonraki kanamalardır. En yüksek risk ise ilk 48-72 saat içindedir ve bütün erken rebleeding epizodlarının %50'sinden fazlası ilk 10 günde ortaya çıkar (%50'si ilk 48 saatte) ve sonrasında giderek azalır. Çok erken kanama 48 saat-5 gün içindeki, erken kanama 6-42 gün içindeki, geç rekürren kanama ise 6-10 hafta arasındaki kanamalardır (Tablo 1)(9). Aktif kanamanın durması sonrasındaki yaklaşık altı hafta rekürren kanama için yüksek risk taşır. Erken rebleeding için risk faktörleri 60 üstü yaş, böbrek yetmezliği, büyük varisler, ilk kanamanın ciddi olmasıdır (Hgb <8 g/dL) ve bu dönemdeki gidişat surveyi belirler (44). Akut varis kanaması yaklaşık %15-20 30 günlük mortaliteyle ilişkilidir (46). Child C grubuna giren sirozlu hastaların %15-30'u varis kanamasını takiben altı hafta içerisinde kaybedilirler (47). Ek olarak bazı veriler non-selektif beta bloker alanların dahi rekürren kanama için artmış risk içinde olduğunu göstermektedir (48). Bununla birlikte bazı çalışmalarda özellikle nadolol ve/veya ISMN ile sekonder proflakside iyi sonuçlar bildirmiş, henüz yayınlanmış bir çalışmada ise karvedilol, sekonder proflakside Nadolol+ISMN kombinasyonu kadar etkin bulunmuştur (49). Sekonder proflaksi için kılavuzlar tarafından önerilen ve meta-analizlerden tarafından da desteklenen ilk seçenek tedavisi EVL + Beta blokerlerdir. Tüm bu çalışmalardan bildirilen rekürren kanamayı azaltmada en üstünken, kapsamlı mortaliteye değiştirmediğidir (Aslında hiçbir yöntem değiştirmemektedir) (50). Bir meta-analiz EVL+Beta bloker + İsosorbid mononitrat şeklindeki tedavinin en iyi tedavi yöntemi olabileceğini ileri sürmüştür, ancak 12 randomize çalışmayı kapsayan bu meta-analizdeki 6 çalışma (N=687) ilginç olarak ISMN eklenmesinde fark bulamamıştır, dahası kümülatif olarak burada da mortaliteye etkisiz olduğu bildirilmiştir. Beta blokerlere (+EVL) ek olarak nitrat kullanılması rekürren kanama riskini azaltmamaktadır (51). Aslında ES'de plesaboya göre rekürren kanamayı azaltmaktadır ancak EVL daha üstün ve yan etkisi daha azdır. EVL ile küçültülmüş ve artık EVL'ye uygun olmayan varislere düşük dozlarda skleroterapi ile obliterasyon sağlanabilir. EVL+ES kombinasyonu, tekli işlem etkinliğinde ancak daha fazla yan etkiye sahip olmasından dolayı önerilmez (52). Sekonder proflaksi de uygulanması gereken tedaviler ve izlem akut kanama kısmında geniş olarak bahsedilmiştir, yukarıda ise algoritmik olarak verilmiştir (Şekil 1). Bu yöntemler ile istenilen sonuca ulaşılamayanlarda ise TIPS, cerrahi yöntemler veya karaciğer transplantasyonu düşünülmelidir (8, 9). Endoskopik yöntemlere göre 1 yıllık rekürren kanama oranları yapılan çalışmalarda EVL için %6-42, ES için %21-73 olarak bildirilmiştir ve rekürren varis kanaması için risk faktörleri tabloda verilmiştir **(Tablo 5)**.

SONUÇ

Portal hipertansiyon nedenlerinden çok sonuçları ile meydan okuyan bir tablodur ve varis kanaması en ölümcül komplikasyonudur. Özofagusta varis gelişimini önlemeye yönelik pre-primer proflaksi önerilmezken, varis gelişmişlerde kanama primer profilaksisinde, varisin durumuna, karaciğer yetmezliğinin evresine ve hastanın toleransına göre β-bloker ve/veya EVL, akut kanamada acil kombine tedavi (EVL+ vazoaktif ilaçlar) ve yoğun bakım ile dikkatli izlem, sekonder profilakside ise varislerin tamamen obliterasyonu ile birlikte HVPG'nin 12 mmHg'nın altına düşürülmesi (NSBB) günümüzün kabul edilen esas yaklaşımlarıdır. Gelecekte, altta yatan hastalığın tedavisinde atılacak başarılı adımlar, portal basıncı etkin düşürebilecek, belki de tek bir ilaç bu mortal komplikasyon için çok daha iyimser olmamızı sağlayabilecektir.

