ISSN 2146-4006

# Bozok Medical Journal

Cilt: 13, Sayı: 3, Eylül 2023

# BOZOK TIP DERGİSİ

Volume: 13, Issue: 3, September 2023

Yozgat Bozok Üniversitesi Tıp Fakültesi Yayın Organıdır

Official Journal of Yozgat Bozok University Medical Faculty

www.bozok.edu.tr

# BOZOK TIP DERGİSİ



Dergimiz Türkiye Atıf Dizini (Türkiye Citation Index) ve Türk Medline Ulusal Sağlık Bilimleri Süreli Yayınlar Veritabanı'na kayıtlıdır.

**Yayın Türü** / Type of Publication
Yerel Süreli Yayın / Periodical Publication

**Tasarım - Dizgi** / Designing- Editing
Mehmet Kaan BAŞER / Mustafa ÇELİKKAYA

**Mizanpaj** / Layout
Mehmet Kaan BAŞER

# BOZOK TIP DERGİSİ

Cilt 13, Sayı 3, 2023



Yozgat Bozok Üniversitesi Tıp Fakültesi Yayın Organıdır. Yılda 4 kez, Mart, Haziran, Eylül ve Aralık aylarında yayınlanır.

**Yazışma Adresi:** Yozgat Bozok Üniversitesi Tıp Fakültesi Çapanoğlu Mah. Cemil Çiçek Cad. Erdoğan Akdağ Yerleşkesi Atatürk Yolu 7. Km 66100 YOZGAT

# BOZOK TIP DERGİSİ

Cilt 13, Sayı 3, 2023



Yozgat Bozok Üniversitesi Tıp Fakültesi Yayın Organıdır. Yılda 4 kez, Mart, Haziran, Eylül ve Aralık aylarında yayınlanır.

**Yazışma Adresi:** Yozgat Bozok Üniversitesi Tıp Fakültesi Çapanoğlu Mah. Cemil Çiçek Cad. Erdoğan Akdağ Yerleşkesi Atatürk Yolu 7. Km 66100 YOZGAT

# İÇİNDEKİLER

# CONTENTS

# CAN THE ROLE OF THE ACROMION INDEX IN THE DIAGNOSIS OF ROTATOR CUFF TEAR BE REDEFINED WITH A DIFFERENT MEASUREMENT TECHNIQUE?

## Rotator Cuff Yırtığı Tanısında Akromion İndeksinin Rolü Farklı Bir Ölçüm Tekniği ile Yeniden Tanımlanabilir mi?

Davut AYDIN[1], Murat KORKMAZ[1], Serhat DURUSOY[1], Hacı Ali OLÇAR[1], Muhammed SARIKAYA[1]

[1]Yozgat Bozok University, Orthopaedics and Traumatology

## ABSTRACT

**Objective:** Many radiographic parameters associated with Rotator Cuff Tears (RCT) have been described. Our aim is to measure the capacity to predict RCT by reinterpreting the Acromion Index (AI) with a new radiographic measurement technique.

**Material and Methods:** The shoulder Magnetic Resonance Imaging (MRI) report of a total of 62 patients and AI measured with the new technique in shoulder radiographs were evaluated. On shoulder radiographs, the glenohumeral length was identified as the length between the lateral humerus tuberculum majus and the anterior midpoint of the glenoid joint. The glenoacromial length was also defined from a different pers-pective as the length between the lateral tip of the acromion and the anterior midpoint of the glenoid joint.

**Results:** There was no significant difference in glenohumeral length between patients with complete and partial RCT and those without RCT (p = 0.163). There was no significant difference in glenoacromial length between these three groups of patients (p = 0.110). It was concluded that there was no significant difference between the three groups of patients in terms of AI that we redefined (p = 0.095).

**Conclusion:** AI of the glenohumeral and glenoacromial lengths, which were redefined with a different measurement technique on the shoulder radiography, did not yield statistically significant results in the diagnosis of shoulder RCT.

**Keywords:** *Rotator Cuff, Acromion Index, Glenohumeral, Glenoacromial*

## ÖZET

**Amaç:** Rotator Manşet Yırtıkları (RCT) ile ilişkili olarak tanımlanan birçok radyografik parametreden birisi olan Akromion indeksini (AI) yeni bir radyografik ölçüm tekniği ile yeniden yorumlayarak RCT'yi tahmin etme kapasitesini ölçmektir.

**Gereç ve Yöntemler:** Toplam 62 hastanın omuz Manyetik Rezonans Görüntüleme (MR) raporu ve omuz grafilerinde yeni teknikle ölçülen glenohumeral ve glenoakromiyal uzunlukla hesaplanan AI değerlendirildi. Omuz grafilerinde glenohumeral uzunluk, lateral humerus tuberculum majus ile glenoid eklemin ön orta noktası arasındaki uzunluk olarak tanımlandı. Glenoakromiyal uzunluk, akromiyonun lateral ucu ile glenoid eklemin ön orta noktası arasındaki uzunluk olarak da farklı bir bakış açısıyla tanımlandı.

**Bulgular:** MR'da tanımlanan tam ve kısmi RCT'li hastalar ile RCT'siz hastalar arasında direk grafideki glenohumeral uzunluk açısından anlamlı fark yoktu (p = 0,163). Bu üç hasta grubu arasında direk grafideki glenoakromiyal uzunluk açısından anlamlı bir fark yoktu (p = 0,110). Direk grafide yeniden tanımladığımız AI açısından üç hasta grubu arasında anlamlı bir fark olmadığı sonucuna varıldı (p = 0,095).

**Sonuç:** Omuz radyografisinde farklı bir ölçüm tekniği ile yeniden tanımlanan glenohumeral ve glenoakromiyal uzunluklarla tanımlanan AI'si, omuz RCT tanısında istatistiksel olarak anlamlı sonuçlar vermemiştir.

**Anahtar Kelimeler:** *Rotator Manşet, Akromion İndeksi, Glenohumeral, Glenoakromiyal*

Davut AYDIN, Dr. Öğr. Ü. (0000-0001-5011-9286)
Murat KORKMAZ, Prof. Dr. (0000-0002-5920-0280)
Serhat DURUSOY, Doç. Dr. (0000-0003-4337-7740)
Hacı Ali OLÇAR, Dr. Öğr. Ü. (0000-0002-3097-3677)
Muhammed SARIKAYA, Arş. Gör. (0000-0002-7814-1562)

**İletişim:**
Dr. Öğr. Ü. Davut AYDIN
Yozgat Bozok University, Yozgat Bozok Medical Faculty, Department of Orthopaedics and Traumatology

**Geliş tarihi/Received:** 05.05.2023
**Kabul tarihi/Accepted:** 14.08.2023
**DOI:** 10.16919/bozoktip.1292828

Bozok Tıp Derg 2023;13(3):21-25
Bozok Med J 2023;13(3):21-25

## INTRODUCTION

Shoulder pain is widespread musculoskeletal discomfort with a prevalence percentage ranging from 7% to 26% in the population (1). The most widespread cause of shoulder pain in the population is rotator cuff tendinopathy which is a multifactorial status (2). The prevalence of Rotator Cuff Tears (RCT) is 22.1% in the community and increases with age. Asymptomatic rupture of the rotator cuff is twice as common as symptomatic rupture (3). The rotator cuff consists of four muscles and tendons of these muscles that fix the humeral head in the shoulder joint and prevent the deltoid muscle from pulling the humeral head up. Therefore, when there is RCT, the humeral head moves upwards. In the evaluation of this condition of the shoulder, radiography is primarily used in the first imaging because it is inexpensive and easily accessible. Although more advanced imaging techniques are available, they are not primarily preferred due to their high cost and difficult accessibility. In previous studies, different measurement methods were applied to evaluate the relationship between shoulder radiography and RCT (4–8). The acromial index, which is the ratio of the glenohumeral length to the glenoacromial length, is one of them. Studies have not found a relationship between the acromial index and the development of RCT (7,8).

In this study, we hypothesized that when Acromion Index (AI) was calculated from a different perspective, it might be associated with RCT. We changed the glenohumeral length and glenoacromial length measurement technique. This study aimed to detect whether there is a relationship between the ratio of glenohumeral length to glenoacromial length measured with the new technique on shoulder radiography and shoulder Magnetic Resonance Imaging (MRI) reports in terms of RCT.

## MATERIAL AND METHODS

We examined the data of patients retrospectively who applied to our orthopedics outpatient clinic with the complaint of shoulder pain, and who had shoulder radiography and MRI. Ethical approval was obtained for the study from the Clinical Research Ethics Committee (2017-KAEK-189_2019.03.13_08). Informed consent was obtained from all patients participating in the study. Those who had a previous surgical procedure in the shoulder region, those who had a fracture in the shoulder region, and those who had any deformity in the shoulder region were excluded from the study. Patients who applied to the orthopedics and traumatology outpatient clinic, who had shoulders MRI and radiographs for any reason and who had no shoulder bone deformation were determined as inclusion criteria.

Shoulder radiography and MRI of a total of 62 patients suitable for our study were evaluated from the hospital archive. These patients were examined in 3 groups; 18 with complete RCT, 25 with partial RCT, and 19 without RCT, according to the MRI report. The glenohumeral length and glenoacromial lengths were measured on the shoulder radiographs of the patients with the new technique we developed (Fig 1).

We measured the glenohumeral length which is the length between the lateral humerus tuberculum majus and the anterior midpoint of the glenoid joint on the shoulder radiograph. We also calculated the glenoacromial length between the lateral tip of the acromion and the anterior midpoint of the glenoid joint from a different perspective. The ratio of the glenohumeral length to the glenoacromial length was recorded. According to the shoulder MRI report of the same patient, the rotator cuff was grouped as complete RCT, partial RCT or intact RCT.

Statistical analysis of this study was evaluated in groups with glenohumeral length, glenoacromial length, glenohumeral length to glenoacromial length, complete RCT, partial RCT and without RCT. The differences between the groups were examined using the Mann-Whitney U test in the paired groups and the Kruskal-Wallis Test in the triple group. Statistical significance was assumed as $p<0.05$.

## RESULTS

The mean glenohumeral length of patients with complete and partial RCT and without RCT was found to be 55.378mm±3.853, 56.944mm±5.207, 58.926mm±5.577, respectively. The mean glenoacromial length in these 3 groups of patients was measured as 56.772mm±4.695, 60.440mm±4.624, and 59.589±5.899, respectively. In addition, the mean ratio of glenohumeral length to glenoacromial

Bozok Tıp Derg 2023;13(3):21-25
Bozok Med J 2023;13(3):21-25

**Figure 1.** Redefined glenohumeral and glenoacromial lengths, GH: Glenohumeral, GA: Glenoacromial


length in these 3 groups of patients was found to be 0.979±0.074, 0.943±0.060, 0.991±0.065, respectively. There was no significant difference in glenohumeral length between patients with partial RCT and complete RCT, patients with partial RCT and without RCT, patients with complete RCT and without RCT ($p = 0.514$, $p = 0.184$, $p = 0.064$, respectively). There was no significant difference in glenoacromial length between patients with partial RCT and complete RCT, patients with partial RCT and without RCT, patients with complete RCT and without RCT ($p = 0.032$, $p = 0.670$, $p = 0.176$, respectively). There was no significant difference in AI between patients with partial RCT and complete RCT, patients with partial RCT and patients without RCT, patients with complete RCT and without RCT ($p = 0.115$, $p = 0.044$, $p = 0.715$, respectively). There was no significant difference in glenohumeral length between patients with complete and partial RCT and patients without RCT ($p = 0.163$) (Table 1). There was no significant difference between these 3 groups of patients in terms of glenoacromial length ($p = 0.110$). In addition, there was no significant difference in AI between these 3 groups of patients ($p = 0.095$).

## DISCUSSION

In this study, we calculated the acromial index from a different perspective. We questioned the usability of the ratio of glenohumeral length to glenoacromial length, which we measured with a new shoulder radiography technique as a diagnostic tool in rotator cuff pathologies. We used shoulder radiography to estimate RCT and MRI reports as references. Shoulder radiography is preferred as primary imaging to rule out possible causes of shoulder pain, such as osteoarthritis, fracture, and shoulder dislocation because more advanced imaging modalities are not usually routinely used in primary clinical examination (9).

In our study, AI results measured with the new technique were similar between patients with complete, and partial RCT and without RCT. Some authors have stated that AI is not a significant indicative value for evaluating rotator cuff rupture (Fig 2) (7,10,11). In a study by Hsu et al., it was stated that AI did not show any difference in predicting supraspinatus tendinopathy in patients with shoulder pain (12). On the other hand, in another study, AI results in rotator cuff pathologies in the Korean population were significantly different between healthy and patient groups, but the relationship between AI and the size of RCT could not be demonstrated (13). Researchers showed that AI was an effective predictive factor for RCT in the Korean population. Some researchers have suggested that RCT may be associated with a larger AI, that is, a longer lateral projection of the acromion (14). Likewise, in other examinations, AI may be an indicator to differentiate preoperative partial and massive RCT. They suggested that a high AI may be one of the associated factors for the progression to massive RCT in rotator cuff disease (15). According to some authors, the different results of studies on AI question the reliability of AI and its relationship with cuff pathologies (7). In a scant study of seven shoulder impingement pain patients with a mean age of 34 years and 13 healthy controls, they found no significant difference in acromiohumeral length between the groups (16). In summary, the acromiohumeral length is primarily genetically detected and is less influenced by external items (17). The upward movement of the

Bozok Tıp Derg 2023;13(3):21-25
Bozok Med J 2023;13(3):21-25

**Table 1.** Distribution of patient groups according to Glenohumoral (GH), Glenoacromial (GA) and Acromion Index (AI)

| | *Tear type* | *N* | *Mean* | *Min.* | *Max.* | *Sd* | *p value** |
|---|---|---|---|---|---|---|---|
| GH Distance | Partial RCT | 25 | 56.944 | 50.1 | 69.1 | 5.206 | 0.163 |
| | Complete RCT | 18 | 55.377 | 47.2 | 63.5 | 3.85 | |
| | Without RCT | 19 | 58.92 | 49.5 | 69.8 | 5.57 | |
| GA Distance | Partial RCT | 25 | 60.44 | 52.2 | 69.4 | 4.62 | 0.11 |
| | Complete RCT | 18 | 56.77 | 46.8 | 64 | 4.69 | |
| | Without RCT | 19 | 59.58 | 49.7 | 67.7 | 5.89 | |
| Ratio (AI) | Partial RCT | 25 | 0.94 | 0.84 | 1.035 | 0.059 | 0.095 |
| | Complete RCT | 18 | 0.978 | 0.845 | 1.120 | 0.074 | |
| | Without RCT | 19 | 0.989 | 0.9 | 1.122 | 0.0662 | |

*= Kruskal Wallis Test, p<0.05, RCT= Rotator Cuff Tears

**Figure 2.** Glenohumeral and glenoacromial lengths, GH: Glenohumeral, GA: Glenoacromial


humeral head is known as the progressive phenomenon caused by the imbalance between the force pairs of the rotator cuff muscles (18). Radiographic assessments of acromiohumeral intervals by independent physicians demonstrated researchers' high reliability when using standard radiographs (19). When it comes to evaluating the inferior surface of the acromion in patients with as distinct from shaped acromions, radiography is more prone to misinterpretation than MRI. In addition, while the shoulder is in internal or external rotation during glenohumeral radiography, it affects the measurements, while MRI is not affected by rotation and accurate measurements are made (20). In contrast, the use of non-standardized radiographs by orthopedic surgeons has shown that the measurement of the acromiohumeral space is not reliable and reproducible (4). Thus, we used only standard anteroposterior shoulder radiographs and MRIs in our study. In this study, we measured the acromial index questioned by previous publications from a different perspective, thus providing a new perspective. We found that AI measured with the new technique was not associated with the RCT. There were no statistically significant results between AI results measured by the new technique between patients with complete or partial RCT and those without RCT. Thus, we supported previous publications stating that the relationship between AI and rotator cuff pathologies was not significant. This study has several limitations. First, the measurement of AI measured by the new technique on radiographs, although non-standardized radiographs are excluded, may have biased the results as it is attached to the quality of the radiographs. Another limitation is the small and different count of patients in all groups. In the end, selection bias may have emerged as we involved only symptomatic patients, potentially reducing the correctness of the control group, which may include asymptomatic individuals with shoulder pathology.

## CONCLUSION

In this study, no relationship was found between the ratio of the glenohumeral length to the glenoacromial length and the RCT status. By looking at it from a different angle, we did not obtain a significant result in terms of radiography diagnosis of shoulder RCT in AI with our newly formed measurement.

## Acknowledgements

The authors declare that they have no conflict of interest. The authors received no financial support for the research and/or authorship of this article. This study was not funded.

## KAYNAKLAR

**1**. Luime JJ, Koes BW, Hendriksen IJM, Burdorf A, Verhagen AP, Miedema HS, et al. Prevalence and incidence of shoulder pain in the general population; a systematic review. Scandinavian Journal of Rheumatology. 2004;33:73–81.

**2.** Lewis JS. Rotator cuff tendinopathy: A model for the continuum of pathology and related management. British Journal of Sports Medicine. 2010;44:918–23.

**3.** Minagawa H, Yamamoto N, Abe H, Fukuda M, Seki N, Kikuchi K, et al. Prevalence of symptomatic and asymptomatic rotator cuff tears in the general population: From mass-screening in one village. Journal of Orthopaedics. 2013;10:8–12.

**4.** Bernhardt GA, Glehr M, Zacherl M, Wurnig C, Gruber G. Observer variability in the assessment of the acromiohumeral interval using anteroposterior shoulder radiographs. European Journal of Orthopaedic Surgery and Traumatology. 2013;23:185–90.

**5.** Fehringer E V, Rosipal CE, Rhodes DA, Lauder AJ, Puumala SE, Feschuk CA, et al. The radiographic acromiohumeral interval is affected by arm and radiographic beam position. Skeletal Radiology. 2008;37:535–9.

**6.** Saupe N, Pfirrmann CWA, Schmid MR, Jost B, Werner CML, Zanetti M. Association between rotator cuff abnormalities and reduced acromiohumeral distance. American Journal of Roentgenology. 2006;187:376–82.

**7.** Björnsson Hallgren HC, Adolfsson L. Neither critical shoulder angle nor acromion index were related with specific pathology 20 years later! Knee Surgery, Sports Traumatology, Arthroscopy. 2021;29:2648–55.

**8.** Liu HX, Xu XX, Xu DL, Hu YZ, Pan XY, Yu Z, et al. The acromion–greater tuberosity impingement index: A new radiographic measurement and its association with rotator cuff pathology. Journal of Orthopaedic Surgery. 2020;28(1):2309499020913348.

**9.** Manske RC, Prohaska D. Diagnosis and management of adhesive capsulitis. Current Reviews in Musculoskeletal Medicine. 2008;1:180–9.

**10.** Hamid N, Omid R, Yamaguchi K, Steger-May K, Stobbs G, Keener JD. Relationship of radiographic acromial characteristics and rotator cuff disease: A prospective investigation of clinical, radiographic, and sonographic findings. Journal of Shoulder and Elbow Surgery. 2012;21:1289–98.

**11.** Lin CL, Chen YW, Lin LF, Chen CP, Liou TH, Huang SW. Accuracy of the Critical Shoulder Angle for Predicting Rotator Cuff Tears in Patients With Nontraumatic Shoulder Pain. Orthopaedic Journal of Sports Medicine. 2020;8(5):2325967120918995.

**12.** Hsu TH, Lin CL, Wu CW, Chen YW, Vitoonpong T, Lin LC, et al. Accuracy of Critical Shoulder Angle and Acromial Index for Predicting Supraspinatus Tendinopathy. Diagnostics. 2022;12:283.

**13.** Kum DH, Kim JH, Park KM, Lee ES, Park YB, Yoo JC. Acromion index in korean population and its relationship with rotator cuff tears. CiOS Clinics in Orthopedic Surgery. 2017;9:218–22.

**14.** Miyazaki AN, Fregoneze M, Santos PD, Da Silva LA, Menegassi Martel É, Debom LG, et al. Radiographic Study On The Acromion Index And Its Relationship With Rotator Cuff Tears. Revista Brasileira de Ortopedia (English Edition). 2010;45:151–4.

**15.** Kim JR, Ryu KJ, Hong IT, Kim BK, Kim JH. Can a high acromion index predict rotator cuff tears? International Orthopaedics. 2012;36:1019–24.

**16.** Desmeules F, Minville L, Riederer B, Côté CH, Frémont P. Acromio-humeral distance variation measured by ultrasonography and its association with the outcome of rehabilitation for shoulder impingement syndrome. Clinical Journal of Sport Medicine. 2004;14:197–205.

**17.** Gumina S, Arceri V, Fagnani C, Venditto T, Catalano C, Candela V, et al. Subacromial space width: Does overuse or genetics play a greater role in determining it?: An MRI study on elderly twins. Journal of Bone and Joint Surgery - American Volume. 2015;97:1647–52.

**18.** Kim SJ, Park JS, Lee KH, Lee BG. The development of a quantitative scoring system to predict whether a large-to-massive rotator cuff tear can be arthroscopically repaired. Bone and Joint Journal. 2016;98-B:1656–61.

**19.** Gruber G, Bernhardt GA, Clar H, Zacherl M, Glehr M, Wurnig C. Measurement of the acromiohumeral interval on standardized anteroposterior radiographs: A prospective study of observer variability. Journal of Shoulder and Elbow Surgery. 2010;19:10–3.

**20.** Singleton N, Agius L, Andrews S. The acromiohumeral centre edge angle: A new radiographic measurement and its association with rotator cuff pathology. Journal of Orthopaedic Surgery. 2017;25:1–9.

# ÜNİVERSİTE ÖĞRENCİLERİNDE UYKU KALİTESİ, DEPRESYON VE OBEZİTE İLİŞKİSİ: TOROS ÜNİVERSİTESİ ÖRNEĞİ

## The Relationship Between Poor Sleep Quality, Depression and Obesity in University Students: The Case of Toros University

Özlem ÖZPAK AKKUŞ[1], Ayşe Gökçe ALP[1], İlayda YORULMAZ[1], Ayşe TEK[1], Esra CANLI[1], Özge AYKUT[1], Ezgi AYKUT[1]

[1]Toros Üniversitesi,
Beslenme ve Diyetetik Bölümü,
Mersin,
Türkiye

Özlem ÖZPAK AKKUŞ, Dyt.
(0000-0002-1471-8000)
Ayşe Gökçe ALP, Uzm. Dyt.
(0000-0001-9931-3362)
İlayda YORULMAZ, Dyt.
(0009-0002-8421-864X)
Ayşe TEK, Dyt.
(0009-0009-8091-9503)
Esra CANLI, Dyt.
(0009-0009-2558-2741)
Özge AYKUT, Dyt.
(0009-0002-1297-9335)
Ezgi AYKUT, Dyt.
(0009-0009-7777-2037)

**İletişim:**
Dr. Öğr. Ü. Özlem ÖZPAK AKKUŞ
Toros Üniversitesi Sağlık Bilimleri Fakültesi Beslenme ve Diyetetik Bölümü
Mersin/Türkiye

**Geliş tarihi/Received:** 15.05.2023
**Kabul tarihi/Accepted:** 04.09.2023
**DOI:** 10.16919/bozoktip.1297411

Bozok Tıp Derg 2023;13(3):26-35
Bozok Med J 2023;13(3):26-35

## ÖZET

**Amaç:** Bu çalışmada Toros Üniversitesi'nde öğrenim gören öğrencilerin depresyon, beslenme durumları ve bazı antropometrik özellikleri ile uyku kaliteleri arasındaki ilişkilerin değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Çalışma Kasım-Aralık 2022 tarihleri arasında Toros Üniversitesi Sağlık Bilimleri Fakültesi'nde okuyan 200 öğrenci ile gerçekleştirilmiştir. Çalışmaya dahil edilme kriterleri 19-40 yaş arası ve çalışmaya gönüllü katılım sağlamış olmaları iken gebe ve emzikliler, kronik hastalığı olanlar, herhangi ilaç, vitamin-mineral ve besin desteği kullanan ve yeme davranış bozukluğu olan öğrenciler çalışma dışında bırakılmışlardır. Çalışmada öğrencilerle yapılan yüz yüze görüşmelerde öğrencilerin; tanımlayıcı özellikleri (yaş, cinsiyet, medeni durum, çalışma durumu, beslenme alışkanlıkları ve fiziksel aktivite kayıtları) sorgulanırken, genel ve santral obezite durumlarının değerlendirilmesi için bazı antropometrik ölçümleri (vücut ağırlığı, boy uzunluğu, bel ve kalça çevresi ölçümleri) ve beslenme durumlarının değerlendirebilmesi içinde 24 saatlik besin tüketim kayıtları alınmıştır. Ayrıca öğrencilerin uyku kalitelerini değerlendirebilmesi için Pittsburgh Uyku Kalite Ölçeği (PUKİ), depresyon durum ve şiddetini saptanabilmesi için de Beck Depresyon Ölçeği (BDÖ) uygulanmıştır.

**Bulgular:** Çalışmada kötü uyku kalitesine sahip olan öğrencilerin vücut ağırlıkları uyku kalitesi iyi olan öğrencilere göre anlamlı düzeyde daha fazla olduğu bulunurken, vücut ağırlığındaki bir birimlik artışın uyku kalitesinin iyi olma düzeyini %3,6 oranında azalttığı saptanmıştır ($p<0,05$). Ayrıca 17'den küçük BDÖ puanına sahip olan öğrencilerin 17'den fazla puana sahip olanlara göre daha iyi uyku kalitesine sahip oldukları saptanmıştır ($p<0,05$).

**Sonuç:** Bu çalışma üniversite öğrencilerinde kötü uyku kalitesinin depresyon durumu ile genel ve santral obezite açısından risk faktörü olabileceğini göstermektedir.

**Anahtar Kelimeler:** *Üniversite Öğrencileri; Uyku Kalitesi; Depresyon; Beslenme Durumu; Obezite*

## ABSTRACT

**Objective:** The aim of this study was to evaluate the relationships between depression, nutritional status, some anthropometric characteristics, and sleep quality of Toros University students.

**Material and Methods:** The study was conducted with 200 students studying at Toros University, Faculty of Health Sciences between November and December 2022. The inclusion criteria were to be between the ages of 19-40 and to participate voluntarily in the study. Pregnant and lactating women, those with chronic diseases, those taking any medication, vitamin-mineral and nutritional supplements, and students with eating behavior disorders were excluded from the study. In the face-to-face interviews conducted with the students in the study, descriptive characteristics (age, gender, marital status, employment status, dietary habits, and physical activity records) were questioned, some anthropometric measurements (body weight, height, waist and hip circumference measurements) were taken to evaluate the general and central obesity status, and 24-hour food consumption records were taken to evaluate the nutritional status. In addition, the Pittsburgh Sleep Quality Inventory (PSQI) was administered to assess sleep quality and the Beck Depression Inventory (BDI) was administered to determine depression status and severity.

**Results:** Body weight of the students with poor sleep quality was significantly higher than that of the students with good sleep quality, and a one-unit increase in body weight decreased the level of good sleep quality by 3.5% ($p<0.05$). In addition, students with a BDI score of less than 17 had better sleep quality than those with a score of more than 17 ($p<0.05$).

**Conclusion:** This study shows that poor sleep quality may be a risk factor for depression and general and central obesity in university students.

**Keywords:** *University Students; Sleep Quality; Depression; Nutritional Status; Obesity*

## GİRİŞ

Sağlıklı bir uyku, iyi kalitede yeterli bir uyku süresi ile karakterize edilmektedir (1). Üniversite öğrencileri ise uyku kalitesi açısından farklı risk faktörlerine karşı savunmasız bir grubu temsil etmekte olup Amerikan Ulusal Uyku Vakfı tarafından bu dönemdeki bireylere günde ortalama 7 ila 9 saat uyku önerilmektedir (2,3). Uyku süresi, uyku kalitesinin önemli bir unsurudur ve üniversite öğrencilerinde yapılan bir araştırmada ≤6, 7-8 ve ≥9 saatlik uyku süresine sahip olan üniversite öğrencilerinin oranlarının sırasıyla %39,2, %46,9 ve %13,9 olduğu bulunarak üniversite öğrencilerinin kısa uyku süreleri açısından risk altında olduğu belirlenmiştir (4). Uyku süresi kaybına ek olarak, özellikle üniversite öğrencilerinde değişen yaşam tarzı ve sosyal medya kullanımına paralel olarak uyku sürekliliğinin bir parçası olan uykuya başlama-sürdürme sorunları ve akabinde görülen sabah yorgunluğu da uyku kalitesinin düşmesinin ana özellikleri olarak sıralanabilmektedir (3). Bu nedenlerle, kötü uyku kalitesinin üniversite öğrencileri arasında önemli bir sorun haline geldiği söylenebilmektedir.

Uykunun fiziksel ve psikolojik iyilik halinin sürdürülmesinde hem yeterliliği hem de kalitesi açısından önemi vurgulanmaktadır (5). Yeterli süreye ve iyi kaliteye sahip olan uyku, mental iyilik halinin sürdürülmesinin yanı sıra metabolizma, iştah düzenleme, solunum sıkıntıları ve hormonal sistemler gibi fizyolojik mekanizmaların güncellenmesine de yardımcı olmaktadır (5,6). Üniversite öğrencilerinde zaman yönetimi becerilerinin eksikliği, okul yaşamı-çalışmaları ve artan sorumluluklar nedeniyle oluşan stres düzeyi ve depresyon durumu genel uyku miktarını ve kalitesini olumsuz yönde etkileyebilmektedir (7). Bunun yanı sıra üniversite öğrencileri arasında yapılan araştırmalar, uyku problemlerinin depresif belirtiler geliştirme riskini artırdığını ve depresif öğrencilerin, olmayanlara göre uyku problemlerini bildirme olasılıklarının daha yüksek olduğunu göstermektedir (7,8).

Uyku sorunları anormal metabolik ve endokrin fonksiyonlar nedeniyle artan vücut ağırlığına neden olabilmektedir. Bu konu için en olası mekanizma ise uyku süresinin azalması ile Leptin ve Ghrelin gibi iştah metabolizmasını düzenleyen bazı önemli hormonların seviyelerinde meydana gelen değişiklikler olarak gösterilmektedir. Uyku süresinin azalmasıyla beraber iştahı uyaran Ghrelin hormonu seviyeleri artarken tokluk hissi sağlayan Leptin hormonu seviyeleri azalmaktadır; bu değişiklikler ise genel ve santral obezite belirteçleri olan beden kitle indeksi (BKİ) ve bel çevresinde artışları teşvik edebilmektedir. Özetle kötü uyku kalitesi, obezitenin tipik bir belirtisi olarak kabul edilmektedir; bununla birlikte artan visseral yağ dokusunda vücudun doğal uyku-uyanıklık döngüsüne müdahale edebilen inflamatuar sitokinlerin salınmasıyla da ilişkilendirilmektedir (7).

Bireylerin diyetinin uyku düzenini kontrol etmede rol oynadığı öne sürülmektedir. Uyku kalitesi, fazla miktarlarda karbonhidrat ve yağ tüketildiğinde zarar görmekte olup süt, balık, meyve ve sebzeler de dahil olmak üzere bazı yiyeceklerin ve artan fiziksel aktivitenin uykuyu artırıcı niteliklere sahip olduğu gösterilmektedir (9). Enerji alımı ve harcaması arasındaki dengesizlik, artan karbonhidrat, toplam kolesterol ve doymuş yağ tüketimi ile ilişkili olarak uyku eksikliği şiddetlenebilmektedir. Üniversite dönemi ise genç yetişkinlerin özellikle beslenme alışkanlıkları konusunda artan özerklikleri nedeniyle değişmeye müsait olan çok önemli bir dönemdir. Yetersiz besin alımı ve fastfood gıda tüketimi ile yetersiz sebze-meyve alımı gibi sağlıksız beslenme davranışlarının bu dönemde ortaya çıkma olasılığı daha yüksek olup bu durumda uyku kalitesini olumsuz yönde etkileyebilmektedir (7).

Bu çalışmada Toros Üniversitesi'nde öğrenim gören öğrencilerin depresyon, beslenme durumları ve bazı antropometrik özellikleri ile uyku kaliteleri arasındaki ilişkilerin değerlendirilmesi amaçlanmıştır.

## GEREÇ VE YÖNTEMLER

Kesitsel ve tanımlayıcı tipte yapılan bu çalışma, Kasım-Aralık 2022 tarihleri arasında Toros Üniversitesi Sağlık Bilimleri Fakültesi'nde okuyan 200 öğrenci ile gerçekleştirilmiştir. Çalışmaya dahil edilme kriterleri 19-40 yaş arası ve çalışmaya gönüllü katılım sağlamış olmaları iken gebe ve emzikliler, kronik hastalığı olanlar, herhangi ilaç, vitamin-mineral ve besin desteği kullanan ve yeme davranış bozukluğu olan öğrenciler çalışma dışında bırakılmışlardır.

Örneklem sayısı için G*Power (Heinrich-Heine-Universitt Dsseldorf, Dsseldorf, Germany; http://www.gpower.hhu.de/) yazılımı ile alfa (α)=0,05, güç

(1-β) =0,95 ve orta düzey etki büyüklüğü (d=0,50) alınarak güç analizi yapılmıştır. Analiz sonucunda bu çalışmada toplam 200 gözlemle çalışıldığı takdirde yaklaşık %100 düzeyinde bir test gücüne ulaşılacağı belirlenmiştir. Bu çalışma için 26.10.2022 tarih 162 no'lu karar ile Toros Üniversitesi Bilimsel Araştırmalar ve Yayın Etik Kurulu'ndan etik kurulu izni ve çalışmaya katılan tüm öğrencilerden çalışma öncesi onam alınmıştır.

Çalışmada öğrencilerle yapılan yüz yüze görüşmelerde öğrencilerin; tanımlayıcı özellikleri (yaş, cinsiyet, medeni durum, çalışma durumu, beslenme alışkanlıkları ve fiziksel aktivite kayıtları) sorgulanırken, genel ve santral obezite durumlarının değerlendirilmesi için antropometrik ölçümleri (vücut ağırlığı, boy uzunluğu, bel çevresi, kalça çevresi), beslenme durumlarının değerlendirebilmesi için de 24 saatlik besin tüketim kayıtları (10) alınmıştır. Ayrıca öğrencilerin uyku kalitelerini değerlendirebilmesi için Pittsburgh Uyku Kalite Ölçeği (PUKİ) (11), depresyon durum ve şiddetini saptanabilmesi için de Beck Depresyon Ölçeği (BDÖ) (12) uygulanmıştır.

Vücut ağırlığı, boy uzunluğu, bel çevresi ve kalça çevresi ölçümleri teknik kapsamlarında araştırmacı tarafından yüz yüze yapılan görüşmelerde ölçülmüştür (13). Vücut ağırlığı ve boy uzunluğu ölçümlerinden BKİ değerleri (vücut ağırlığı (kg) / boy uzunluğu ($m^2$)) hesaplanmış ve Dünya Sağlık Örgütü (DSÖ) sınıflamasına (BKİ: <18,5 $kg/m^2$ olanlar zayıf, 18,5-24,9 $kg/m^2$ arasında olanlar normal, 25,0-29,9 $kg/m^2$ arasında olanlar fazla kilolu, ≥30,0 $kg/m^2$ olanlar obez) göre değerlendirilmiştir (14). Santral obezite durumlarının belirlenebilmesi için ölçülen bel çevresi ölçümleri de DSÖ sınıflamasına (erkekler: <94 cm normal, 94-101 cm riskli, ≥102 cm yüksek riskli, kadınlar: <80 cm normal, 80-87 cm riskli, ≥88 cm yüksek riskli) (15) göre değerlendirilirken, ölçülen bel çevresi ölçümlerinden kalça çevresi ile bel-kalça oranı hesaplanarak, DSÖ sınıflamasına (bel-kalça oranı: erkekler >0,90, kadınlar >0,85) (14) göre, boy uzunluğu ölçümleriyle de bel-boy oranı hesaplanarak, Ashwell ve ark. (16) tarafından geliştirilen sınıflandırmaya (bel-boy oranı: <0,5 olanlar normal, 0,5-0,6 riskli, ≥0,6 yüksek riskli) göre santral obezite durumları değerlendirilmiştir.

Çalışmaya katılan öğrencilerin 24 saatlik fiziksel aktivite kayıtları alınarak gün içerisinde yapılan fiziksel aktiviteler için Türkiye Beslenme Rehberi'nde belirlenmiş olan katsayılar ile yapılan fiziksel aktivitenin süresi ve öğrencilerin vücut ağırlığı çarpılarak toplam enerji harcaması değeri (TEH) elde edilmiştir. Elde edilen TEH değeri ise Schofield formülü kullanılarak hesaplanan bazal metabolizma hızı (BMH) değerine bölünmesiyle öğrencilerin fiziksel aktivite katsayıları (PAL) değerleri (TEH (kcal) / BMH (kcal)) hesaplanmıştır (17). Öğrencilerin 24 saatlik besin tüketim kayıtları yapılan yüz yüze görüşme sırasında "Yemek ve Besin Fotoğraf Kataloğu'' (18) kullanılarak alınırken, dışarıda tüketilen yemeklerin porsiyon ölçüsü ve bir porsiyon içine giren besinlerin hesabında ise "Standart Yemek Tarifeleri" kitabı kullanılmıştır(19). Akabinde alınan bu besin tüketim kayıtları Beslenme Bilgi Sistemleri (BeBiS) ile değerlendirilerek öğrencilerin almış oldukları günlük enerji ve besin öğeleri alım miktarları hesaplanmış ve makro besin öğelerini karşılama yüzdeleri ise Türkiye Beslenme Rehberi'ne (referans değerler; erkekler için (%10-20 protein, %20-35 yağ, %45-60 karbonhidrat); kadınlar için (%12-20 protein, %20-35 yağ, %45-60 karbonhidrat) göre değerlendirilmiştir (17).

Öğrencilerin uyku kalitelerinin değerlendirilebilmesi için 24 sorudan oluşan PUKİ ölçeği kullanılmıştır. Bu ölçek Buysse ve ark. tarafından geliştirilmiş olup, Türkçe geçerlilik ve güvenirliliği Ağargün ve ark. tarafından yapılmıştır(11,20). Uyku kalitesini nicel olarak ölçmeyi hedefleyen bu ölçekte 7 bileşene (öznel uyku kalitesi, uykuya dalma süresi, uyku süresi, alışılmış uyku etkinliği, uyku bozukluğu, uyku ilacı kullanımı ve gündüz işlev bozukluğu) ait değerler elde edilebilmektedir. Bu değerlerin toplamı toplam PUKİ değerini (0–21 puan) vermektedir ve toplam PUKİ puanının <5 puan olması "iyi", ≥5 puan olması ise "kötü" uyku kalitesi olarak değerlendirilmektedir.