Tablo 5. Rekürren varis kanaması için risk faktörleri* (9)

Erken rekürren kanama	- Yaş >60 - Başlangıç kanamasının şiddeti (hipotansiyon, derin anemi) - Böbrek yetmezliği - İleri evre MELD > 18 & CPH skoru - Assit - Endoskopi sırasında aktif kanama - Kırmızı işaretler - Varis üzerinde trombosit pıhtısı - Agresif volüm replasmanı - Enfeksiyon - Yüksek HVPG (> 20 mmHg) - Endoskopik tedavinin komplikasyonları - Böbrek yetmezliği - Portal Ven Trombusü
Geç rekürren kanama	- İleri evre MELD > 18 & CPH skoru - Assit - Hepatoma - Aktif alkol kullanımı - Büyük varis çapı

*Erken kanama; İlk kanamadan 6 haftadan az sürede, Geç kanama; 6 haftadan sonraki kanama

KAYNAKLAR

1. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology 2007; 46:922.
2. Grace ND. Prevention of initial variceal hemorrhage. Gastroenterol Clin North Am 1992; 21:149.
3. Odelowo OO, Smoot DT, Kim K. Upper gastrointestinal bleeding in patients with liver cirrhosis. J Natl Med Assoc 2002; 94:712.
4. Merli M, Nicolini G, Angeloni S, Rinaldi V, De Santis A, Merkel C, et al. Incidence and natural history of small esophageal varices in cirrhotic patients. J Hepatol. 2003;38(3):266-72.
5. Pagliaro L, D'Amico G, Pasta L, Politi F, Vizzini G, Traina M, et al. Portal hypertension in cirrhosis: Natural history. In: Bosch J, Groszmann RJ. Portal Hypertension. Pathophysiology and Treatment. Oxford, UK:Blackwell Scientific, 1994: 72-92.
6. Albillos A, Bañares R, González M, Ripoll C, Gonzalez R, Catalina MV, et al. Value of the hepatic venous pressure gradient to monitor drug therapy for portal hypertension: a meta-analysis. Am J Gastroenterol. 2007 May;102(5):1116-26.
7. D'Amico G, Garcia-Pagan JC, Luca A, Bosch J. Hepatic vein pressure gradient reduction and prevention of variceal bleeding in cirrhosis: a systematic review. Gastroenterology 2006; 131:1611.
8. Sarin SK, Kumar A, Angus PW, Baijal SS, Baik SK, Bayraktar Y, et al. Asian Pacific Association for the Study of the Liver (APASL) Working Party on Portal Hypertension. Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations. Hepatol Int. 2011 Jun;5(2):607-24.
9. de Franchis R, Baveno V Faculty. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol 2010; 53:762.
10. Gana JC, Turner D, Mieli-Vergani G, Davenport M, Miloh T, Avitzur Y, et al. A clinical prediction rule and platelet count predict esophageal varices in children. Gastroenterology 2011; 141:2009.
11. Chawla S, Katz A, Attar BM, Gupta A, Sandhu DS, Agarwal R. Platelet count/spleen diameter ratio to predict the presence of esophageal varices in patients with cirrhosis: a systematic review. Eur J Gastroenterol Hepatol. 2012 Apr;24(4):431-6.
12. Vlachogiannakos J, Goulis J, Patch D, Burroughs AK. Review article: primary prophylaxis for portal hypertensive bleeding in cirrhosis. Aliment Pharmacol Ther 2000; 14:851.
13. Chalasani N, Kahi C, Francois F, Pinto A, Marathe A, Bini EJ, et al. Improved patient survival after acute variceal bleeding: a multicenter, cohort study. Am J Gastroenterol 2003; 98:653.
14. Garcia-Tsao G, Bosch J, Groszmann RJ. Portal hypertension and variceal bleeding--unresolved issues. Summary of an American Association for the study of liver diseases and European Association for the study of the liver single-topic conference. Hepatology. 2008 May;47(5):1764-72.
15. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. N Engl J Med 1988;319:983.
16. Li L, Yu C, Li Y. Endoscopic band ligation versus pharmacological therapy for variceal bleeding in cirrhosis: a meta-analysis. Can J Gastroenterol 2011;25:147.
17. Liu J, Petersen BT, Tierney WM, Chuttani R, Disario JA, Coffie JM, et al. Endoscopic banding devices. Gastrointest Endosc. 2008;68(2):217-21.
18. Ramirez FC, Colon VJ, Landan D, Grade AJ, Evanich E. The effects of the number of rubber bands placed at each endoscopic session upon variceal outcomes: a prospective, randomized study. Am J Gastroenterol 2007;102:1372.

19. Gluud LL, Krag A. Banding ligation versus beta-blockers for primary prevention in oesophageal varices in adults. Cochrane Database Syst Rev. 2012 Aug 15;8:CD004544.
20. Soares-Weiser K, Brezis M, Tur-Kaspa R, Leibovici L. Antibiotic prophylaxis for cirrhotic patients with gastrointestinal bleeding. Cochrane Database Syst Rev 2002; :CD002907.
21. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila F, Soares-Weiser K, Mendez-Sanchez N, Gluud C, et al. Meta-analysis: antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding - an updated Cochrane review. Aliment Pharmacol Ther 2011; 34:509.
22. Hou MC, Lin HC, Liu TT, Kuo BI, Lee FY, Chang FY, et al. Antibiotic prophylaxis after endoscopic therapy prevents rebleeding in acute variceal hemorrhage: a randomized trial. Hepatology 2004;39:746.
23. Bosch J, Thabut D, Bendtsen F, D'Amico G, Albillos A, González Abraldes J, et al. Recombinant factor VIIa for upper gastrointestinal bleeding in patients with cirrhosis: a randomized, double-blind trial. Gastroenterology 2004;127:1123.
24. Martí-Carvajal AJ, Karakitsiou DE, Salanti G. Human recombinant activated factor VII for upper gastrointestinal bleeding in patients with liver diseases. Cochrane Database Syst Rev 2012; 3:CD004887.
25. Wells M, Chande N, Adams P, Beaton M, Levstik M, Boyce E, et al. Meta-analysis: vasoactive medications for the management of acute variceal bleeds. Aliment Pharmacol Ther. 2012 Jun;35(11):1267-78.
26. D'Amico G, Pagliaro L, Pietrosi G, Tarantino I. Emergency sclerotherapy versus vasoactive drugs for bleeding oesophageal varices in cirrhotic cirrhotic patients. Cochrane Database Syst Rev. 2010;(3):CD002233.
27. Bai Y, Guo JF, Li ZS. Meta-analysis: erythromycin before endoscopy for acute upper gastrointestinal bleeding. Aliment Pharmacol Ther. 2011 Jul;34(2):166-71.
28. Hou MC, Lin HC, Kuo BI, Chen CH, Lee FY, Lee SD. Comparison of endoscopic variceal injection sclerotherapy and ligation for the treatment of esophageal variceal hemorrhage: a prospective randomized trial. Hepatology 1995;21:1517.
29. Chen WT, Lin CY, Sheen IS, Huang CW, Lin TN, Lin CJ, et al. MELD score can predict early mortality in patients with rebleeding after band ligation for variceal bleeding. World J Gastroenterol 2011;17:2120-5.
30. Garcia-Pagan JC, Bosch J: Endoscopic band ligation in the treatment of portal hypertension. Nat Clin Pract Gastroenterol Hepatol 2005;2:526–535.
31. Yoshida H, Mamada Y, Taniai N, Yamamoto K, Kawano Y, Mizuguchi Y, et al. A randomized control trial of bi-monthly versus bi-weekly endoscopic variceal ligation of esophageal varices. Am J Gastroenterol 2005;100:2005-9.
32. Petrasch F, Grothaus J, Mössner J, Schiefke I, Hoffmeister A. Differences in bleeding behavior after endoscopic band ligation: a retrospective analysis. BMC Gastroenterol 2010; 10:5.
33. Vanbiervliet G, Giudicelli-Bornard S, Piche T, Berthier F, Gelsi E, Filippi J, et al. Predictive factors of bleeding related to post-banding ulcer following endoscopic variceal ligation in cirrhotic patients: a case-control study. Aliment Pharmacol Ther 2010;32:225-32.
34. Croffie J, Somogyi L, Chuttani R, DiSario J, Liu J, Mishkin D, et al. Sclerosing agents for use in GI endoscopy. Gastrointest Endosc. 2007;66(1):1-6.
35. Sarin SK, Nanda R, Sachdev G, Chari S, Anand BS, Broor SL. Intravariceal versus paravariceal sclerotherapy: a prospective, controlled, randomised trial. Gut 1987; 28:657–662.