Öğrencilerin güncel depresyon belirti şiddetlerinin ölçülmesi amacıyla Beck ve ark. oluşturduğu BDÖ kullanılmıştır (21). Hisli ve ark. tarafından Türkçe geçerlilik ve güvenirliliği yapılmış olan ve depresyonda görülen vejetatif, duygusal, bilişsel ve motivasyonel belirtileri ölçen bu ölçeğin amacı depresyon tanısı koymak değil depresyon derecesinin sayısal karşılığı elde edebilmektir (12). Yirmi bir sorudan oluşan bu ölçekte her soru depresyona özgü bir davranışsal örüntüyü belirlemekte olup azdan çoğa (0 puan-3 puan) doğru giden dört seçenekli değerlendirme cümlelerini içermektedir. Ölçekten alınabilecek toplam puan 0-63

Bozok Tıp Derg 2023;13(3):26-35
Bozok Med J 2023;13(3):26-35

puan (0-9 puan=Minimal Depresyon, 10-16 puan= Hafif Depresyon, 17-29 puan= Orta Depresyon, 30 puan ve üzeri= Şiddetli Depresyon) arasında değişmekte olup kesme puanı 17 olarak belirlenmiştir.

Çalışmanın istatistiksel analiz aşamasında ortalama karşılaştırma testleri ve lojistik regresyon analizleri yapılmıştır. Elde edilen değişkenlerin normal dağılım varsayımına uygunluk testi için Shapiro-Wilk testi sonuçları incelenmiştir. Normal dağılıma uygun olmayan iki gruplu karşılaştırmalar için Mann Whitney U testi, ikiden fazla gruplu karşılaştırmalar için Kruskal-Wallis testi kullanılmıştır. Çoklu karşılaştırmalarda ise Bonferroni düzeltmeli Dann testi kullanılmıştır. Çalışmada uyku kalitesi ve uyku süresi değişkenlerinin gruplarını etkileyen faktörleri belirlemek için lojistik regresyon analiz uygulanmıştır. İstatistiksel hipotez testlerin değerlendirilmesinde hata payı %5 olarak alınmıştır. Hipotez testlerine dair bulgular ise IBM SPSS 26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.) programı kullanılarak elde edilmiştir.

## BULGULAR

Tablo 1'de araştırmaya dahil olan öğrencilerin genel özelliklerinin uyku kaliteleri ve uyku sürelerine göre karşılaştırma sonuçları verilmiştir. Sonuçlara bakıldığında akşam öğününden sonra besin tüketim ve sigara kullanım durumları ile PUKİ puanları arasında istatistiksel olarak anlamlı bir farklılık olduğu görülürken bu farklılıklar incelendiğinde akşam öğününden sonra besin tüketmeyenlerin besin tüketen ve bazen tüketen gruplara göre, sigara kullanmayan öğrencilerin ise sosyal içici olan öğrencilere göre istatistiksel olarak anlamlı düzeyde daha iyi uyku kalitesine sahip oldukları belirlenmiştir ($p<0,05$). Ayrıca araştırmaya katılan öğrencilerin BDÖ puanı ve PUKİ puanları arasında da istatistiksel olarak anlamlı bir farklılığın olduğu ve BDÖ puanına göre depresyon riski olan öğrencilerin olmayanlara göre daha kötü uyku kalitesine sahip oldukları bulunmuştur ($p<0,05$). Ayrıca uyku süresi kısa olan öğrencilerin daha kötü uyku kalitesine sahip olduğu da saptanmıştır ($p<0,05$). Yine aynı tabloda öğrencilerin cinsiyet, yaşanılan yer, sigara ve alkol kullanım durumları ile uyku süreleri arasında istatistiksel olarak anlamlı bir farklılık bulunmaktadır ($p<0,05$). Bu farklılıklar incelendiğinde erkeklerin uyku sürelerinin kadınlara göre, öğrenci evi ve öğrenci yurdunda yaşayan öğrencilerin aile yanında yaşayan öğrencilere göre, alkol kullanmayan öğrencilerin kullanan öğrencilere göre uyku sürelerinin anlamlı düzeyde daha düşük olduğu ($p<0,05$), sigara kullanmayan öğrencilerin ise uyku sürelerinin sosyal içici olan öğrencilere göre anlamlı düzeyde daha fazla olduğu görülmektedir ($p<0,05$) (Tablo 1).

Tablo 2'ye bakıldığında uyku kalitesi iyi ve kötü olan öğrencilerin vücut ağırlıklarının ortalamaları arasında istatistiksel olarak anlamlı bir farklılık olduğu görülmektedir. Farklılıklar incelendiğinde uyku kalitesi iyi olan öğrencilerin vücut ağırlıklarının, uyku kalitesi kötü olan öğrencilere göre anlamlı düzeyde daha düşük olduğu bulunmuştur ($p<0,05$). Yine aynı tabloda kötü uyku kalitesine sahip ve bel çevresi ölçümleri riskli düzeyde olan erkek öğrencilerin bel çevresi ölçümlerinin iyi uyku kalitesine sahip olanlara göre istatistiksel olarak daha fazla olduğu görülmektedir ($p<0,05$). Ayrıca iyi uyku kalitesine sahip olan öğrencilerden bel boy oranı riskli düzeyde olanların bel boy oranlarının ve PAL değerlerinin kötü uyku kalitesine sahip olanlara göre istatistiksel olarak anlamlı düzeyde daha yüksek olduğu görülmektedir ($p<0,05$). Çalışmaya katılan öğrenciler uyku süresine göre değerlendirildiğinde ise uyku süresi kısa olan öğrencilerin vücut ağırlıklarının normal ve uzun süre uyuyanlara göre istatistiksel olarak anlamlı düzeyde daha yüksek olduğu görülmektedir ($p<0,05$).

Tablo 4'te uyku kalitesi ve uyku süresi değişkenlerine ait lojistik regresyon sonuçları verilmiştir. Tabloya göre bel çevresi, bel boy oranının uyku kalitesi üzerinde istatistiksel olarak anlamlı bir etkiye sahip olmadığı bulunurken, vücut ağırlığı ve uyku süresinin uyku kalitesi üzerinde istatistiksel olarak anlamlı bir etkiye sahip olduğu bulunmuştur ($p<0,05$). Bulgulara göre vücut ağırlığı bir birim arttığında, uyku kalitesinin iyi olma düzeyinin %3,6 oranında azaldığı saptanırken, uyku süresi normal/uzun olan öğrencilerin, kısa olan öğrencilere göre uyku kalitesinin iyi olma düzeyinin %78,8 oranında daha az olduğu saptanmıştır. Yine aynı tabloda uyku süresine ait lojistik regresyon sonuçları da verilmiş olup vücut ağırlığı değişkeninin uyku süresi üzerinde istatistiksel olarak anlamlı bir etkiye sahip olduğu görülmektedir ($p<0,05$). Bulgulara göre vücut ağırlığı bir birim arttığında, uyku süresinin normal/uzun olma düzeyinin %2,2 oranında azalmakta olduğu

Bozok Tıp Derg 2023;13(3):26-35
Bozok Med J 2023;13(3):26-35

**Tablo 1.** Öğrencilerin genel özelliklerine göre PUKİ puanı ve uyku süresi ortalamaları

| | **PUKİ ±SS** | **p** | **Uyku Süresi ±SS** | **p** |
|---|---|---|---|---|
| **Yaş (yıl)** | | | | |
| 19-29 | 7,3±2,5 | 0,175 | 7,2±1,7 | 0,672 |
| 30-39 | 6,0±2,2 | | 7,1±0,8 | |
| **Cinsiyet** | | | | |
| Erkek | 7,4±2,6 | 0,311 | 6,9±1,7 | 0,003[U] |
| Kadın | 7,1±2,5 | | 7,5±1,5 | |
| **Yaşadığınız yer** | | | | |
| Öğrenci evi[a] | 7,7±2,6 | 0,315 | 6,6±1,9 | 0,006[KW] (a-c, b-c) |
| Öğrenci yurdu[b] | 7,8±2,3 | | 6,5±2,2 | |
| Aile yanı[c] | 7,0±2,5 | | 7,5±1,4 | |
| **Akşam öğününden sonra besin tüketiyor mu** | | | | |
| Evet[a] | 7,4±2,4 | 0,018[KW] (a-b, b-c) | 7,2±1,6 | 0,502 |
| Hayır[b] | 5,8±2,6 | | 7,4±2,0 | |
| Bazen[c] | 7,6±2,7 | | 7,2±1,5 | |
| **Kafein tüketim durumu** | | | | |
| Evet | 7,1±2,5 | 0,296 | 7,3±1,6 | 0,477 |
| Hayır | 7,8±2,8 | | 6,8±1,7 | |
| **Sigara kullanım durumu** | | | | |
| Kullanıyor[a] | 9,0±1,8 | 0,002[KW] (b-c) | 6,5±1,0 | 0,028 [KW] (b-c) |
| Kullanmıyor[b] | 6,8±2,4 | | 7,5±1,5 | |
| Sosyal içiciyim[c] | 7,9±2,6 | | 6,8±1,8 | |
| **Alkol kullanım durumu** | | | | |
| Kullanıyor[a] | 7,8±2,5 | 0,206 | 7,5±1,7 | 0,047[KW] (a-b) |
| Kullanmıyor[b] | 6,9±3,1 | | 6,8±1,8 | |
| Sosyal içiciyim[c] | 7,4±2,2 | | 7,1±1,4 | |
| **Beck Depresyon Ölçeği** | | | | |
| Depresyon riski var (<17) | 6,9±2,4 | <0,001[U] | 7,2±1,7 | 0,482 |
| Depresyon riski yok (≥17) | 8,9±2,5 | | 7,1±1,4 | |
| **Uyku kalitesi** | | | | |
| İyi (<5) | 3,4±0,8 | <0,001[U] | 8,1±1,2 | <0,001[U] |
| Kötü (≥5) | 7,9±2,1 | | 7,1±1,7 | |
| **Uyku süresi (saat)** | | | | |
| Kısa (<7[a]) | 8,5±2,4 | <0,001[KW] (a-b, b-c, a-c) | 5,2±1,3 | <0,001[KW] (a-b, a-c, b-c) |
| Normal (7-8[b]) | 7,1±2,3 | | 7,4±0,6 | |
| Uzun (>8[c]) | 5,8±2,5 | | 9,4±0,8 | |

PUKİ: Pittsburgh Uyku Kalite Ölçeği, U: Mann Whitney-U test KW: Kruskal Wallis testi p: anlamlılık değeri

Bozok Tıp Derg 2023;13(3):26-35
Bozok Med J 2023;13(3):26-35

**Tablo 2.** Öğrencilerin uyku kalite ve sürelerine göre antropometrik ölçümleri

| | İyi Uyku Kalitesi Olanlar (<5) (n=30) ±SS | Kötü Uyku Kalitesi Olanlar (≥5) (n=170) ±SS | p | Kısa Süre Uyuyanlar (< 7 saat) (n=52) ±SS | Normal ve Uzun Süre Uyuyanlar (≥7 saat) (n=148) ±SS | p |
|---|---|---|---|---|---|---|
| **Antropometrik ölçümler** | | | | | | |
| **Vücut ağırlığı (kg)** | 66,4±16,5 | 73,3±17,0 | **0,018**[U] | 71,8±16,9 | 65,9±16,4 | **0,017**[U] |
| **BKİ (kg/m²)** | 23,9±4,3 | 23,6±12,7 | 0,163 | 23,6±3,8 | 23,7±13,6 | 0,088 |
| **Bel çevresi (cm)** | 81,8±11,1 | 78,9±13,7 | 0,140 | 82,0±13,8 | 78,4±13,0 | 0,092 |
| **Erkekler** | | | | | | |
| Normal (<94) | 83,5±7,5 | 80,2±10,2 | 0,333 | 82,1±7,3 | 79,9±10,8 | 0,416 |
| Riskli (94-101) | 94,3±0,6 | 97,8±2,7 | **0,031**[U] | 96,7±3,0 | 97,4±2,8 | 0,689 |
| Yüksek riskli (≥102) | 106,0 | 112,5±8,3 | 1,000 | 113,0±10,5 | 111,2±7,6 | 0,905 |
| **Kadınlar** | | | | | | |
| Normal (<88) | 70,1±4,9 | 69,2±4,8 | 0,706 | 68,7±5,6 | 69,4±4,6 | 0,727 |
| Riskli (80-87) | 84,0±3,6 | 82,7±2,8 | 0,600 | - | 83,0±2,9 | - |
| Yüksek riskli (≥88) | 100,0 | 95,1±8,5 | 0,667 | 98,0±12,7 | 95,0±7,6 | 1,000 |
| **Bel kalça oranı** | 0,8±0,1 | 0,8±0,1 | 0,315 | 0,8±0,0 | 0,8±0,1 | 0,059 |
| **Erkekler** | | | | | | |
| Normal (<0,90) | 0,8±0,1 | 0,8±0,1 | 0,799 | 0,8±0,2 | 0,8±0,1 | 0,431 |
| Riskli (≥0,90) | 0,9±0,0 | 0,9±0,2 | 0,226 | 0,9±0,1 | 0,9±0,2 | 1,000 |
| **Kadınlar** | | | | | | |
| Normal (<0,85) | 0,8±0,1 | 0,7±0,1 | 0,075 | 0,7±0,1 | 0,8±0,1 | 0,096 |
| Riskli (≥0,85) | 0,9 | 0,9±0,0 | 1,000 | 0,9±0,0 | 0,9±0,1 | 0,099 |
| **Bel boy oranı** | 0,5±0,2 | 0,5±,0,1 | 0,137 | 0,5±0,2 | 0,5±0,1 | 0,146 |
| Normal (<0,5) | 0,4±0,1 | 0,4±0,1 | 0,793 | 0,4±0,1 | 0,4±0,1 | 0,413 |
| Riskli (0,5-0,6) | 0,6±0,1 | 0,5±,0,1 | **0,030**[U] | 0,5±0,1 | 0,6±0,0 | 0,164 |
| **PAL değeri** | 1,8±0,4 | 1,7±0,3 | **0,011**[U] | 1,8±0,4 | 1,8±0,3 | 0,356 |

U: Mann Whitney-U test PAL: fiziksel aktivite katsayıları p: anlamlılık değeri

**Tablo 3.** Öğrencilerin uyku kalite ve sürelerine göre günlük ortalama enerji değerleri ve makro besin öğelerini karşılama durumları

| | İyi Uyku Kalitesi Olanlar (<5) (n=30) ±SS | Kötü Uyku Kalitesi Olanlar (≥5) (n=170) ±SS | p | Kısa Süre Uyuyanlar (< 7 saat) (n=52) ±SS | Normal ve Uzun Süre Uyuyanlar (≥7 saat) (n=148) ±SS | p |
|---|---|---|---|---|---|---|
| **Enerji ve besin öğeleri** | | | | | | |
| **Enerji (kcal)** | 1631,6±574,9 | 1696,6±522,9 | 0,811 | 1692,2±432,7 | 1684,9±561,6 | 0,703 |
| **CHO (g)** | 180,2±77,4 | 184,3±74,9 | 0,929 | 193,0±68,8 | 180,3±77,1 | 0106 |
| **CHO (%)** | 45,9±12,6 | 44,1±10,1 | 0,653 | 46,4±11,8 | 43,7±10,0 | 0,120 |
| **Protein (g)** | 65,2±25,2 | 70,7±28,6 | 0,541 | 69,3±27,1 | 69,9±28,6 | 0,891 |
| **Protein (%)** | 16,6±4,7 | 17,4±5,5 | 0,484 | 16,9±4,9 | 17,4±5,6 | 0,853 |
| **Yağ (g)** | 68,1±28,9 | 72,5±27,7 | 0,847 | 69,3±27,4 | 72,7±28,1 | 0,496 |
| **Yağ (%)** | 36,7±12,2 | 38,3±9,5 | 0,880 | 36,7±11,4 | 38,5±9,4 | 0,264 |

CHO: Karbonhidrat p: anlamlılık değeri

Bozok Tıp Derg 2023;13(3):26-35
Bozok Med J 2023;13(3):26-35

**Tablo 4.** Uyku kalitesi ve süresi değişkenlerine ait lojistik regresyon modelinin sonuçları

| **Uyku Kalitesi** | **OR** | **Wald** | **p** | **%95 OR Güven Aralığı** | |
|---|---|---|---|---|---|
| | | | | **Alt Sınır** | **Üst Sınır** |
| **Katsayı** | | | | | |
| Vücut ağırlığı | 0,964 | 5,152 | **0,023** | 0,933 | 0,995 |
| Bel boy oranı (Ref=normal) | | | | | |
| Bel boy oranı (riskli) | 0,726 | 0,272 | 0,602 | 0,218 | 2,421 |
| Bel boy oranı (yüksek risk) | 1,930 | 0,204 | 0,652 | 0,111 | 33,585 |
| Bel çevresi (Ref= normal) | | | | | |
| Bel çevresi (riskli) | 1,175 | 0,060 | 0,807 | 0,323 | 4,268 |
| Bel çevresi (yüksek risk) | 3,269 | 1,382 | 0,240 | 0,454 | 23,552 |
| Uyku süresi (Ref=Kısa) | | | | | |
| Uyku süresi (Normal/Uzun) | 0,212 | 5,501 | **0,019** | 0,058 | 0,775 |
| Sabit terim | 251,790 | 18,864 | **<0,001** | | |
| **Uyku Süresi** | **OR** | **Wald** | **p** | **%95 OR Güven Aralığı** | |
| | | | | **Alt Sınır** | **Üst Sınır** |
| **Katsayı** | | | | | |
| Vücut ağırlığı | 0,978 | 4,835 | **0,028** | 0,958 | 0,998 |
| Bel kalça oranı | 1,477 | 0,407 | 0,524 | 0,445 | 4,902 |
| PAL değeri | 0,512 | 1,906 | 0,167 | 0,198 | 1,325 |
| Sabit terim | 42,853 | 10,989 | **<0,001** | | |

OR: Odds oranı

saptanmıştır. Uyku kalitesinin ve uyku süresinin bağımlı değişken olarak alındığı lojistik regresyon modelinin Nagelkerke R2 değerleri sırasıyla 0,127 ve 0,050'dir, bu değerler 0'dan oldukça uzaktır. Bu modellerin doğru sınıflama oranları ise sırasıyla %85,5 ve %74 düzeylerindedir ve bu oranlar oldukça yüksektir.

## TARTIŞMA

Üniversite dönemi öğrencilerin ileriye yönelik bireysel alışkanlıklarının yerleştiği kritik bir dönemdir. Toros Üniversitesi Sağlık Bilimleri Fakültesinde okuyan öğrencilerde uyku, beslenme durumu ve depresyon arasındaki ilişkiyi belirlemek amacıyla yapılan bu araştırma üniversite öğrencilerinde kötü uyku kalitesinin depresyon durumu ile genel ve santral obezite açısından risk faktörleri olabileceğini göstermektedir.

Uyku kalitesini etkileyen en önemli faktörlerin başında demografik faktörler gelmektedir; yaş ise bu faktörlerin en önemli unsurlarından birini oluşturmaktadır. Yaş almaya bağlı olarak bireylerde uykunun süresi, derinliği ve verimi azalırken; gece uyanık kalma süresi ve uykudan uyanma sıklığı artış göstermektedir (22). Bu konuda yapılan bir meta-analizde erişkin bireylerde yaşla birlikte uyku gecikmesinin arttığı, REM uyku yüzdesinin ise azaldığı gösterilmektedir (23). Bu çalışmada ise yaş ile uyku kalitesi arasındaki ilişki değerlendirildiğinde anlamlı olarak bir ilişki bulunamamıştır (p>0,05) (Tablo 1). Bunun nedeninin çalışmaya katılan öğrencilerin yaş aralığının çok geniş olmamasından kaynaklı olduğu düşünülmektedir. Fiziksel aktivite uyku kalitesini iyileştirmek için en umut verici alternatiflerden biri olarak gösterilmektedir. Bu ilişkinin nedenleri ise yapılan düzenli fiziksel aktivitedeki artışın vücut ağırlığı ile kronik hastalıkların temeli olan inflamasyondaki azalma ve psikolojik iyilik halindeki artış olarak gösterilmektedir (24). Yakın tarihli bir meta-analizde fiziksel aktivitenin uyku kalitesi ve süresi üzerindeki etkilerini kıyaslamak için bireylerin yaptığı egzersiz akut (bir günlük) ve düzenli (bir hafta

veya daha fazla) olarak gruplandırmış ve sonuçta her iki egzersiz türünün de uykuya dalma süresini kısaltıp, uykuda geçirilen süre ve kaliteyi arttırdığı belirlenmiştir (25). Literatürü destekler nitelikte bu çalışmada da iyi uyku kalitesine sahip olan öğrencilerin PAL değerlerinin kötü uyku kalitesine sahip olanlara göre daha yüksek olduğu bulunmuştur (p<0,05) (Tablo 2).