36. Park WG, Yeh RW, Triadafilopoulos G. Injection therapies for variceal bleeding disorders of the GI tract. Gastrointest Endosc. 2008 Feb;67(2):313-23.
37. H. Snady, M.A. Korsten, J.D. Waye. The relationship of bacteremia to the length of injection needle in endoscopic variceal sclerotherapy. Gastrointest Endosc, 1985;31:243–246.
38. de Paulo GA, Ardengh JC, Nakao FS, Ferrari AP. Treatment of esophageal varices: a randomized controlled trial comparing endoscopic sclerotherapy and EUS-guided sclerotherapy of esophageal collateral veins Gastrointest Endosc, 63 (2006), pp. 396–402.
39. De Franchis R, Primignani M: Endoscopic treatments for portal hypertension. Semin Liver Dis 1999;19:439– 455.
40. Harras F, Sheta el S, Shehata M, El Saadany S, Selim M, Mansour L. Endoscopic band ligation plus argon plasma coagulation versus scleroligation for eradication of esophageal varices. J Gastroenterol Hepatol. 2010 Jun;25(6):1058-65.
41. Cipolletta L, Bianco MA, Rotondano G, Marmo R, Meucci C, Piscopo R. Argon plasma coagulation prevents variceal recurrence after band ligation of esophageal varices: preliminary results of a prospective randomized trial. Gastrointest Endosc. 2002 Oct;56(4):467-71.
42. Monici LT, Meirelles-Santos JO, Soares EC, Mesquita MA, Zeitune JM, Montes CG, et al. Microwave coagulation versus sclerotherapy after band ligation to prevent recurrence of high risk of bleeding esophageal varices in Child-Pugh's A and B patients. J Gastroenterol. 2010 Feb;45(2):204-10.
43. Fuad Maufa and Firas H. Al-Kawas. Role of Self-Expandable Metal Stents in Acute Variceal Bleeding. International Journal of Hepatology Volume 2012, Article ID 418369, doi:10.1155/2012/418369.
44. Bureau C, Garcia Pagan JC, Layrargues GP, Metivier S, Bellot P, Perreault P, et al. Patency of stents covered with polytetrafluoroethylene in patients treated by transjugular intrahepatic portosystemic shunts: long-term results of a randomized multicentre study. Liver Int 2007;27:742.
45. Burroughs AK. The natural history of varices. J Hepatol 1993; 17(2):S10.
46. D'Amico G, De Franchis R, Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology 2003;38:599.
47. Carbonell N, Pauwels A, Serfaty L, FourdanO, Levy VG, Poupon R. Improved survival after variceal bleeding in patients vith cirrhosis over the past two decades. Hepatology 2004;40:652-9.
48. de Souza AR, La Mura V, Reverter E, Seijo S, Berzigotti A, Ashkenazi E, et al. Patients Whose First Episode of Bleeding Occurs While Taking a β-Blocker Have High Long-term Risks of Rebleeding and Death. Clin Gastroenterol Hepatol 2012;10:670.
49. Lo GH, Chen WC, Wang HM, Yu HC. A Randomized, Controlled Trial Of Carvedilol VS. Nadolol Plus Isosorbide Mononitrate For The Prevention Of Variceal Rebleeding. J Gastroenterol Hepatol. 2012 Jul 31. doi: 10.1111/j.1440-1746.2012.07244.x.
50. Thiele M, Krag A, Rohde U, Gluud LL. Meta-analysis: banding ligation and medical interventions for the prevention of rebleeding from oesophageal varices. Aliment Pharmacol Ther. 2012 May;35(10):1155-65. .
51. Gluud LL, Langholz E, Krag A. Meta-analysis: isosorbide-mononitrate alone or with either beta-blockers or endoscopic therapy for the management of oesophageal varices. Aliment Pharmacol Ther. 2010 Oct;32(7):859-71.
52. Singh P, Pooran N, Indaram A, Bank S. Combined ligation and sclerotherapy versus ligation alone for secondary prophylaxis of esophageal variceal bleeding: a meta-analysis. Am J Gastroenterol. 2002 Mar;97(3):623-9.