Sigara ve alkol tüketimi, uyku kalitesini ve süresini olumsuz yönde etkileyebilmektedir. Sigara tüketimi solunum yollarında olumsuz fonksiyonlara neden olarak uyku apnesi ve artan uyku gecikmesiyle birlikte uyku kalitesini bozmaktadır. Alkolün ise uyku kalitesi üzerindeki olumsuz etkileri alkolün uyku regülasyonu ile ilişkili GABAerjik sistemler üzerindeki akut etkileri ve dopamin gibi nörotransmiterler üzerindeki etkileri ile ilişkili olabilmektedir (26). Yapılan bir araştırmaya göre, sigara ve alkol kullanan üniversite öğrencilerinin, kullanmayanlara göre daha kötü uyku kalitesine sahip oldukları ve derste uyuklama oranının ise daha yüksek olduğu bildirilmiştir (27). Bu çalışmada da sigara kullanmayan öğrencilerin sosyal içici olan öğrencilere göre daha iyi uyku kalitesine sahip oldukları bulunurken (p<0,05), alkol kullanmayan öğrencilerin de kullanan öğrencilere göre daha kısa uyku süresine sahip oldukları bulunmuştur (p>0,05) (Tablo 1). Bu sonuçlar literatürü destekler niteliktedir.

Uyku bozuklukları ve depresyon mental sağlık temeli üzerinden genellikle ilişkilendirilmektedir. Depresyon gibi duygudurum bozukluklarına sıklıkla uyku güçlükleri eşlik edebildiği gibi tam tersi bir durumda söz konusu olabilmektedir (8). Bu karşılıklı ilişkiye istinaden yapılan gözlemsel bir çalışmada uykusuzluğu olan bireylerin klinik olarak anlamlı düzeyde depresyon tanısı alma olasılığının uykusuz olmayanlara göre 10 kat daha fazla olduğu bulunmuştur (28). Müdahale çalışmalarını içeren bir meta-analizde ise uyku kalitesini iyileştirmenin depresyon, kaygı ve stres düzeylerini azalttığı ortaya koyulmuştur (29). Bu çalışmada ise literatüre uyumlu olacak şekilde BDÖ puanına göre depresyon riski olan öğrencilerin olmayanlara göre daha kötü uyku kalitesine sahip oldukları saptanmıştır (p<0,05) (Tablo1).

Akut uyku kısıtlamalarından sonra özellikle toplam enerji, toplam yağ ve doymuş yağ alımındaki artışlar ile birlikte karbonhidrat ve protein açısından zengin gece atıştırmalarının sıklığı artmaktadır ve bu durumda uyku kalitesini olumsuz yönde etkileyebilmektedir (30). Yaşları 20-79 arasında değişen ve yüksek katılım içeren bir çalışmada bireylerin uyku süresi ile makro besin ögesi alımları arasındaki ilişki incelenmiş ve kısa uyku süresine sahip olan bireylerde günlük alınan protein miktarının normal ve uzun süre uyuyan bireylere göre anlamlı düzeyde daha düşük olduğu saptanmıştır. Yine aynı çalışmada kısa uyku süresine sahip olan erkek bireylerin tükettikleri yağ miktarı ile kadın bireylerin günlük tükettikleri karbonhidrat miktarının da diğer gruplara göre anlamlı düzeyde daha yüksek olduğu bulunmuştur (31). Yakın tarihte yapılan başka bir çalışmada ise günlük alınan yağ miktarındaki artışla beraber bireylerin halsizlik/yorgunluk durumunun arttığı ve toplam uyku süresinde azalmaların olduğu bulunurken, tüketilen yağ miktarının uyku ve uyanıklık sürecini kontrol eden Leptin ve Ghrelin hormonu seviyelerinde de değişikliklere yol açtığı da bulunmuştur. Bu sonuçlara istinaden aynı çalışmada akşam saatlerinde tüketilen besinlerin yağ miktarının sınırlandırılmasıyla da uyku kalitesinin arttırılabileceği de belirlenmiştir (32). Mevcut olan bu çalışmada da akşam öğününden sonra besin tüketen öğrencilerin tüketmeyenlere göre kötü uyku kalitesine sahip olduğu bulunurken (p<0,05), aile yanında yaşayan öğrencilerin, öğrenci evi ve öğrenci yurdunda yaşayanlara göre daha uzun uyku süresine sahip oldukları bulunmuştur (p<0,05) (Tablo 1). Çıkan bu sonuçlar sağlıklı beslenme konusunda daha avantajlı olan ailelerinin yanında yaşayan öğrencilerin daha iyi uyku kalitesine sahip olması ile de desteklenmektedir (33).

Kısa süreli uyku ve uyku kalitesinin bozulması hem iştah metabolizmasını düzenleyen hormonlar aracılığıyla beynin açlık ve tokluk mekanizmasını açlık yönüne kaydırarak hem de enerji ve karbonhidrat açısından zengin atıştırmalıklara zaman oluşturarak enerji alımını arttırmakta ve uzun dönemde düzensiz yeme alışkanlığı oluşturarak da daha yüksek BKİ ve santral obezite belirteçleriyle ilişkilendirilmektedir (34). Yapılan çalışmalar sürekli artan vücut ağırlığı artışı ile azalan uyku süresinin arasında bir ilişki olduğunu göstermektedir (35,36). Spiegel ve ark. kısa vadeli uyku kısıtlanmasının Leptin ve Ghrelin gibi iştah metabolizmasında önemli bazı hormonların değişimini de beraberinde getirdiğini göstermiştir (37). Yapılan başka bir çalışmaya göre ise uyku süresindeki

her 1 saatlik azalmanın obezite riskinde %24'lük artışa neden olduğu saptanmıştır (35). Gupta ve ark. yapmış oldukları bir çalışmada da bireylerin BKİ değerleri arttıkça uyku kalitelerinin azaldığı bulunmuştur (34). Bu çalışmaların aksine Türközü ve Aksoydan'ın üniversite öğrencileri ile yapmış oldukları bir çalışmada ise farklı uyku süresi ve uyku kalitesine sahip öğrencilerin antropometrik ölçümleri arasında anlamlı bir fark bulunamamıştır (36). Mevcut olan çalışmada da kötü uyku kalitesine sahip olan öğrencilerin vücut ağırlıkları uyku kalitesi iyi olan öğrencilere göre anlamlı düzeyde daha fazla olduğu bulunurken ($p<0,05$) (Tablo 2), vücut ağırlığındaki bir birimlik artışın uyku kalitesinin iyi olma düzeyini %3,6 oranında azalttığı saptanmıştır ($p<0,05$) (Tablo 4). Genel obezite belirteci olan beden kütle indeksinden ziyade santral obeziteyi belirleyen ve daha hassas bir obezite belirteci olan bel çevresi ölçümlerine yönelik değerlendirmelerde ise normal süre uyuyan bireylere kıyasla kısa süre uyuyan bireylerin daha yüksek BKİ ile bel çevresine sahip olduğu bulunmuştur (38). Bu çalışmanın aksine İspanya'da yapılan bir çalışmada ise uyku kalitesi ile bel çevresi ölçümleri arasında istatistiksel olarak anlamlı bir ilişki bulunmamıştır, bunun nedeni ise çalışmanın popülasyonunun yaşlı bireylerden oluşması olarak gösterilmiştir (39). Bu çalışmada da kötü uyku kalitesine sahip ve bel çevresi ölçümleri riskli düzeyde olan erkek bireylerin bel çevresi ölçümlerinin iyi uyku kalitesine sahip olanlara göre istatistiksel olarak anlamlı düzeyde daha yüksek olduğu görülmektedir ($p<0,05$) (Tablo 2). Bu sonuçlar literatür ile uyum göstermektedir.

Bu çalışmanın birkaç kısıtlaması bulunmaktadır. Bunlardan ilki çalışma kesitsel bir tasarıma sahip olduğu için genellemeye imkân vermemektedir. Bir diğer kısıtlılık ise antropometrik ölçümler dışında uyku verileri dahil olmak üzere tüm bilgilerin kişisel bildirime dayalı olmasıdır. Son olarak da uyku latansı bilinerek uyku süresinin değerlendirmesi daha objektif bir değerlendirme sağlayacaktır.

## SONUÇ

Üniversite öğrencilerinde uyku, mental sağlık ve beslenme karşılıklı olarak birbirini etkileyebilen ve insan hayatı için elzem ihtiyaçlar arasındadır. Bu süreçlerin kontrolü eş zamanlı gerçekleştirilemediğinden iştahı olumsuz yönde etkileyebilen farklı hormonal süreçler ön plana çıkarak bireyler obeziteye ve ilintili olduğu kronik hastalıklara yönelebilmektedir. Bu yüzden mental sağlığı, uyku süresi ve kalitesini iyileştirmeye yönelik alanında uzman kişiler tarafından gerekli koruyucu girişimlerin uygulanmasının bu konunun çözümünde etkili olabileceği düşünülmektedir. Bu çalışmada kötü uyku kalitesine ve kısa uyku süresine sahip olan üniversite öğrencilerinin obezite açısından riskte oldukları görülmektedir. Bu konuda bir beslenme uzmanı tarafından öğrencilere özellikle ideal vücut ağırlıklarına ulaşmaları ve bu ağırlıkları korumaları, öğün düzenleri, gece yeme alışkanlığı ve kafein gibi uyarıcı besinlerin tüketimi başta olmak üzere sağlıklı beslenme eğitimi verilmesinin bir diğer koruyucu uygulama ve tedavi edici girişim olacağı düşünülmektedir. İlerleyen yıllarda üniversite öğrencilerinde uyku, depresyon ve obezite arasındaki ilişkilerin daha net ortaya koyulabilmesi için geniş katılımın sağlandığı, uyku ve depresyon ile ilgili verilerin nicel olarak değerlendirildiği çalışmaların yapılmasına ihtiyaç duyulmaktadır.

## Tasdik ve Teşekkür

Bu çalışma için finansal destek alınmamıştır. Çalışmaya katılan öğrencilere teşekkür ederiz. Yazarlar arasında herhangi bir çıkar çatışması bulunmadığı beyan ederler.

## KAYNAKLAR

**1**. Institute of Medicine (US) Committee on Sleep Medicine and Research. Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. Colten HR, Altevogt BM, eds. Washington (DC), National Academies Press (US). 2006.

**2.** Cappuccio FP, Taggart FM, Kandala N-B. Meta-analysis of short sleep duration and obesity in children and adults. Sleep. 2008;31:619–26.

**3.** Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Sleep Health. 2015;1:40–3.

**4.** Peltzer K, Pengpid S. Sleep duration and health correlates among university students in 26 countries. Psychol Health Med. 2016;21(2):208–20.

**5.** Clement-Carbonell V, Portilla-Tamarit I, Rubio-Aparicio M, Madrid-Valero JJ. Sleep Quality, Mental and Physical Health: A Differential Relationship. Int J Environ Res Public Health. 2021;18(2):460.

**6.** Zee PC, Badr MS, Kushida C, Mullington JM, Pack AI, Parthasarathy S, et al. Strategic opportunities in sleep and circadian

research: report of the Joint Task Force of the Sleep Research Society and American Academy of Sleep Medicine. Sleep. 2014;37(2):219-27.

**7.** Alafif N, Alruwaili NW. Sleep duration, body mass index, and dietary behaviour among KSU students. Nutrients. 2023;15:510.

**8.** Dinis J, Bragança M. Quality of sleep and depression in college students: a systematic review. Sleep Sci. 2018;11(4):290-301.

**9.** Chaput JP, Després JP, Bouchard C, Tremblay A. The association between sleep duration and weight gain in adults: a 6-year prospective study from the Quebec Family Study. Sleep. 2008;31:517–23.

**10.** Pekcan G. Beslenme durumunun saptanması, (Baysal A, ed,) Diyet el kitabı, Ankara, Hatipoglu Yayınevi. 2008. p. 67-141.

**11.** Ağargün MY, Kara H, Anlar Ö. Pittsburgh Uyku Kalitesi İndeksi'nin geçerliliği ve güvenilirliği. Türk Psikiyatri Dergisi. 1996;7:107–15.

**12.** Hisli N. Beck Depresyon Envanteri'nin üniversite öğrencileri için geçerliği ve güvenirliği. Psikoloji Dergisi. 1989;23:3-13.

**13.** Gordon C, Chumlea WC, Roche AF. Measurement descriptions and techniques. In: Lohman T, Roche AF, Martorell R, eds. Anthropometric standardization reference manual, Human Kinetics Books. IL, Champaign. 1988. p. 3-12.

**14.** Türkiye Beslenme Rehberi (TÜBER)-2022. TC. Sağlık Bakanlığı Yayın No:1031, Ankara, 2022. p.40.

**15.** Pekcan G. Beslenme durumunun saptanması. (Baysal A, ed). Diyet El Kitabı. Ankara: Hatipoğlu Yayınevi, 2008. p.64-141.

**16.** Ashwell M, Gibson S. Waist-to-height ratio as an indicator of 'early health risk': simpler and more predictive than using a 'matrix' based on BMI and waist circumference. BMJ Open. 2016;6(3):e010159.

**17.** Türkiye Beslenme Rehberi (TÜBER)-2015. TC. Sağlık Bakanlığı Yayın No:1031, Ankara, 2016.

**18.** Rakıcıoğlu N, Ayaz A, Pekcan G. Yemek ve besin fotoğraf kataloğu ölçü ve Miktarları. Ankara, Nadir Kitap, 2012.

**19.** Kutluay Merdol T. Toplu beslenme yapılan kurumlar için standard yemek tarifleri. Ankara, Hatipoğlu Yayınları, 2003.

**20.** Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989 May;28(2):193-213.

**21.** Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4:561-71.

**22.** Li J, Vitiello MV, Gooneratne NS. Sleep in normal aging. Sleep Med Clin. 2008;13(1):1-11.

**23.** Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep. 2004;1;27(7):1255-73.

**24.** Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ. 2006;174(6):801-9.

**25.** Kredlow MA, Capozzoli MC, Hearon BA, Calkins AW, Otto MW. The effects of physical activity on sleep: a meta-analytic review. J Behav Med. 2015;38(3):427-49.

**26.** Koob GF, Colrain IM. Alcohol use disorder and sleep disturbances: a feed-forward allostatic framework. Neuropsychopharmacology. 2020;45(1):141-65.

**27.** Aysan E, Karaköse S, Zaybak A, İsmailoğlu EG. Üniversite Öğrencilerinde Uyku Kalitesi ve Etkileyen Faktörler. Dokuz Eylül Üniversitesi Hemşirelik Fakültesi Elektronik Dergisi. 2014;7(3):15-8.

**28.** Taylor DJ, Lichstein KL, Durrence HH, Reidel BW, Bush AJ. Epidemiology of insomnia, depression, and anxiety. Sleep. 2005;28(11):1457-64.

**29.** Scott AJ, Webb TL, Martyn-St James M, Rowse G, Weich S. Improving sleep quality leads to better mental health: a meta-analysis of randomised controlled trials. Sleep Med Rev. 2021;60:101556.

**30.** Dashti HS, Scheer FA, Jacques PF, Lamon-Fava S, Ordovás JM. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. Adv Nutr. 2015;6(6):648-59.

**31.** Doo M, Kim Y. Association between sleep duration and obesity is modified by dietary macronutrients intake in Korean. Obes Res Clin Pract. 2016;10:424-31.

**32.** Cao Y, Taylor A, Pan X, Adams R, Apleton S, Shi Z. Dinner fat intake and sleep duration and self-reported sleep parameters over five years: findings from the Jiangsu nutrition study of Chinese adults. Nutrition. 2016;32(9):970-4.

**33.** Ermiş E, Doğan E, Erilli N, Satıcı A. Üniversite öğrencilerinin beslenme alışkanlıklarının incelenmesi: Ondokuz Mayıs Üniversitesi örneği. Spor ve Performans Araştırmaları Dergisi. 2015;6(1):30-40.

**34.** Gupta P, Srivastava N, Gupta V, Tiwari S, Banerjee M. Association of sleep duration and sleep quality with body mass index among young adults. J Family Med Prim Care. 2022;11(6):3251-6.

**35.** Patel SR, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity 2008;16(3):643-53.

**36.** Türközü D, Aksoydan E. Uyku süresi ve kalitesinin beslenme ve vücut bileşimine etkisi. Journal of Sted. 2015;24(1):10

**37.** Spiegel K, Tasali E, Penev P, Van Cauter E. Brief communication. Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med. 2004;141:846-50.

**38.** Haglöw J, Berglund L, Janson C, Lindberg E. Sleep duration and central obesity in women- differences between short sleepers and long sleepers. Sleep Medicine. 2012;13:1079-85.

**39.** López-García E, Faubel R, León-Muñoz L. Sleep duration, general and abdominal obesity, and weight change among the older adult population of Spain. Am J Clin Nutr. 2008;87(2):310-6.

# EVALUATION OF THE RESULTS OF HEMATOLOGICAL PARAMETERS OF PATIENTS WITH GASTRIC CANCER

## Mide Kanserli Hastaların Hematolojik Parametre Sonuçlarının Değerlendirilmesi

Mehmet Ali GUL[1], Duygu TOZCU[2], Nezahat KURT[3], Mustafa CAPRAZ[4]

[1]Department of Medical Biochemistry, Faculty of Medicine, Amasya University, Amasya, Türkiye
[2]Department of Physiology, Faculty of Medicine, Amasya University, Amasya, Türkiye
[3]Department of Medical Biochemistry, Faculty of Medicine, Erzincan Binali Yildirim University, Türkiye
[4]Department of Internal Diseases, Faculty of Medicine, Amasya University, Amasya, Türkiye

Mehmet Ali GÜL, Dr. (0000-0002-5849-0116)
Duygu TOZCU, Dr. (0000-0002-3972-5442)
Nezahat KURT, Dr. (0000-0002-1685-5332)
Mustafa ÇAPRAZ, Dr. (0000-0001-9586-6509)

**İletişim:**
Dr. Mehmet Ali GÜL
Department of Medical Biochemistry, Faculty of Medicine, Amasya University, Amasya, 05100, Türkiye

**Geliş tarihi/Received:** 05.06.2023
**Kabul tarihi/Accepted:** 08.09.2023
**DOI:** 10.16919/bozoktip.1307841

Bozok Tıp Derg 2023;13(3):36-42
Bozok Med J 2023;13(3):36-42

## ABSTRACT

**Objective:** Gastric cancer is a major health concern which fourth leading cause of cancer death and fifth most common cancer. It has difficulties such as having a poor prognosis and diagnoses at an advanced stage. There are studies to find prognostic indicators that are easily and less invasively obtained in gastric cancer and hematological tests are one of them. In this study, we aimed to investigate the relation between hematological test and gastric cancer.

**Material and Methods:** 48 patients diagnosed with gastric cancer and 45 healthy adults in the control group were examined prospectively. All participants' demographic data and laboratory results were obtained from the hospital database and recorded.