Letter to Editor (Editöre Mektup)

A Case of Iatrogenic Botulism with a Toxin of Unknown Formulation

Bilinmeyen Formülasyonlu Toksinle İyatrojenik Botulizm Vakası

Fatih KOCTURK[1]

[1] Sutcu Imam University, Faculty of Medicine, Department of Neurology, Kahramanmaras, Turkiye

Özet

Amaç: Botulinum toksini estetik ve terapötik pek çok alanda yaygın olarak kullanılan, genel olarak güvenli bir ajandır. Ancak önerilen dozların aşılması veya onaylanmamış/sahte ürünlerin kullanılması iatrojenik botulizme yol açabilmektedir. Bu olguda estetik amaçlı botulinum toksini uygulaması sonrası gelişen iatrojenik botulizm tablosu sunulmaktadır.

Olgu: Daha önce alın ve aksilla bölgelerine botulinum toksini uygulanan, 10 gün sonra ise ayak tabanına hiperhidroz nedeniyle tekrar enjeksiyon yapılan kadın hasta, son uygulamadan 5 gün sonra yaygın halsizlik, üst ekstremite proksimal kaslarında belirgin güçsüzlük, yutma güçlüğü, solunum yavaşlaması ve hafif pitoz yakınmaları ile başvurdu. Nörolojik muayenede bilinci açıktı, kraniyal sinirler sağlamdı; üst ekstremite proksimal kas gücü 4/5 idi. Solunum fonksiyonu stabildi. Klinik izlemde hastanın yutma fonksiyonları düzeldi, oral alımı sağlandı ve destek tedavisi ile taburcu edildi. Olgunun klinik seyri, botulinum toksininin sistemik yayılımı ile uyumlu değerlendirildi.

Sonuç: Bu olgu, standardizasyonu bilinmeyen veya sahte botulinum toksini ürünlerinin ciddi iatrojenik botulizm riskine yol açabileceğini göstermektedir. Estetik uygulamalarda ürün güvenilirliğinin sağlanması, doz ve uygulama protokollerine uyulması ve şüpheli durumlarda erken tanı-klinik yönetimin önem taşıdığı vurgulanmaktadır.

Anahtar Kelimeler: İyatrojenik botulizm, Toksin, Botulinum toksin

Abstract

Objective: Botulinum toxin is widely used for therapeutic and cosmetic purposes and is generally considered safe. However, exceeding recommended doses or using unapproved/counterfeit products may lead to iatrogenic botulism. This report presents a case of iatrogenic botulism following cosmetic botulinum toxin injections.

Case: A female patient received botulinum toxin injections to the forehead and axillae, followed by plantar injections for hyperhidrosis Ten days later, Botox was administered again to the soles of the feet for sweating. Five days after the last procedure, she developed progressive generalized weakness, marked proximal upper-extremity weakness, slowed breathing, mild dysphagia, and ptosis. Neurological examination revealed normal consciousness, intact cranial nerves, and 4/5 proximal upper-extremity strength. Respiratory function remained stable. During clinical follow-up, swallowing improved, oral intake was achieved, and the patient was discharged with supportive treatment. The clinical picture was considered consistent with systemic spread of botulinum toxin.

Conclusion: This case highlights the potential for iatrogenic botulism associated with counterfeit or non-standardized botulinum toxin products. Ensuring the authenticity of the toxin, adhering to recommended dosing protocols, and maintaining strict clinical oversight are essential for safe application. Early recognition and appropriate management of suspected cases are critical to prevent severe complications.