**Results:** In the gastric cancer group compared to the healthy control group, while red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean cell hemoglobin concentration (MCHC), platelet distribution width (PDW), lymphocyte (LYM), eosinophil (EO) values were statistically lower, mean corpuscular hemoglobin (MCH), red cell distribution width-standard deviation, red cell distribution width-coefficient of variation (RDW-CV), nucleated red blood cells (NRBC), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) values were observed statistically higher ($p<0.05$). RBC, HGB, HCT, LYM, RDW-SD, RDW-CV, NLR, PLR, and MLR exhibited considerably higher area under the curve (AUC) values in the receiver operating characteristic (ROC) analysis of these parameters ($p<0.001$).

**Conclusion:** RBC, HGB, HCT, LYM, RDW-SD, RDW-CV, NLR, PLR, and MLR levels can be used as a supportive test to eliminate endoscopic delays in gastric cancer diagnosis.

**Keywords:** *Stomach; Adenocarcinoma; Laparoscopic Gastrectomy; Blood Cell Count*

## ÖZET

**Amaç:** Mide kanseri, kansere bağlı ölümlerde dördüncü ve en sık görülen kanserlerde beşinci sırada yer alan önemli bir sağlık sorunudur. Prognozun kötü olması ve ileri evrede tanı konması gibi güçlükleri vardır. Mide kanserinde kolay ve daha az invaziv olarak elde edilen prognostik göstergeleri bulmaya yönelik çalışmalar vardır ve hematolojik testler bunlardan biridir. Bu çalışmada hematolojik test sonuçları ile mide kanseri arasındaki ilişkiyi araştırmayı amaçladık.

**Gereç ve Yöntemler:** Bu çalışmada mide kanseri tanısı almış 48 hasta ve kontrol grubunda yer alan 45 sağlıklı yetişkin retrospektif olarak incelendi. Tüm katılımcıların demografik verileri ve laboratuvar sonuçları hastane veri tabanından elde edildi ve kaydedildi.

**Bulgular:** Mide kanserli grupta sağlıklı kontrol grubuna göre; kırmızı kan hücreleri (RBC), hemoglobin (HGB), hematokrit (HCT), ortalama hücre hemoglobin konsantrasyonu (MCHC), trombosit dağılım genişliği (PDW), lenfosit (LYM), eozinofil (EO) değerleri istatistiksel olarak daha düşüktü, ortalama eritrosit hemoglobin (MCH), kırmızı hücre dağılım genişliği-standart sapma, kırmızı hücre dağılım genişlik-varyasyon katsayısı (RDW-CV), çekirdekli kırmızı kan hücreleri ( NRBC), nötrofil lenfosit oranı (NLR), trombosit lenfosit oranı (PLR) ve monosit lenfosit oranı (MLR) değerlerinin istatistiksel olarak daha yüksek olduğu gözlendi ($p<0,05$). RBC, HGB, HCT, LYM, RDW-SD, RDW-CV, NLR, PLR ve MLR, bu parametrelerin alıcı çalışma karakteristiği (ROC) analizinde oldukça yüksek eğri altı alan (AUC) değerleri sergiledi ($p<0,001$).

**Sonuç:** RBC, HGB, Hct, LYM, RDW-SD, RDW-CV, NLR, PLR ve MLR seviyeleri mide kanseri tanısında endoskopik gecikmeleri ortadan kaldırmak için destekleyici test olarak kullanılabilir.

**Anahtar Kelimeler:** *Mide; Adenokarsinom; Laparoskopik Gastrektomi; Kan Hücre Sayımı*

## INTRODUCTION

Gastric cancer (GC) is one of the most common type of cancer and is an aggressive disease which is front row cause of cancer-related death (1-2). While the incidence of GC decreases due to some factors such as early diagnosis, healthy life and reduced incidence of disease-causing bacteria, but still there is an increase in mortality rates and incidence of the disease in some geographies (3). GC development affected by both genetic and environmental factors (4). Various genetic changes such as mutations at the cytogenetic level in the somatic cell or loss of function of the DNA mismatch repair system in some types of GC have been shown in the occurrence of the disease (5-7). Environmental and nutritional factors play a role in the development of the disease. Consumption of salty and salt-preserved foods, nitrates or pickled foods have been associated with an increased risk of developing stomach cancer (8-9). Content of the diet, eating habits and smoking can increase the risk of disease (9-10). The early stages of the disease may be asymptomatic or have minimal symptoms, so the disease is difficult to diagnose and constantly diagnosed at an advanced stage (11).

Currently, the gold standard method for detecting GC is upper endoscopy with tissue biopsy. However, these methods have disadvantages such as being invasive, costly and time-consuming. Therefore, rapid, economical, non-invasive method researches continue. Studies on genetic, biochemical and hematological parameters that have the potential to one of the biomarkers on blood, urine, saliva and gastric juice are in progress. However, although some results are very promising, further studies with larger sample sizes with larger numbers of healthy patients are needed (12-14). The prognostic significance of some hematology test results, such as leukocyte and platelet count, and mean platelet volume, has been demonstrated in various malignancies (15-16). We aimed to investigate the status of hematological tests in evaluating hematological changes associated with GC, as well as other medical tests and imaging modalities, regarding the diagnosis or treatment of GC.

## MATERIAL AND METHODS

This study was based on retrospective analysis of 48 patients diagnosed with GC and 45 healthy adults. A patient group was formed from individuals who underwent curative laparoscopic (assisted) gastrectomy and diagnosed with gastric adenocarcinoma in Sabuncuoğlu Şerefeddin Training and Research Hospital between January 2021 and January 2023. An informed consent form was obtained from the individuals before the laparoscopic (assisted) gastrectomy procedure. For both groups, individuals with chronic diseases, ongoing infections, diabetes mellitus, autoimmune disease, under the age of 18, and blood transfusions were excluded. Amasya University Rectorate Non-Invasive Clinical Research Ethics Committee (Jan 2023 Number of Meeting 02 Decision Number 2023/05).

Laboratory values of white blood cell (WBC), red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean cell hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet (PLT), red cell distribution width-standard deviation (RDW-SD), red cell distribution width-coefficient of variation (RDW-CV), platelet distribution width (PDW), mean platelet volume (MPV), plateletcrit (PCT), nucleated red blood cells (NRBC#), nucleated red blood cells (NRBC), neutrophil (NEUT#), lymphocyte (LYMPH#), monocyte (MONO#), eosinophil (EO #), basophil (BASO#), LYMP, MONO, NEUT, EO and BASO measured in Sysmex XN-1000 analyzer and demographics and data were extracted from the hospital database records.

SPSS 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) software was used for statistical analysis of data. First of all, Kolmogorov-Smirnov test was used to determine the data distribution, and Independent Samples t-test was used for pairwise comparison of parametric tests for data showing normal distribution according to this test, and Mann Whitney-U test, which is one of the nonparametric tests, was used for data that did not show normal distribution. Evaluating the discrimination of these analyzes between the patient group and the healthy group was evaluated with the Receiver Operating Characteristic (ROC) test. $p<0.05$ was considered statistically significant.

## RESULTS

Demographic data of the patient and control groups included in the study are given in Table 1. Accordingly, there was no difference between the mean age of the

Bozok Tıp Derg 2023;13(3):36-42
Bozok Med J 2023;13(3):36-42

**Table 1.** Demographic data of Control and Patient Groups

| | Control (n=45) | Patient (n=48) |
|---|---|---|
| **Age (year)** | 62.22±11.85 | 65.812±9.55 |
| **Gender (Woman/Man)** | 9/39 | 11/34 |

**Table 2.** Levels of Hematological Values in Control and Patient Groups

| | Control (n=45) | Patient (n=48) | p values |
|---|---|---|---|
| **RBC ($x10^6$)** | 4.786±0.542 | 3.948±0.669 | .000 |
| **WBC ($x10^3$)** | 7.054±1.085 | 8.157±4.470 | .863 |
| **PLT ($x10^6$)** | 227.555±46.256 | 206.062±91.826 | .162 |
| **HGB (g/dL)** | 14.000±1.498 | 11.320± 2.058 | .000 |
| **HCT** | 37.866±2.0108 | 35.025± 5.781 | .000 |
| **NEU ($x10^3$)** | 3.948±0.867 | 5.945±4.352 | .056 |
| **MCH** | 29.226±1.850 | 28.816±2.900 | .442 |
| **MCHC** | 33.091±1.233 | 32.054±2.186 | .007 |
| **RDW-CV** | 13.444±1.092 | 16.477±4.176 | .000 |
| **RDW-SD** | 42.264±2.650 | 53.904±14.25 | .000 |
| **NRBC** | 0.000±0.002 | 0.014±0.040 | .000 |
| **PDW** | 12.306±2.233 | 11.172±2.553 | .005 |
| **PCT** | 0.235±0.052 | 0.212±0.068 | .030 |
| **LYMPH ($x10^3$)** | 2.279±0.657 | 1.227±0.769 | .000 |
| **EO ($x10^3$)** | 0.186±0.186 | 0.116±0.159 | .000 |
| **LYM%** | 32.404±8.080 | 16.836±10.906 | .000 |
| **MONO%** | 8.295±2.067 | 6.872±4.888 | .003 |
| **NEUT%** | 55.917±7.851 | 69.630±19.532 | .000 |
| **EOS%** | 2.400±1.133 | 1.563±1.743 | .000 |
| **BASO%** | 0.544±0.298 | 0.371±0.321 | .006 |
| **NLR** | 1.922±0.878 | 6.9123±6.773 | .000 |
| **PLR** | 108.063±40.191 | 224.027±174.241 | .000 |
| **MLR** | 0.280±0.162 | 0.567±0.478 | .007 |

red blood cells (RBC), white blood cell (WBC), platelet (PLT), hemoglobin (HGB), hematocrit (HCT), neutrophil (NEUT#), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), red cell distribution width-coefficient of variation (RDW-CV), red cell distribution widt-h-standard deviation (RDW-SD), nucleated red blood cells (NRBC), platelet distribution width (PDW), plateletcrit (PCT), lymphocyte (LYMPH), eosinophil (EO), lymphocyte percentile (LYM%), monocyte percentile (MONO%), neutrophil percentile (NEUT%), eosinophil percentile (EOS %), basophil percentile (BASO%), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) P<0.05 statistically significant

patient group and the mean age of the control group (p= 0.110).

In the GC group compared to the healthy control group, RBC, HGB, HCT, mean cell MCHC, PDW, LYM, EO values were statistically lower, MCH, RDW-SD, RDW-CV, NRBC, neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) values were observed statistically higher (p<0.05). On the other hand, no difference was observed in MCH, PLT and WBC values between the two groups. (Table 2 presents hematological data.) RBC, HGB, HCT, MCHC, PDW, PCT, LYM, EO, RDW-SD, RDW-CV, NLR, PLR, and

Bozok Tıp Derg 2023;13(3):36-42
Bozok Med J 2023;13(3):36-42

**Figure 1.** ROC analysis curves of hematological data

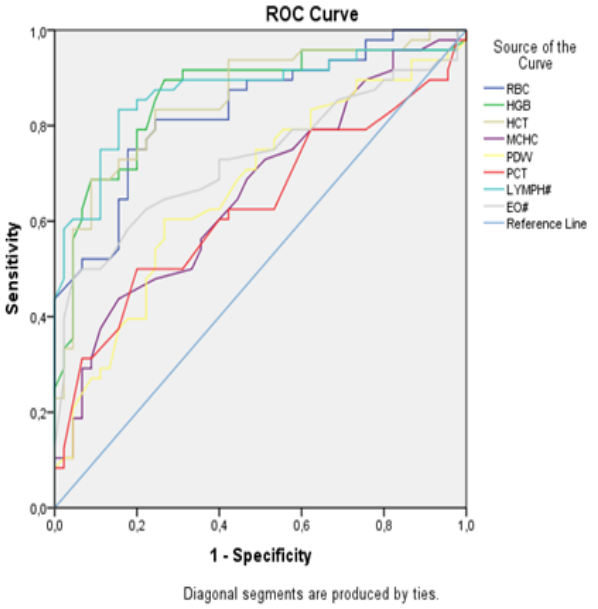



**Figure 2.** ROC analysis curves of hematological data

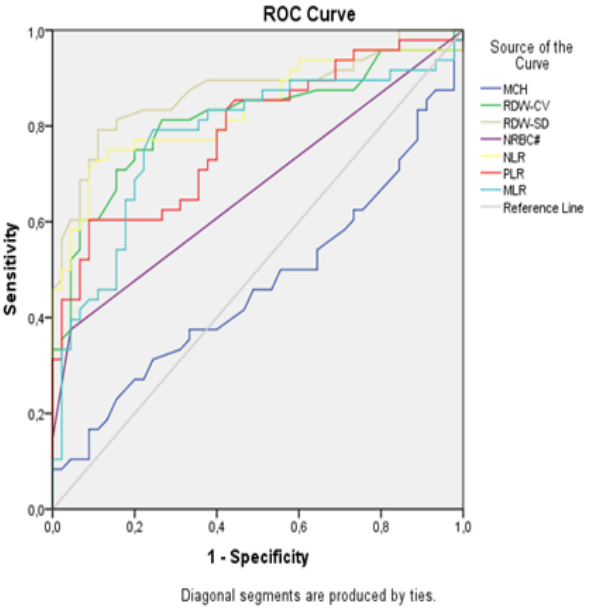



**Table 3.** ROC analysis data for hematological testing

| | AUC | Std. Error | P value | Asymptotic 95% Confidence Interval | |
|---|---|---|---|---|---|
| | | | | Lower Bound | Upper Bound |
| **RBC** | .834 | .041 | .000 | .752 | .915 |
| **HGB** | .862 | .040 | .000 | .784 | .941 |
| **HCT** | .854 | .040 | .000 | .777 | .932 |
| **MCHC** | .663 | .056 | .007 | .554 | .773 |
| **PDW** | .669 | .056 | .005 | .559 | .780 |
| **PCT** | .631 | .058 | .030 | .516 | .745 |
| **LYMPH** | .871 | .039 | .000 | .794 | .947 |
| **EO** | .732 | .053 | .000 | .628 | .836 |
| **MCH** | .465 | .061 | .564 | .347 | .584 |
| **RDW-CV** | .814 | .046 | .000 | .724 | .904 |
| **RDW-SD** | .872 | .038 | .000 | .797 | .947 |
| **NRBC#** | .669 | .056 | .005 | .558 | .779 |
| **NLR** | .834 | .043 | .000 | .750 | .919 |
| **PLR** | .783 | .047 | .000 | .691 | .876 |
| **MLR** | .778 | .050 | .000 | .679 | .876 |

red blood cells (RBC),hemoglobin (HGB), hematocrit (HCT), mean cell hemoglobin concentration (MCHC), platelet distribution width (PDW), plateletcrit (PCT), lymphocyte (LYMPH), eosinophil (EO), mean cell hemoglobin (MCH),red cell distribution width-coefficient of variation (RDW-CV), red cell distribution width-standard deviation (RDW-SD), nucleated red blood cells (NRBC),lymphocyte percentile (LYM%), monocyte percentile (MONO%), neutrophil percentile (NEUT%), eosinophil percentile (EOS %), basophil percentile (BASO%), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR)

Bozok Tıp Derg 2023;13(3):36-42
Bozok Med J 2023;13(3):36-42

MLR exhibited considerably higher area under the curve (AUC) values ($p<0.001$) in the receiver operating characteristic (ROC) analysis of these parameters. (Figure 1, Figure 2 and Table 3 show ROC analysis data.)

## DISCUSSION

In this study, we examined the whole blood hematology results of GC patients and healthy individuals. Because recent studies and new data on GC are needed. Due to the nature of the disease, it is difficult to diagnose the disease in the early stages. In addition, current methods used in diagnosing the disease are expensive and laborious (14). The tumor microenvironment is associated with a tumor-associated systemic state of inflammation, thereby accelerating tumor progression (17). Although recent studies suggest that cytokines secreted by inflammatory cells in the tumor microenvironment affect tumor cell proliferation and migration, the exact mechanisms are still unknown (18-19). Some genetic tests, such as the application of cfDNA use, is difficult to study for early GC detection due to the low level in early stage of GC and technical difficulties in its detection (20).

The NLR and PLR are indicator of systemic inflammation. In line with our results, Fang et. all, found that the systemic inflammatory markers NLR and PLR were higher in GC cancer and showed diagnostic sensitivity (21). Furthermore, they indicate NLR and PLR were more valuable for the diagnosis of GC than the traditional tumor markers CEA and CA19-9. Zhao et al. noted that both preoperative high NLR and PLR collected from routine blood tests are associated with poor overall survival, but they emphasized that only NLR can be an independent prognostic marker in patients with metastatic GC. Consequently, they reported that high NLR and PLR levels may contribute to adverse anti-tumor function (22). Lian et al., showed that preoperative PLR and NLR levels were significantly higher in patients with GC than in healthy individuals, and they stated that they could provide important diagnostic and prognostic results in patients with resectable GC (23).

RDW is predictor of inflammation and related with erythrocyte volume variability and erythrocyte homeostasis (24). It has been shown RDW associated with many diseases, and in studies on GC, Wang et al. suggested that high pre-treatment RDW level may be a negative predictor for cancer prognosis (25). And parallel with our RDW-CV results, Pietrzyk et all. showed that GC patients higher mean RDW values than healthy individuals (26). In cancer-induced inflammation, the survival of red blood cells is short. The number of immature red blood cells increases, resulting in high RDW. Therefore, high RDW is often seen in GC patients (27).

Aksoy et al. found that HGB, MLR and WBC results were significantly different in the GC patient group. HGB and MLR results are consistent with our results, while WBC results are not. Because according to our data, there was no significant difference in WBC between the groups (28). In their study on patients with GC who received neoadjuvant chemotherapy, Cheng et al. showed similar results and stated that MLR can be used as a convenient and inexpensive prognostic marker (29). Song et al., reported that MLR may be biomarkers to predict overall survival in patients with advanced GC (30).

It has been shown that PDW may be effective as an indicator of inflammation, and there is a close relationship between PDW, white blood cell count and serum C-reactive protein level (31). In parallel with our results, Cheng et al. showed decreased PDW associated with GC, but Saito et al. showed opposite to our results increased PDW increases in GC patients. They explained that this may be due to differences in diagnosis and different analysis methods chosen among studies, such as median value cut-off and optimal cut-off (27-32).

## CONCLUSION

In our study, there were limitations such as being subject to bias, because it was retrospective, and the small number of patients included in our study. However, among the findings we obtained regarding the hematological parameters we examined, the RBC, HGB, HCT, MCHC, PDW, LYM, EO values were statistically lower in patients with GC compared to the control group. The fact that it is higher than the mean value indicates that endoscopic intervention can be evaluated as a prognostic marker in the diagnosis of GC. We believe that our findings will contribute to further research to be conducted.

## Acknowledgments

The authors declare that there is no conflict of interest. No financial support was received for this research. We would like to thank all the doctor and staff of Sabuncuoğlu Şerefeddin Training and Research Hospital, especially in the laboratory, diagnosis and imaging departments and individuals who participated in this study.

## REFERENCES

**1**. Ferro A, Peleteiro B, Malvezzi M, BosettiC, Bertuccio P, Levi Fabio, et al. Worldwide trends in gastric cancer mortality (1980-2011), with predictions to 2015, and incidence by subtype. Eur J Cancer. 2014;50(7):1330-44.

**2.** Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61(2):69-90.

**3.** Topi S, Santacroce L, Bottalico L, Ballini A, Inchingolo AD, Dipalma G, et al. Gastric Cancer in History: A Perspective Interdisciplinary Study. Cancers (Basel). 2020;12(2):264.

**4.** Fock KM. Review article: the epidemiology and prevention of gastric cancer. Aliment Pharm Ther. 2014;40(3):250-60.

**5.** Chen ZD, Zhang PF, Xi HQ, Wei B, Chen L, Tang Y. Recent Advances in the Diagnosis, Staging, Treatment, and Prognosis of Advanced Gastric Cancer: A Literature Review. Frontiers in medicine. 2021;8:744839.

**6.** Fuchs CS, Tomasek J, Yong CJ, Dumitru F, Passalacqua R, Goswami C, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2014;383(9911):31-9.

**7.** Bae JM, Kim EH. Epstein-Barr. Virus and Gastric Cancer Risk: A Meta-analysis With Meta-regression of Case-control Studies. J Prev Med Public Health. 2016;49(2):97-107.

**8.** Correa P. Gastric cancer: overview. Gastroenterol Clin North Am. 2013;42(2):211-7.

**9.** Carcas LP. Gastric cancer review. J Carcinog. 2014;13:14.

**10.** La Vecchia C, Negri E, D'Avanzo B, Franceschi S. Electric refrigerator use and gastric cancer risk. Br J Cancer. 1990;62(1):136-7.

**11.** Hartgrink HH, Jansen EPM, van Grieken NCT, van de Velde CJH. Gastric cancer. Lancet. 2009;374(9688):477-90.

**12.** Herrera-Pariente C, Montori S, Llach J, Bofill A, Albeniz E, Moreira L. Biomarkers for Gastric Cancer Screening and Early Diagnosis. Biomedicines. 2021;9(10):1448.

**13.** Choi KS, Jun JK, Park EC, Park S, Jung KW, Han MA, et al. Performance of different gastric cancer screening methods in Korea: a population-based study. PLoS One. 2012;7(11):e50041.

**14.** Matsuoka T, Yashiro M. Biomarkers of gastric cancer: Current topics and future perspective. World J Gastroenterol. 2018;24(26):2818-32.

**15.** Yamanaka T, Matsumoto S, Teramukai S, Ishiwata R, Nagai Y, Fukushima M. The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in advanced gastric cancer. Oncology. 2007;73(3-4):215-20.

**16.** Smith RA, Ghaneh P, Sutton R, Raraty M, Campbell F, Neoptolemos JP. Prognosis of resected ampullary adenocarcinoma by preoperative serum CA19-9 levels and platelet-lymphocyte ratio. J Gastrointest Surg. 2008;12(8):1422-8.

**17.** Kumari N, Dwarakanath BS, Das A, Bhatt AN. Role of interleukin-6 in cancer progression and therapeutic resistance. Tumour Biol. 2016;37(9):11553-72.

**18.** Katheder NS, Rusten TE. Microenvironment and tumors-a nurturing relationship. Autophagy. 2017;13(7):1241-3.

**19.** Hirahara N, Tajima Y, Fujii Y, Kaji S, Yamamoto T, Hyakudomi R, et al. Comprehensive Analysis of Red Blood Cell Distribution Width as a Preoperative Prognostic Predictor in Gastric Cancer. Anticancer Res. 2019;39(6):3121-30.

**20.** Huang ZB, Zhang HT, Yu B, Yu DH. Cell-free DNA as a liquid biopsy for early detection of gastric cancer. Oncol Lett. 2021;21(1):3.

**21.** Fang T, Wang Y, Yin X, Zhai Z, Zhang Y, Yang Y, et al. Diagnostic Sensitivity of NLR and PLR in Early Diagnosis of Gastric Cancer. J Immunol Res. 2020 Mar 7;2020:9146042.

**22.** Zhao G, Liu N, Wang S, Guo J, Song X, Qi Y, et al. Prognostic significance of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in patients with metastatic gastric cancer. Medicine (Baltimore). 2020;99(10):e19405.

**23.** Lian L, Xia YY, Zhou C, Shen XM, Li XL, Han SG, et al. Application of platelet/lymphocyte and neutrophil/lymphocyte ratios in early diagnosis and prognostic prediction in patients with resectable gastric cancer. Cancer Biomark. 2015;15(6):899-907.

**24.** Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci. 2015;52(2):86-105.

**25.** Wang PF, Song SY, Guo H, Wang TJ, Liu N, Yan CX. Prognostic role of pretreatment red blood cell distribution width in patients with cancer: A meta-analysis of 49 studies. J Cancer. 2019;10(18):4305-17.

**26.** Pietrzyk L, Plewa Z, Denisow-Pietrzyk M, Zebrowski R, Torres K. Diagnostic Power of Blood Parameters as Screening Markers in Gastric Cancer Patients. Asian Pac J Cancer Prev. 2016;17(9):4433-7.

**27.** Saito H, Shimizu S, Shishido Y, Miyatani K, Matsunaga T, Fujiwara Y. Prognostic significance of the combination of preoperative red cell distribution width and platelet distribution width in patients with gastric cancer. BMC Cancer. 2021;21(1):1317.

**28.** Aksoy EK, Kantarci S, Torgutalp M, Akpınar MY, Sapmaz FP, Yalçın

GŞ, et al. The importance of complete blood count parameters in the screening of gastric cancer. Prz Gastroenterol. 2019;14(3):183-7.

**29.** Chen XQ, Xue CR, Hou P, Lin BQ, Zhang JR. Lymphocyte-to-monocyte ratio effectively predicts survival outcome of patients with obstructive colorectal cancer. World J Gastroenterol. 2019;25(33):4970-84.

**30.** Song S, Li C, Li S, Gao H, Lan X, Xue Y. Derived neutrophil to lymphocyte ratio and monocyte to lymphocyte ratio may be better biomarkers for predicting overall survival of patients with advanced gastric cancer. Onco Targets Ther. 2017;10:3145-54.

**31.** Santimone I, Di Castelnuovo A, De Curtis A, Spinelli M, Cugino D, Gianfagna F, et al. White blood cell count, sex and age are major determinants of heterogeneity of platelet indices in an adult general population: results from the MOLI-SANI project. Haematologica. 2011;96(8):1180-8.

**32.** Cheng S, Han F, Wang Y, Xu Y, Qu T, Ju Y, et al. The red distribution width and the platelet distribution width as prognostic predictors in gastric cancer. BMC Gastroenterol. 2017;17(1):163.

# THE EFFICACY OF COMPUTED TOMOGRAPHY GUIDED PERCUTANEOUS CORDOTOMY ON INTRACTABLE PAIN IN PATIENTS WITH LUNG CANCER

## Bilgisayarlı Tomografi Eşliğinde Yapılan Perkütan Kordotomi Uygulamasının Akciğer Kanserli Hastalardaki İnatçı Ağrı Üzerine Etkisi

Ferhat EGE[1], Mert AKBAS[2], Gozde DAGISTAN[3]

[1]Department of Algology,
Hatay Training and Research Hospital,
Hatay,
Türkiye
[2]Department of Algology,
Akdeniz University Faculty of Medicine,
Antalya,
Türkiye
[3]Department of Algology,
Akdeniz University Faculty of Medicine,
Antalya,
Türkiye

Ferhat EGE, Dr.
(0000-0002-5187-1856)
Mert AKBAS, Prof. Dr.
(0000-0001-9545-0642)
Gozde DAGISTAN, Dr.
(0000-0002-1777-3507)

**İletişim:**
Dr. Ferhat EGE
Department of Algology, Hatay Training and Research Hospital Hatay/Türkiye

**Geliş tarihi/Received:** 18.07.2023
**Kabul tarihi/Accepted:** 11.09.2023
**DOI:** 10.16919/bozoktip.1329518

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

## ABSTRACT

**Objective:** This study was carried out to evaluate the efficacy of Computed tomography (CT) guided percutaneous cordotomy(PCC) and postoperative complications in the treatment of intractable pain associated with lung cancer.

**Material and Methods:** CT – guided cordotomy was performed on 10 lung cancer patients unresponsive to medical and interventional pain management methods.

**Results:** The mean pretreatment and post treatment visual analog pain scale (VAS) scores of the patients were determined as 10 ± 0.0001 and 1.00 ± 0.67, respectively. Additionally, the mean pretreatment and post treatment Karnofsky Performance Scale (KPS) scores of the patients were calculated as 40± 9.42 and 73±10.59, respectively. Accordingly, there was a statistically significant difference between the pretreatment and post treatment VAS and KPS scores. Furthermore, the mean pretreatment and post treatment morphine equivalent dose of the patients were found as 860.2±199.8 mg and 220.7±69.08 mg, respectively.

**Conclusion:** The findings of this study suggest that CT guided PCC is a valuable treatment option for intractable pain problems in patients suffering from lung cancer.

**Keywords:** *CT Guided; Cordotomy; Pain, Cancer*

## ÖZET

**Amaç:** Akciğer kanserine bağlı dirençli ağrı tedavisinde, BT kılavuzluğunda perkütan kordotominin etkinliğini ve işlem sonrası komplikasyonları değerlendirmeyi amaçladık.

**Gereç ve Yöntemler:** Medikal ve girişimsel ağrı tedavi yöntemlerine yanıt vermeyen 10 akciğer kanser hastaya bilgisayarlı tomografi (BT) eşliğinde kordotomi uygulandı.

**Bulgular:** Hastaların tedavi öncesi ve tedavi sonrası görsel analog ağrı skalası (VAS) puan ortalamaları sırasıyla 10±0,0001 ve 1±0,67 olarak belirlendi. Ayrıca hastaların tedavi öncesi ve tedavi sonrası ortalama Karnofsky Performans Ölçeği (KPS) puanları sırasıyla 40± 9,42 ve 73±10,59 olarak hesaplandı. Buna göre tedavi öncesi ve tedavi sonrası VAS ve KPS skorları arasında istatistiksel olarak anlamlı fark vardı. Ayrıca hastaların tedavi öncesi ve tedavi sonrası ortalama morfin eşdeğer dozları sırasıyla 860,2±199,8 mg ve 220,7±69,08 mg olarak bulundu.

**Sonuç:** Kordotominin akciğer kanserinden muzdarip bazı hastalarda inatçı ağrı sorunları için en iyi çözüm olduğuna inanıyor ve öneriyoruz.

**Anahtar Kelimeler:** *BT Kılavuzluğu; Kordotomi; Ağrı; Kanser*

## INTRODUCTION

Lung cancer was the second most frequently diagnosed cancer worldwide in 2020 and the leading cause of cancer-related deaths. The diagnosis of lung cancer is usually made in the late stages (1). Pain associated with lung cancer depends on the localization of the primary tumor and the presence of metastases. Pain in primary lung cancer is usually observed in patients with pleura, and chest wall involvement characterized by pain in the arm and shoulder or classic Pancoast's Syndrome (2). There are a wide variety of treatment options available for clinicians in the treatment of cancer pain, ranging from pharmacological therapies to invasive interventions. Interventional pain management techniques can be used to attempt to control refractory pain in patients for whom standard therapy cannot provide effective pain relief or cannot tolerate medication adjustments. In general, standard invasive treatment options should be preferred (sympathetic block, epidural drug applications). In cases where standard invasive interventional treatment options are insufficient, high-risk invasive procedures can be used. Cordotomy reportedly provides more benefits to patients with limited life expectancy (3). Computed tomography (CT)-guided percutaneous cervical cordotomy (PCC) is indicated for pain levels below C5. It is a useful procedure in patients with unilateral, localized, persistent, and somatic cancer-related pain which may not be adequately treated with other invasive methods (3). CT-guided PCC targets the lateral spinothalamic tract in the anterolateral region of the spinal cord. The spinothalamic tract carries nociceptive signals from the contralateral side of the body, heat, and non-discriminatory sense of touch (4). The percutaneous technique was developed by Mullan et al. in 1963 (5) and radiofrequency current was used by Rosomoff et al. to produce the lesion in 1965 (6). The introduction of CT-guided PCC, which was described by Kanpolat et al., has led to greater safety and efficacy (7). Complications related to the CT-guided PCC procedure may include motor weakness, dysesthesia, mirror pain, urinary dysfunction, respiratory failure, headache, hypotension, hemorrhage, infection, neural damages caused by damages inflicted on other pathways (reticulospinal, somatosensory or corticospinal), Horner's syndrome, and sensory-motor changes including death. Contraindications include a history of respiratory distress on the contralateral side the procedure performed or midline pain (8-9).

In light of the foregoing, the objective of this study is to evaluate the efficacy of CT-guided PCC and post treatment complications in the treatment of intractable pain associated with lung cancer.

## MATERIAL AND METHODS

The study sample included 10 lung cancer patients unresponsive to invasive interventional methods other than medical treatment and PCC. All patients underwent CT-guided PCC at the Algology Department of Akdeniz Faculty of Medicine. Of the 10 patients, 4 had adenocarcinoma, 4 had squamous cell cancer, 1 had small cell cancer and 1 had Pancoast tumor. Written informed consent was obtained from each patient. The study was conducted in accordance with the principles set forth in the Declaration of Helsinki. The study protocol was approved by the Akdeniz University institutional ethics committee (KAEK 425-24/05/2023). Cancer type, disease duration, the localization of pre-processing pain symptoms and type, pain intensity and the quality of life of pre-processing and post processing, types of pain treatment applied before CT-guided PCC, morphine equivalent dose (MED) and the complications emerged after the procedure were recorded. Pain levels were recorded with Visual Analogue Pain Scale (VAS) before the procedure and on the 7th-day after the procedure.

Karnofsky Performance Scale (KPS) was used to evaluate the quality of life of the patients before and after the procedure. KPS assesses patient's symptoms, ability to perform daily activities, dependency status, and need for medical care (10). The total score that can be obtained from KPS ranges between 0 point and 100 points. 100 points indicate normal health, each ten-point reduction in the total score indicates a deterioration in functions, and 0 points correspond to death (10). According to the KPS scores, patients are divided into 3 categories: Category A consisted of patients who scored between 80 and 100 points, thus do not require special care, can continue their normal activities and work; Category B consisted of patients who scored between 50 and 70 points, thus can take care of themselves with assistance, but cannot work;

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

and Category C consisted of patients who scored between 0 point and 40 points, thus cannot take care of themselves and the disease progresses rapidly towards death (11). Patients included in the study filled out the scales under the supervision of a physician according to the pretreatment KPS scores, of the 10 patients included in this study, 8 (80%) patients were in Category C, 2 (20%) patients were in Category B, and there was no patient that could be classified as Category A patient. The patients had pain in the shoulder and/or upper extremity and upper chest region due to unilateral cancer. In this context, unilateral and bilateral PCC procedures were performed in 9 patients and in 1 patient with intractable pain, respectively. The patient, who underwent cordotomy due to intractable pain in the left chest, armpit and shoulder region, and whose pain regressed in the left shoulder and chest pain after the procedure, yet re-emerged in the right chest and shoulder region, was performed left PCC procedure 1 month later. Cordotomy procedure was performed as per the instructions described by Yegül in the literature (12).

## Processing Technique

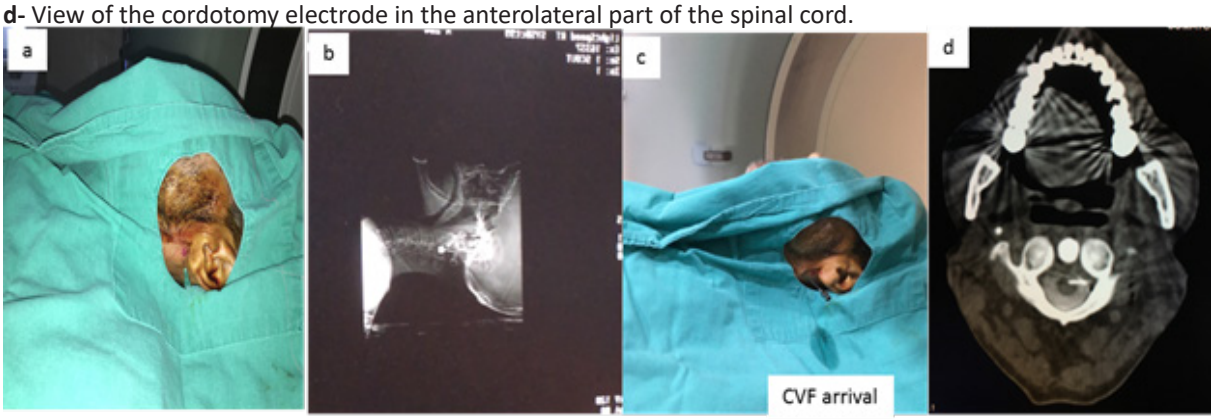
Patients were placed in supine position. The head is placed in a head holder and fixed in a slightly flexed position in order to 'open' the C2 foramen. They were provided oxygen via nasal cannula. Their vital signs were constantly monitored during the procedure. The patient has to remain reasonably still and should not move head while taking CT scans. Movement of the head and neck will make the pictures blurred and it is going to be hard to identify the position of the needle tip. Patients who have suffered too much pain cannot be stayed calm. Therefore, adequate premedication with opioid analgesics is necessary. We have preferred 50 – 100 mcg of fentanyl intravenously 5 minutes before operation, if the patient have pain. The needle entry area was sterilized. The entrance is located near the mastoid process. The C1-C2 (first and second cervical vertebrae) range was determined based on CT-imaging, and the area that lie just below the mastoid protrusion was marked. Local anesthesia was applied to the marked area using 2% lidocaine with an injection needle 21G (0.8mm x 25mm) (Figure-1a). Under the guidance of CT, Crawford type 20 G spinal needle was perpendicularly inserted to the apex of C2 foraminal opening. (Figure-1b). After puncturing the dura-mater membrane and cerebrospinal fluid was observed (Figure 1c). The spinal cord was visualized by injecting 7 mL of water-soluble contrast Omnipaque® (350 mg/mL) and 3 mL of saline mixture into the subarachnoid space using the barbotage method. The injection was done slowly doing barbotage to avoid increasing intracranial pressure and patient discomfort. If barbotage is performed the dye evenly spreads around the spinal cord. A disposable insulated radiofrequency cordotomy electrode with adjustable active tip (Minta) was inserted through the needle and connected to the generator (Neurotherm® NT1100) to start impedance monitoring. With continuous impedance monitoring, the needle was advanced and when its tip reached the anterolateral borderline of the spinal cord, the electrode was quickly, short (0.1 - 0.2 mm), and precisely inserted into the pia mater (Figure 1d). Once the electrode enters the anterolateral quadrant of the spinal cord and electrical impedance monitoring reaches intramedullary levels (Impedance is in the range of 200 ohms (CSF) to 1435 ohms), electrostimulation is performed. Electrostimulation was performed, 2 Hz to identify if there is motor response and 50 Hz to identify the region of original pain. Sensory test was performed to identify the region of original pain, also motor tests to search for motor response each response was documented with an axial CT scan. Sensory changes and motor contractions were recorded during stimulation. In the sensory testing coldness or hotness was felt in the site of original pain and in the motor testing neck muscles fasciculation. After it was verified that the patients felt the stimulus in the targeted area, they were administered radiofrequency current at 80 °C for 10, 20 and 30 seconds, respectively. Patients were kept under observation for 5 hours after the procedure, considering the possible complications that might arise.

## Statistical Analysis

The research data were analyzed using the SPSS 21 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp) software package. Descriptive statistics were expressed using mean, standard deviation, minimum, and maximum. Shapiro-Wilk test was used to determine whether the variables

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

**Figure 1.**
**a-** Use of local infiltration anesthesia between the first and the second cervical vertebrae
**b-** CT image of the needle while between the C1 and C2
**c-** As the needle passed through the dura, CVF discharge has occurred
**d-** View of the cordotomy electrode in the anterolateral part of the spinal cord.




CVF: cerebrospinal fluid

conform to normal distribution. Subsequently, Wilcoxon test were used for statistical analyses. The significance level was set at 0.05.