Keywords: Iatrogenic botulism, Toxin, Botulinum toxin

Correspondence: Fatih KOCTURK, Sutcu Imam Universitesi Tıp Fakültesi Nöroloji Anabilim Dalı, Kahramanmaraş, Türkiye

Phone: +90 546 246 10 75 **e-mail:** drfatihkocturk@gmail.com

ORCID No: 0000000291792685

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Dear Editor,

All serotypes block the release of the essential neurotransmitter acetylcholine at the neuromuscular junction, causing muscle paralysis. Weakness caused by botulinum toxin A injection usually lasts for about three months. Botulinum toxins play a very important role, especially in the treatment of strabismus and focal dystonia, hemifacial spasm, various spastic movement disorders, headaches, hypersalivation, and hyperhidrosis. Cosmetological applications include a range of treatments, from correcting lines, wrinkles, and creases on the face, chin, neck, and chest area to dermatological applications such as hyperhidrosis. Botulinum toxin injections are generally well tolerated and have few side effects (1).

We present a case of botulism that was affected by Botox treatment of the forehead and axillae in an external clinic. Ten days later, Botox was administered to the soles of the feet for sweating. According to her statement, she received spinal anesthesia. 5 days after the last Botox treatment, complaints of weakness in the arms and general weakness occurred. About a week after the onset of these complaints, when the patient was at home, her breathing slowed, she had weakness in the proximal muscles, difficulty swallowing, and mild ptosis. The patient, whose complaints had increased over the past 2 days, contacted our emergency department with these complaints. She was taken to the hospital by car. With these complaints, the patient was consulted in the emergency room and admitted to the neurology clinic for further examination and follow-up care.

First examination revealed; no chronic illnesses were present in history. The patient was conscious, oriented, and cooperative. Light reflex was bilaterally positive. Cranial nerves were intact. Motor examination revealed that muscle strength in the proximal bilateral upper extremities was 4/5, distal was 5/5, and muscle strength in the lower extremities was bilateral 5/5. Deep tendon reflexes were normoactive; plantar responses were bilateral flexor. Uvula was in the midline, and there was no edema. The patient could swallow semi-solid liquid food.

The patient, who was admitted to the neurology clinic with the preliminary diagnosis of iatrogenic botulism and whose vitals had stable vitals. Swallowing functions improved, was fed orally, and monitored with spontaneous respiration and planned to be discharged. The patient, who had upper respiratory tract infection symptoms, was discharged with Amoxicillin 1 g / 2x1, mouthwash, and Mestinon 60mg 3x1 treatment. Infection, neurology outpatient clinic control was recommended; in terms of acetylcholine receptor antibody for underlying myasthenia gravis. And imaging will be checked.

Participant was included in the study voluntarily by obtaining their consent via a form.

Doctors who perform cosmetic procedures in their clinics use different types of botulinum toxin. Some doctors also stated; they perform sweating, masseter, and upper face botox at the same time. They also often attend conferences with courses and learn the maximum doses for these different types. At an international conference where botulism cases were discussed, the Ministry of Health's regulation on the subject is shown on screen, and the upper limits for each type of botulinum toxin are discussed. In the presentation, the upper limit for abobotulinum toxin was set at 2500 units of abobotulinum (Dysport) and 1000 units for onabotulinum toxin (Allergan-Botox) in the regulation of the Social Insurance Institution (2-5). In a publication where botulismus cases were collected, it was stated that the consumption should not exceed 500 units in a month (6).

Based on the recommended doses in the FDA botulinum toxin A catalogs, in a review article covering the studies on cases received abobotulinum toxin of unknown formulation, 33 of the 63 individual cases in the review had received doses that were on average 3.2 ± standard deviation (SD) 1.6 times higher than the recommended dose for the specific formulation of botulinum toxin A. For example, nine patients with the specific indication of spasticity all received onabotulinum toxin A at a higher dose than the FDA-recommended dose of 200 units (7,8). In the review, the symptoms those included were generalized weakness in 67.2 % and shortness of breath in 24.5 %. More than half of the cases were treated conservatively (57.1%). In terms of degree of impairment, 20.6% were minimally impaired, 60.3 % had generalized muscle weakness, 7.9 % had respiratory insufficiency requiring support, and 11.1 % had to be admitted to the intensive care unit. The mean time from injection to the onset of symptoms or signs of systemic muscle weakness was 10.9 ± 8.0 days, and the mean duration of symptoms was 3.1 ± 3.0 months (7).

In addition, the patients reported in the recent studies developed a syndrome similar to botulism after intramuscular injections of therapeutic doses of onabotulinum toxin derived from two different batches of the drug. In the first patient, these symptoms occurred after only one dose, while in the second patient, they occurred after five years of regular treatment with the toxin. Clinically detectable weakness was present in the extraocular, bulbar, trunk, and limb muscles, and EMG changes were recorded in all muscles tested. The muscle weakness and EMG changes resolved a few weeks later (8,9).

Given the otherwise excellent safety record of botulinum toxin products, an accidental overdose, possibly due to an unauthorised product or a change in procedure, would be a plausible explanation for the incident described here. This case demonstrates a previously unrecognised potential for large outbreaks of iatrogenic botulism, and there are several lessons to be learned. The systematic error that appears to have led to toxin overdose and subsequent botulism in patients needs to be elucidated so that it can be actively avoided in the future. At the very least, in light of the WHO's 2022 warning about a counterfeit product in Turkey (10). The regulatory mechanisms designed to remove counterfeit toxin products from the market may need to be reviewed. It is an unethical practice for clinics to use counterfeit botox products to make more profit.

We know that some antibiotics enhance the effect of Botox, but it is not really strong enough to have a toxic effect. Its mechanism of action, as with high doses of aminoglycosides, may prevent the release of acetylcholine at the neuromuscular junction and cause a botulism-like clinical condition (11). Previous use of antibiotics has not been reported in our case, but we recommend that doctors take a break of several days after taking antibiotics, depending on the half-life, which reduces the interaction to almost zero.

The Social Security institution revealed Botox toxic doses as 2500 units (5 ampoules) at a time for abobotulinum toxin (Dysport) and 1000 units for onabotulinum toxin (Allergan). In fact, it is emphasized that you do not have to worry about toxicity if you are using an approved product; however, there is a danger with unapproved (counterfeit) products because the number of units is not exactly known. Some of the products are specifically for abobotulinum toxin of unknown formulation, while the toxin dose is zero; in some cases, it is 255 times higher than it should be (12). About toxin poisoning cases, there is the poison control center, calling 114 in Türkiye. There are only 3 provinces in Turkey: Kayseri, Ankara, and Izmir. However, they are sending the antitoxin by ambulance if you are admitted to a hospital with an intensive care unit.

Conflict of interest: The authors declare no conflict of interest.

Informed consent: An informed consent form was taken from the participant.

REFERENCES

1. Nigam PK and Nigam A. Botulinum toxin. Indian J Dermatol. 2010 Jan-Mar; 55(1): 8– 14.
2. Mestfest medical aesthetic medicine festival, international congress (May 30-June 2-2024). Cyprus.
3. Health application communiqué, social security institution . sut_2010-26.03.2010.pdf (tdb.org.tr).
4. www.drhuseyintirman.com, internet page site.
5. www.safakgoktas.com., internet page site.
6. Bhatia K, et al. Generalised muscular weakness after botulinum toxin injections for dystonia: a report of three cases. J Nerol Neurosurg Psyciatry, 1999 Jul; 67(1): 90–93.
7. Locke J., et al. Systemic muscular weakness after botulinum toxin A administration: a review of the literature. Drugs & Therapy Perspectives (2021) 37:315–327.
8. Highlights of prescribing information (onabotulinumtoxinA and abobotulinumtoxinA). 2009.https://www.accessdata.fda.gov/326drugsatfda_docs/label/2011/103000s5236lbl.pdf. Accessed 26 Apr 2021.
9. Bakheit AM, et al. Generalised botulism-like syndrome after intramuscular injections of botulinum toxin type A: a report of two cases. J Neurol Neurosurg Psychiatry. 1997 Feb; 62(2): 198.
10. Dorner MD, et al. A large travel-associated outbreak of iatrogenic botulism in four European countries following intragastric botulinum neurotoxin injections for weight reduction, Türkiye, February to March 2023. EuroSurveill, 2023 Jun 8; 28(23): 2300203.
11. Samizadeh S., De Boulle K. Botulinum neurotoxin formulations: overcoming the confusion. Clin Cosmet Investig Dermatol. 2018; 11: 273–287.
12. Denizbasi A. If I am toxicology expert, from then? , Oral presentation. 7th Eurasian congress on Emergency Medicine /25-28 November 2021