## RESULTS

The study sample consisted of 10 lung cancer patients with intractable pain who did not respond adequately to medical treatments or invasive interventional treatments other than cordotomy or who could not be administered higher opioid doses (more than 100 mg morphine equivalent dose) due to side effects and thus underwent CT-guided PCC at the Algology Department of Akdeniz Faculty of Medicine. Demographic characteristics, pain localizations, pain types and types of pain treatment applied before cordotomy of the patients are given in Table 1. The mean age of the patients, of whom 7 (70%) were male and 3 (30%) were female, was 60.1±10.3 years. Of the 10 patients, 4 had adenocarcinoma, 4 had squamous cell cancer, 1 had small cell cancer and 1 had Pancoast tumor. All patients had metastases to peripheral tissue and bone metastases or distant organs and were using high-dose narcotic analgesics (more than 100 mg morphine equivalent dose). Unilateral and bilateral PCC procedures were performed in 9 patients and in 1 patient with intractable pain, respectively. The mean disease duration was 4.9 months. The electrostimulation data of the patients and the cordotomy application side are given in Table 2. PCC was applied through the left C1-2 and right C1-2 spaces in 5 (50%) and 4 (40%) patients, respectively. One (10%) patient was performed bilateral C1-2 PCC. The mean VAS scores of the patients before and after the cordotomy were 10 ± 0.0001 and 1.30 ± 0.67, respectively. All patients experienced significant pain relief after PCC (Table 3). Additionally, the mean KPS scores of the patients before and after cordotomy were determined as 40± 9.42 and 73±10.59, respectively. There was a statistically significant difference between the pretreatment and post treatment VAS and KPS scores (Table 4) ($p<0.05$). Furthermore, the mean pretreatment and post treatment opioid dose equivalences of the patients were calculated as 860.2±199.8 mg and 220.7±69.08 mg, respectively (Table 4) ($p<0.05$). There was a statistically significant difference between the pretreatment and post treatment MED (Table 3). Analysis of the complications related to the PCC procedure revealed mirror pain in 10% of patients, head and neck pain in 90%, opioid withdrawal in 40%, walking imbalance in 30%, and urinary retention in 10%. One complication was observed in 20% of the patients, and two complications were observed in 80% (Table 3). Mirror pain complication occurred in one patient two days after the procedure and completely resolved spontaneously after 5 days. Walking imbalance complication occurred in 3 patients. In one of these patients, walking imbalance started 2 days after the procedure and completely resolved spontaneously in 5

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

**Table 1.** Clinical Characteristics of the Patients who underwent Percutaneous Cervical Cordotomy

| | Gender | Age | Cancer Type | Disease duration (Month) | Metastasis | Pain Localization | Pain type | Types of Pain Treatment Applied Before Cordotomy | Treatments For Cancer |
|---|---|---|---|---|---|---|---|---|---|
| 1st Patient | Male | 60 | Small cell | 6 | Peripheral tissue, distant organ and bone metastases | Right chest, right upper extremity, lumbar region and right leg irradiation | Mixed | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | CT |
| 2nd Patient | Male | 65 | Adenocarcinoma | 4 | Peripheral tissue and bone metastases | Right chest, right shoulder | Nociceptive | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | RT+CT |
| 3rd Patient | Male | 67 | Squamous cell | 4 | Peripheral tissue, distant organ and bone metastases | Left chest, left upper extremity and lumbar region | Mixed | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | CT |
| 4th Patient | Male | 64 | Squamous cell | 3 | Peripheral tissue, distant organ and bone metastases | Left chest, left upper extremity, lumbar region and right leg irradiation | Nociceptive | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | CT |
| 5th Patient | Male | 65 | Squamous cell | 4 | Peripheral tissue and bone metastases | Left chest, left shoulder | Nociceptive | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | RT+CT |
| 6th Patient | Male | 69 | Pancoast | 5 | Peripheral tissue and bone metastases | Left chest, left upper extremity | Mixed | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | RT+CT |
| 7th Patient | Female | 71 | Adenocarcinoma | 6 | Peripheral tissue and bone metastases | Left chest, left shoulder | Nociceptive | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | RT+CT |
| 8th Patient | Male | 55 | Adenocarcinoma | 5 | Peripheral tissue and bone metastases | Left chest, left upper extremity | Mixed | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | RT+CT |
| 9th Patient | Female | 41 | Adenocarcinoma | 6 | Peripheral tissue, bone and distant organ metastasis | Right shoulder and right chest before the 1st procedure and left chest, armpit and shoulder region before the 2nd procedure | Nociceptive | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | CT |
| 10th Patient | Male | 44 | Squamous cell | 6 | Peripheral tissue and bone metastases | Right chest, right shoulder | Nociceptive | Oral opioid + Transdermal fentanyl + Sympathetic block + Epidural drug applications | RT+CT |

CT: Chemotherapy, RT: Radiotherapy

days. In another patient, walking imbalance started 3 days after the procedure and completely resolved after 1 week. In the third patient, walking imbalance started 2 days after the procedure and resolved after 8 days. Urinary retention occurred in one patient 1 day after the procedure and resolved after 4 days. Mild head and neck pain was reported in 90% of all patients, however, did not require any additional treatment in any patient, including the patients who developed opioid withdrawal.

## DISCUSSION

Pain is reportedly experienced by 47% of the lung cancer patients. Lung cancer is one of the cancers that inflicts the most pain (1, 2). Pain affects the physical functions, daily activities, psychological-emotional status and social life of individuals. It is extremely important that the intractable pain is addressed not only as a health problem, but also as a humane problem. Patients with cancer differ from other patients in that they require their quality of life to be improved and the symptoms

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

**Table 2.** Electrostimulation data of patients who underwent percutaneous cervical cordotomy.

| | Procedure Side of the Body | Impedance | Motor Stimulation | Sensory Stimulation | Sensation During Motor Stimulation | Sensation During Sensory Stimulation |
|---|---|---|---|---|---|---|
| 1st Patient | Left | 217-1282 ohms | 2 Hz / 1ms / 0.48 - 1V | 50Hz / 1ms / 0.24V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |
| 2nd Patient | Left | 204-1167 ohms | 2 Hz / 1ms / 0.42 - 1V | 50Hz / 1ms / 0.25V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |
| 3rd Patient | Right | 208-1204 ohms | 2 Hz / 1ms / 0.33 - 1V | 50Hz / 1ms / 0.27V | Neck Muscles Fasciculation (Needle Site) | Hotness Sensation on Pain Site |
| 4th Patient | Right | 200-1235 ohms | 2 Hz / 1ms / 0.37 - 1V | 50Hz / 1ms / 0.23V | Neck Muscles Fasciculation (Needle Site) | Hotness Sensation on Pain Site |
| 5th Patient | Right | 211-1275 ohms | 2 Hz / 1ms / 0.41 - 1V | 50Hz / 1ms / 0.2V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |
| 6th Patient | Right | 223-1297 ohms | 2 Hz / 1ms / 0.39- 1V | 50Hz / 1ms / 0.24V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |
| 7th Patient | Right | 201-1232 ohms | 2 Hz / 1ms / 0.32- 1V | 50Hz / 1ms / 0.26V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |
| 8th Patient | Right | 225-1285 ohms | 2 Hz / 1ms / 0.44 - 1V | 50Hz / 1ms / 0.27V | Neck Muscles Fasciculation (Needle Site) | Hotness Sensation on Pain Site |
| 9th Patient | Bilateral | 209-1266 ohms | 2 Hz / 1ms / 0.3- 1V | 50Hz / 1ms / 0.25V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |
| 10th Patient | Left | 211-1281 ohms | 2 Hz / 1ms / 0.38 - 1V | 50Hz / 1ms / 0.23V | Neck Muscles Fasciculation (Needle Site) | Coldness Sensation on Pain Site |

that may develop as a result of primary treatment to be avoided.

The analysis of the VAS and KPS scores of ten lung cancer patients who underwent PCC included in this study revealed a significant difference between the pretreatment and post treatment scale scores. Accordingly, a significant reduction in pain was achieved in patients. In parallel, the daily MED decreased from 860 mg before PCC to 240 mg after PCC. All of the complications resolved within 10 days. No permanent deficit was observed in any patient. All of the patients stated their satisfaction with PCC outcomes 1 week after the procedure. CT-guided PCC is considered one of the useful procedures in patients with persistent pain due to unilateral cancer. As a matter of fact, it was reported that 95% of the patients who underwent CT-guided PCC had sufficient pain relief after the procedure (7). In this context, patients with unilateral cancer pain who do not respond to medical treatment and standard algological interventional procedures constitute the target patient group for cordotomy (12). It has been reported in the literature that patients with unilateral upper body pain due to lung cancer, mesothelioma or Pancoast tumors and unilateral lower body pain due to malignancies may benefit from CT-guided unilateral PCC (13). PCC is an effective procedure in reducing cancer pain, but its use has not increased in parallel with technological developments. The classical technique under fluoroscopy guidance is a blind technique and requires a fat-soluble contrast medium. For PCC we should use the CT guide because the active electrode can be easily detected by CT scanning. It is difficult to obtain such an image under fluoroscopy. CT-scan also allows localization of the electrode on the anteromedial and posterolateral sides of the lateral spinothalamic tract. When the procedure is performed under fluoroscopy, the dentate ligament should be visible, and the contrast medium used in this case should be fat-soluble. All contrast agents used today are water-soluble and it is not possible to visualize the dentate ligament with water-soluble contrast. Also, imaging of the dentate ligament is not necessary when using CT during the procedure. Kanpolat et al. reported that the success rate of CT-guided PCC was 92% in patients

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

**Table 3.** Pre- and post-procedure; VAS, KPS scores, morphine equivalent doses and complications

| | Pain type | BP-VAS | AP-VAS | BP- KPS | AP-KPS | BP- Category KPS | AP- Category KPS | BP- Morphine Equivalent Dose | AP- Morphine Equivalent Dose | Type of Complication |
|---|---|---|---|---|---|---|---|---|---|---|
| 1st Patient | Mixed | 10 | 2 | 40 | 70 | C | B | 1320 | 360 | Mirror Pain + Walking Imbalance |
| 2nd Patient | Nociceptive | 10 | 1 | 40 | 70 | C | B | 858 | 198 | Opioid Withdrawal+ Head and Neck Pain |
| 3rd Patient | Mixed | 10 | 2 | 30 | 50 | C | B | 960 | 300 | Opioid Withdrawal+ Head and Neck Pain |
| 4th Patient | Nociceptive | 10 | 2 | 60 | 90 | B | A | 618 | 138 | Walking Imbalance+ Head and Neck Pain |
| 5th Patient | Nociceptive | 10 | 1 | 50 | 80 | B | A | 840 | 180 | Head and Neck Pain+ Urinary Retention |
| 6th Patient | Mixed | 10 | 1 | 40 | 70 | C | B | 738 | 198 | Head and Neck Pain |
| 7th Patient | Nociceptive | 10 | 0 | 30 | 70 | C | B | 778 | 258 | Opioid Withdrawal+ Head and Neck Pain |
| 8th Patient | Mixed | 10 | 1 | 40 | 80 | C | A | 1020 | 240 | Opioid Withdrawal+ Head and Neck Pain |
| 9th Patient | Nociceptive | 10 | 2 | 30 | 70 | C | B | 720 | 180 | Walking Imbalance + Head and Neck Pain |
| 10th Patient | Nociceptive | 10 | 1 | 40 | 80 | C | A | 750 | 155 | Head and Neck Pain |

VAS: Visual analogue scale, KPS: Karnofsky Performance Scale, BP: Before Procedure, AP: After procedure

**Table 4.** Before and after the procedure; Statistics of VAS, KPS scores and morphine equivalent doses

| VARIABLES | BEFORE PROCEDURE | | AFTER PROCEDURE | | |
|---|---|---|---|---|---|
| | **Mean ± SD** | **Min-Max** | **Mean ± SD** | **Min-Max** | **p value** |
| VAS | 10 ±0.0 | 10 -10 | 1.3 ± 0.67 | 0-2 | 0.004 |
| KPS | 40 ± 9.4 | 30 – 60 | 73 ± 10.59 | 50-90 | 0.004 |
| MORPHINE EQUIVALENT DOSE | 860.2±199.8 | 618-1320 | 220.7±69.08 | 138-360 | 0.005 |

Wilcoxon test was used for statistical analyses. VAS: Visual analogue scale, KPS: Karnofsky Performance Scale

with intractable pain, including patients with malignancies such as pulmonary malignancies, mesothelioma, gastrointestinal tumors, and Pancoast tumor (4). In another study by Kanpolat et al., the success rate of CT-guided PCC was reported as 98% in patients with excruciating pain due to lung tumors (14). In the study of Raslan et al., 98% and 80% procedural success was found in patients with persistent cancer pain who underwent CT-guided PCC at the end of one-month and six-month follow-up, respectively (15). In a study by Kanpolat et al. conducted with lung cancer patients, the mean VAS score decreased by 98% and the mean KPS score increased by 75% after the procedure (4). On the other hand, in another study, the mean VAS score decreased by 66% and the mean KPS score increased by 22% after the procedure (15). In comparison, in this study, which was conducted with lung cancer patients as in the study of Kanpolat et al., the mean VAS score decreased by 90% and the mean KPS score increased by 82.5% after the procedure. Therefore, pain palliation was achieved in lung cancer patients with severe pain, and it was concluded that cordotomy is effective in this patient group. According to the pretreatment KPS scores, 8 (80%) patients were in Category C, whereas 2 (20%) patients were in Category B. According to the posttreatment KPS scores,

Bozok Tıp Derg 2023;13(3):43-51
Bozok Med J 2023;13(3):43-51

on the other hand, 6 (60%) patients were in Category B, and 4 (40%) patients were in Category A. Thus, the normal activity levels and the independence of patients had increased. Furthermore, the mean MED of patients decreased by 76% after the procedure. In addition, there was a decrease in the frequency of the side effects of high-dose opioid analgesic drugs such as constipation, loss of appetite, nausea and drowsiness which were more frequent before the procedure. Therefore, the increase in the KPS scores is due not only to the reduction of pain but also to the reduction of side effects. Nevertheless, further studies which feature reduced analgesic doses and assess patient survival times in larger patient groups would reveal more concrete results on the cost effectiveness of the procedure. The patients included in this study could not be followed up for extended periods. However, the research data suggest that cordotomy is effective for intractable lung cancer pain, since a significant reduction in pain was achieved in all patients included in this study. The most common complications associated with PCC are mild neck and headache, urinary retention, arterial hypotension, sensory ataxia, hypotonia, opioid withdrawal, and ipsilateral hemiparesis. Motor and sphincter or sexual disorders occur in less than 10% of cases. Other less common complications associated with PCC include respiratory dysfunction and sleep apnea (Ondine's Curse). Of the two complications, the latter is more commonly associated with bilateral PCC (16). In addition, there is a risk of recurrence of other previously masked pains or "mirror pain", that is, emergence of pain on the contralateral side. New pain often reflects the original pain in the same region on the contralateral side of the body. The incidence of such pain syndromes ranges from 9% to 63% (17). The complications encountered after cordotomy in patients included in this study were mirror pain, headache, urinary retention, mild gait instability and opioid withdrawal. Head and neck pain, which was observed in 90% of the patients, was the most common complication. All complications were temporary and did not require additional treatment. Mirror pain developed in 1 patient two days after the procedure and spontaneously resolved 5 days later. All complications disappeared within 10 days after the procedure. Major complications reported in other studies might have stemmed from the use of fluoroscopy-guided procedure. In addition, the absence of major complications in this case series might be attributed to the fact that the procedure was performed under the guidance of CT and by experienced physicians. Recovery of the spinothalamic tract and recurrence of pain are likely after a certain period of time following cordotomy (18). This post-regeneration pain may present as dysesthetic symptoms or pain syndromes and be difficult to treat as in the case of neuropathic pain seen after spinal cord injury. Nevertheless, such cases were not mentioned in a case series with a follow-up period of 5 years after cordotomy (19). Similarly, there were no symptoms suggestive of neuropathic pain observed in the patients included in this study during the follow-up period after cordotomy. Studies involving bilateral PCC have revealed that both procedures have low complication rates, with the success rate on the second side similar to that on the first side (12-13). In comparison, there was one patient who developed contralateral pain after the procedure in this study. A significant regression was observed in the pain of the patient who underwent the second PCC procedure 1 month after the first PCC procedure. The bilateral PCC results reported by both Kanpolat et al. and Yegül et al. indicated that the procedures performed on different sides both had low complication rates and similar success rates. The VAS score of the patient who underwent bilateral PCC was found to be 0 after both procedures, and no complications related to either procedure were observed. CT-guided PCC continues to be an effective and safe method in the treatment of cancer pain resistant to medical treatments. In addition, considering that cancer is a systemic and progressive disease, CT-guided PCC can be repeated if pain reoccurs in the same area or in another part of the body. Bilateral PCC should be considered as one of the methods to be preferred at different times due to its positive effect on the quality of life of patients with refractory bilateral extremity pain associated with cancer.

## CONCLUSION

It is extremely important that the intractable pain is addressed not only as a health problem, but also as a humane problem. In this context, CT-guided PCC offers the best solution for refractory pain problems

experienced by lung cancer patients. The safety of the CT-guided PCC procedure depends on the skill of the physician and choosing the patients suitable to the procedure. In conclusion, CT-guided PCC should be performed as soon as possible.in individuals who do not respond to standard algological interventional procedures and conservative treatment options.

## Acknowledgements

Findings of this study can be provided by the corresponding author upon reasonable request. The authors have no conflicts of interest to declare. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## REFERENCES

**1.** Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-49.

**2.** Kuzeyli Y, Uyar M, Fadıllıoğlu Ç. Kanser ağrısı ve yaşam kalitesine etkisi (Review). Ağrı Dergisi. 2005;17(4):17-22.

**3.** Zuurmond WW, Perez RS, Loer SA. Role of cervical cordotomy and other neurolytic procedures in thoracic cancer pain. Curr Opin Support Palliat Care. 2010;4(1):6-10.

**4.** Kanpolat Y, Ozdemir M, Al-Beyati ESM. Ct-Guided Percutaneous Cordotomy for Intractable Pain in What is More than a Disease: Lung Malignancies. Turkish Neurosurgery. 2013;23(1): 81-7.

**5.** Mullan S, Harper Pv, Hekmatpanah J, Torres H, Dobbin G. Percutaneous Interruption of Spinal-Pain Tracts by Means of A Strontium90 Needle. J Neurosurg. 1963;20:931-9

**6.** Rosomoff, H.L., P. Sheptak, and F. Carroll, Modern pain relief: percutaneous chordotomy. JAMA. 1966;196(6): p. 482-6.

**7.** Kanpolat Y, Deda H, Akyar S, Bilgiç S. CT-guided percutaneous cordotomy. Acta Neurochir Suppl (Wien). 1989;46:67-8.

**8.** France BD, Lewis RA, Sharma ML, Poolman M. Cordotomy in mesothelioma-related pain: a systematic review. BMJ Support Palliat Care. 2014;4(1):19-29.

**9.** Chai T, Suleiman ZA, Roldan CJ. Unilateral Lower Extremity Pain Due to Malignancy Managed With Cordotomy: A Case Report. PMR 2018;10(4):442-5.

**10.** Yıldız Çeltek N, Süren M, Demir O, Okan İ. Karnofsky Performance Scale validity and reliability of Turkish palliative cancer patients. Turk J Med Sci. 2019;49(3):894-8.

**11.** Péus D, Newcomb N, Hofer S. Appraisal of the Karnofsky Performance Status and Proposal of a Simple Algorithmic System for its Evaluation. BMC MedInform. 2013;13: 72.

**12.** Yegul I, Erhan E. Bilateral CT-guided percutaneous cordotomy for cancer pain relief. Clin Radiol. 2003;58(11):886-9.

**13.** Kanpolat Y, Savas A, Caglar S, Temiz C, Akyar S. Computerized tomography-guided percutaneous bilateral selective cordotomy. Neurosurg Focus. 1997;2(1): e4.

**14.** Kanpolat Y, Ugur HC, Ayten M, Elhan AH. Computed tomography-guided percutaneous cordotomy for intractable pain in malignancy. Neurosurgery 2009;64:ons187-93; discussion 193-4.

**15.** Raslan AM. Percutaneous computed tomography-guided radiofrequency ablation of upper spinal cord pain pathways for cancer-related pain. Neurosurgery. 2008;62:226-33; discussion 233-4.

**16.** Sarturi NM, Zicarelli CA. Cervical cordotomy for the treatment of oncological pain. Rev Chil Neurocirugía. 2014;40(1):152-7

**17.** Jones B, Finlay I, Ray A, Simpson B. Is there still a role for open cordotomy in cancer pain management? J Pain Symptom Manage. 2003;25(2):179-84.

**18.** Cetas JS, Saedi T, Burchiel KJ. Destructive procedures for the treatment of nonmalignant pain:a structured literature review. J Neurosurg. 2008;109:389-404.

**19.** Meeuse JJ, Vervest ACM, van der Hoeven JH, Reyners AK. Five-year follow up of a cordotomy. Pain Res Manag. 2008;13:506-10.

# ASSOCIATION OF SERUM ANNEXIN A3 (ANXA3) LEVELS WITH AGE-RELATED MACULAR DEGENERATION

## Yaşa Bağlı Makula Dejenerasyonu İle Serum Anneksin A3 (Anxa3) Düzeylerinin İlişkisi

Alpaslan OZTURK[1], Mehmet Ali GUL[2], Tugba AGBEKTAS[3], Cemile ZONTUL[4], Cem Hakan CİFTCİ[5], Ayca TAS[6], Duygu YALINBAS YETER[5], Yavuz SILIG[3]

[1]Clinical Biochemistry, Etlik City Hospital, Ankara, Türkiye
[2]Department of Medical Biochemistry, Faculty of Medicine, Amasya University, Amasya, Türkiye
[3]Department of Food Processing Technologies Services, Yıldızeli Vocational School, Sivas Cumhuriyet University, Sivas, Türkiye
[4]Department of Chemistry and Chemical Processing Technologies Services, Yıldızeli Vocational School, Sivas, Türkiye
[5]Department of Ophthalmology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Türkiye
[6]Department of Nutrition and Diet, Faculty of Health Sciences, Sivas Cumhuriyet University, Sivas, Türkiye

Alpaslan OZTURK, Dr. (0000-0003-4525-3477)
Mehmet Ali GUL, Dr. Öğr. Ü. (0000-0002-5849-0116)
Tugba AGBEKTAS, Öğr. Gör. (0000-0003-3433-8870)
Cemile ZONTUL, Öğr. Gör. (0000-0002-1436-5145)
Cem Hakan CIFTCI, Dr. (0009-0000-6391-7260)
Ayca TAS, Doç. Dr. (0000-0002-7132-1325)
Duygu YALINBAS YETER, Doç. Dr. (0000-0001-9001-0277)
Yavuz SILIG, Prof. Dr. (0000-0002-0562-7457)

**İletişim:**
Dr. Alpaslan OZTURK,
Clinical Biochemistry, Etlik City Hospital,
Ankara, Türkiye

**Geliş tarihi/Received:** 24.07.2023
**Kabul tarihi/Accepted:** 11.09.2023
**DOI:** 10.16919/bozoktip.1331935

Bozok Tıp Derg 2023;13(3):52-57
Bozok Med J 2023;13(3):52-57

## ABSTRACT

**Objective:** Age-related macular degeneration (AMD) is the most common cause of advanced visual loss in developed societies. Annexin A3 (ANXA3) contributes to tumor development by affecting cell signaling pathways, cell profiling, invasion, metastasis and cell apoptosis. The aim of this study was to compare serum ANXA3 levels in wet type and dry type macular degeneration patients with the control group and to investigate whether there is a significant difference between the groups.

**Material and Methods:** A total of 78 patients (39 patients with wet AMD, 39 patients with dry AMD diagnosed at the same time period and 39 healthy controls without any previous diagnosis of macular degeneration) were enrolled in this study. ANXA3 levels were determined by enzyme-linked immunosorbent assay (ELISA).

**Results:** Serum ANXA3 levels were found to be significantly higher in wet AMD than in the control group (p=0.005). In addition, the difference between serum ANXA3 levels of wet and dry AMD patients was found to be significant. It was observed that there was a significant increase in wet type AMD patients (p=0.004). However, no significant difference was found in ANXA3 levels in dry type AMD compared to the control group (p=0.444).

**Conclusion:** These findings suggest that ANXA3 protein may play an important role in age-related macular degeneration.

**Keywords:** *Age-Related Macular Degeneration, ANXA3, ELISA*

## ÖZET

**Amaç:** Yaşa bağlı maküler dejenerasyon (YBMD) gelişmiş toplumlarda ileri derecede görme kaybının en sık nedenidir. Anneksin A3 (ANXA3), hücre sinyal yolakları, hücre profilerasyonu, invazyon, metastaz ve hücre apoptozuna etki ederek tümör gelişimine katkı sağlamaktadır. Bu çalışmanın amacı, yaş tip ve kuru tip makula dejenerasyonu hastalarında serum ANXA3 düzeylerini kontrol grubu ile karşılaştırmak ve gruplar arasında anlamlı bir fark olup olmadığını araştırmaktır.

**Gereç ve Yöntemler:** Bu çalışma yaş tip YBMD tanısı alan 39 hasta, aynı zaman diliminde kuru tip YBMD tanısı alan 39 olmak üzere toplam 78 hasta ve daha önce herhangi bir maküler dejenerasyon tanısı almamış sağlıklı 39 kontrol grubundan oluşturuldu. ANXA3 düzeyleri enzim bağlantılı immünosorbent tahlil (ELISA) yöntemi ile tespit edildi.

**Bulgular:** Serum ANXA3 düzeylerinin yaş tip YBMD hastalığında kontrol grubuna göre anlamlı olarak yüksek düzeyde olduğu tespit edildi (p=0,005). Ayrıca yaş tip ve kuru tip YBMD hastalarının serum ANXA3 düzeyleri arasındaki farklılık anlamlı bulundu. Yaş tip YBMD hastalarında anlamlı ölçüde yükseklik olduğu görüldü (p=0,004). Ancak kontrol grubuna göre kuru tip YBMD hastalığında ANXA3 seviyelerinde anlamlı bir farklılık saptanmadı (p=0,444).

**Sonuç:** Bu bulgular sonucunda ANXA3 proteininin yaşa bağlı maküler dejenerasyon hastalığında önemli rol oynayabileceği düşünülmektedir.

**Anahtar Kelimeler:** *Yaşa Bağlı Maküler Dejenerasyon, ANXA3, ELİSA*

## INTRODUCTION

Age-related macular degeneration (AMD) affects millions of people worldwide and is one of the leading causes of blindness (1). There are 2 main types of the disease, neovascular and non-neovascular, which can be further classified according to their specific features. The main reason for this distinction is whether or not new blood vessels form. If new vascularization is present, it is referred to as wet AMD, neovascular AMD, exudative AMD or disciform AMD. Wet AMD accounts for 20% of all patients. If no new vessel formation is present, it is called non-exudative or dry AMD or Geographic atrophy (GA). Dry AMD accounts for 80% of all patients and generally carries a more favorable prognosis. Wet AMD accounts for the overwhelming majority (75%) of visual loss (2,3). Neovascular AMD ("wet" AMD) affects the remaining 15% to 20% and accounts for approximately 80% of severe vision loss (4).

Annexins (AnxA) are a large family of proteins widely distributed in various organisms, tissues and cell types (5). AnxA binds calcium and phospholipids to form calcium-dependent ion voltage channels (6). It has been suggested that calcium binding underlies the effect of AnxA in processes such as anticoagulation, endocytosis and exocytosis, signal transduction, cellular proliferation and apoptosis (7,8). In mammals, 12 different annexins named A1-A11 and A13 have been identified (9). Changes in tissue or cellular expression of AnxA have been associated with various conditions such as asthma (10), atherosclerosis (11), autoimmune diseases (12), cancers (13), Parkinson's disease (14) and Alzheimer's disease (15). It has been shown that AnxA may also play a role in many ocular diseases and may be a target for treatment (16). The roles of some AnxAs have been investigated in the visual system, leaving room to explore the promising therapeutic potential these proteins may have in ocular diseases. Others AnxAs have been studied in infectious and autoimmune diseases (17-18). Considering that eye diseases can have many etiologies, further research on the role of AnxAs in the eye could advance the field of ophthalmology because the eye is an organ that can be exposed to many microorganisms and can be affected by certain autoimmune diseases. Therefore, a better understanding of the function of AnxAs in the eye could lead to at least partial elucidation of disease mechanisms in the visual system.

There is no study investigating the relationship between serum ANXA3 levels in patients with age-related macular degeneration (dry and wet types). The aim of this study was to compare serum ANXA3 levels in wet and dry macular degeneration patients with the control group and to investigate whether there is a significant difference between the groups.

## MATERIAL AND METHOD

### Patients and Controls

In this study, a total of 78 patients, including 39 patients who were first diagnosed with wet AMD and 39 patients who were diagnosed with dry AMD in the same period of time, who presented to Sivas Cumhuriyet University Faculty of Medicine Ophthalmology Outpatient Clinic with complaints of decreased vision and curved vision, were included in the study. Patients were informed about the diseases in their eyes. The treatments applied worldwide and the treatments they would receive in our hospital were explained in detail. The consent document was read to the patients and their consent was obtained by making explanations about the exclusion criteria.

The control group consisted of 39 healthy volunteers who had not been diagnosed with macular degeneration before and who were similar in age and gender to the patients in the same period.

Patients who had previously initiated anti-vasculer endothelial growth factor (VEGF) therapy and used other anti-VEGF agents during the treatment period, patients who could not be started on bevacizumab due to cardiovascular and cerebrovascular reasons, patients who could not complete 3 intravitreal bevacizumab injections during the treatment period, patients who had previous eye surgery for any reason, patients with additional retinal pathology such as diabetic retinopathy, branch vein occlusions, Patients with anterior chamber inflammation for any reason or whose vision was affected as a result of this inflammation, patients diagnosed with glaucoma, patients with ±3D refractive error, patients with media opacities such as corneal opacity, vitreous hemorrhage, and patients with systemic diseases such as diabetes mellitus, hypertension, and malignancy that may

Bozok Tıp Derg 2023;13(3):52-57
Bozok Med J 2023;13(3):52-57

affect serum ANXA3 levels were excluded from the study. In the control group, patients with any retinal abnormality, glaucoma, previous intravitreal anti-VEGF disease, systemic disease, previous ocular surgery, and corneal opacities, cataracts, vitreous haze that would prevent Optic coherence tomography (OCT) were excluded from the control group. Systemic and ocular findings of the patients were recorded in the data. All patients underwent a complete ophthalmologic examination before enrollment in the study. Visual acuity was recorded using Snellen's threshold. Biomicroscopic examination was recorded by measuring intraocular pressure and refraction values with Tonoref 2 (Nidek, Gamagori, Japan). Following pupil dilatation, fundus examination was performed using a 90 diopter lens. Fundus fluorescein angiography (CLARUS 700™, Carl Zeiss Meditec Inc., Californea, USA, FFA), optical coherence tomography (OCT RS- 25 3000 Advance, NIDEK CO., LTD., JAPAN, OCT) and Solix Fullrange optical coherence tomography-angiography (Optovue Inc, Freemont CA, USA, OCT-A) imaging modalities were performed in all patients at the initial examination and wet AMD and dry AMD were diagnosed. Our study was performed using human serum samples obtained from the blood of patients and controls collected within the scope of the project with ethical decision number 2021-11/03.

Blood samples were collected in 5 ml vacuum tubes containing citrate. The samples were centrifuged at 3000 rpm (1400xg) for 10 minutes at room temperature to obtain serum. These serum samples were placed in sterile eppendorf tubes and stored at -80°C.

ANXA3 (ELK Biotechnology, Denver, CO 80202 USA, Cat: ELK3218) levels were determined using a commercially available human enzyme-linked immunosorbent assay (ELISA) kit. The range of detection was 0.16-10 ng/mL with <8% intra-assay and <10% inter-assay variation coefficient. The sensitivity of this kit is 0.065 ng/mL.

The statistical analysis of the data in our study was performed by loading into the SPSS Software (Version 26.0) program. The normality of the obtained data was evaluated with the Kolmogorov-Smirnov test. Levene's test was used for homogeneity of variances. Mann-Whitney U test, Kruskal-Wallis test and chi-square test was used to compare data that did not show normal distribution. Tukey post-hoc test of variances was recorded to determine the differences between groups after ANOVA. Statistical significance level was considered as $p<0.05$.

An application was made to the Sivas Cumhuriyet University Clinical Research Ethics Committee (Sivas, Türkiye), and the necessary ethics committee approval was obtained (Number: 2022-12/54). The study was carried out in compliance with the ethical principles of the Declaration of Helsinki.

## RESULTS

The control group was compatible with the wet AMD group and the dry AMD group in terms of age and gender ($p>0.05$). Active leakage areas were observed on Fundus fluorescein angiography (FFA) in 39 (100.0) patients with wet AMD and active membrane was observed on Optical coherence tomography angiography (OCT-A) in 32 (82.0) patients (Table 1).

In the control group, mean serum ANXA3 levels were 3.94 ng/mL (minimum: 1.43 ng/mL, maximum: 10.84 ng/mL). In the wet type group, mean serum ANXA3 levels were 5.39 ng/mL (minimum: 1.46 ng/mL, maximum: 11.95 ng/mL). In the dry type group, mean serum ANXA3 levels were 3.51 ng/mL (minimum: 1.19 ng/mL, maximum: 8.52 ng/mL).

In this study, serum ANXA3 levels were significantly different in wet type AMD compared to the control group ($p=0.005$). In addition, the difference between serum ANXA3 levels of wet type and dry type AMD patients was significant ($p=0.004$). However, no significant difference was found in ANXA3 levels in dry AMD compared to the control group ($p=0.444$). These statistical results between groups are shown in table 2.

## DISCUSSION

In our study, serum ANXA3 levels were investigated in dry AMD and wet AMD patients. ANXA3 levels were found to be higher in wet type AMD patients compared to dry AMD group and normal population. These results showed that high serum ANXA3 levels may play a role in the pathogenesis of AMD, especially wet type AMD.

Age-related macular degeneration is a chronic macular degenerative disorder that causes age-related central vision loss in individuals. It is a multifactorial disease resulting from irregularities in the angiogenic, inflammatory, lipid and extracellular matrix pathways

Bozok Tıp Derg 2023;13(3):52-57
Bozok Med J 2023;13(3):52-57

**Table 1.** Demographic characteristics of wet AMD, dry AMD and control group

| | CONTROL n (%) | WET AMD n (%) | DRY AMD n (%) | *p* |
|---|---|---|---|---|
| **Number of individuals** | 39 | 39 | 39 | |
| **Gender** | | | | |
| Female | 21 (53,8) | 21 (53,8) | 21 (53,8) | |
| Male | 18 (46,2) | 18 (46,2) | 18 (46,2) | |
| **Average age** | | | | |
| Female | 72.00 ± 7.77 | 72.42 ± 7.78 | 71.76 ± 7.74 | |
| Male | 72.88 ± 6.79 | 73.11 ± 6.38 | 74.00 ± 6.59 | |
| **Cigarette story** | 19 (48,7) | 18 (46,1) | 22 (56,4) | *p>0.05* |
| **Eye** | | | | |
| Right | 21 | 21 | 20 | *p>0.05* |
| Left | 22 | 22 | 23 | |
| **Leakage in fundus fluorescein angiography** | - | 39 (100,0) | - | |
| **Active membrane in optical coherence tomography** | | 32 (82,0) | | |

AMD: Age-related macular degeneration

**Table 2.** Comparison of ANXA3 levels in wet AMD, dry AMD and control groups

| ANXA3 | n | Mean ± SD | *p value* |
|---|---|---|---|
| CONTROL – DRY TYPE | 39 | 3.94 ± 2.50<br>3.51 ± 2.21 | *p=0.444** |
| CONTROL – WET TYPE | 39 | 3.94 ± 2.50<br>5.39 ± 2.96 | ***p=0.005**** |
| DRY TYPE – WET TYPE | 39 | 3.51 ± 2.21<br>5.39 ± 2.96 | ***p=0.004**** |

*p<0.05

(1). Studies have reported that reduced risk of neovascular AMD is associated with higher carotenoid serum levels (19). In a study conducted with 100 patients diagnosed with AMD and 100 healthy individuals, a significant difference was found in interleukin 17 serum levels compared to the control group (20). ANXA3 is a Ca2±dependent phospholipid and membrane-binding protein (21,22). It has important functions in membrane transport and other calmodulin-dependent activities on the membrane surface and is also involved in the regulation of inflammatory responses, cell differentiation and interactions of cytoskeletal proteins. It has been reported that ANXA3 expression may be associated with many human diseases.

ANXA3 contributes to tumor development by affecting cell signaling pathways, cell profiling, invasion, metastasis and cell apoptosis (23-27) reported that ANXA3 is important in gastric cancer cell proliferation by using fluorescent two-dimensional differential gel electrophoresis and liquid chromatography-mass spectrometry methods in a study conducted in gastric cancer. In another study by Xie et al (28), ANXA3 expression was investigated in rectal tumor tissues and ANXA3 expression was found to be high in rectal cancer tissues. As a result of this study, overexpression of ANXA3 was reported to be associated with poor prognosis of patients. In a study conducted in serum samples of patients with cholelocele cancer, ANXA3 serum levels were found to be significantly higher than healthy controls (29). In a study conducted in hepatocellular

carcinoma (HCC) patient sera, ANXA3 levels were found to be at the highest level and it was determined that ANXA3 could differentiate patients with HCC from individuals at risk of Hepatocellular carcinoma (HCC) (30). In our study, serum ANXA3 levels were found to be significantly higher in patients with dry AMD compared to the control group. Our study supports the use of serum ANXA3 levels as a biomarker for AMD. Histopathologic studies have reported that dry atrophic AMD is characterized by loss of the retinal pigment epithelium (RPE) component of the blood-retinal barrier in the macula in the absence of clinical exudation (31,32). In the dry lesion, pigment masses accumulate at the edge of the atrophy zone (33). Holz et al. in patients with AMD suggested that increased fundus autofluorescence induced by lipofuscin (LF) in eyes with geographic atrophy (GA) may reflect variable reactive changes in RPE cells (34). VEGF expression is controlled by many cellular factors such as growth factors and hormones. VEGF has a specific and strong angiogenic effect and contributes to tumor development by regulating tumor neovascularization. There are studies reporting that ANXA3 may affect vascular signaling by directly or indirectly regulating VEGF expression. In a study to investigate whether VEGF production is involved in tube formation in ANXA3-stimulated human umbilical vein endothelial cells (HUVECs), it was found that cells overexpressing ANXA3 produced significantly more VEGF than control cells. As a result of this study, it is thought that increased VEGF levels may be associated with ANXA3-induced angiogenic activity involved in migration and tube formation (35).

Our study resulted in increased serum levels of ANXA3 in accordance with the mentioned studies and this result suggests that vascularization may occur in ischemic ocular retinopathy and may be protective in the course of the disease. In this study, the difference between serum ANXA3 levels in wet and dry AMD patients was also significant. Therefore, serum ANXA3 levels may be meaningful as a biomarker to differentiate wet and dry AMD in patients diagnosed with the disease.

**Study Limitations:** The most important limitations of our study were that the study population was small, ANXA3 molecule levels were affected by many factors, and that only ELISA analysis was performed and not confirmed by genetic tests.

## CONCLUSIONS

As a result of this study, we think that ANXA3 protein can be used as a diagnostic and therapeutic option for AMD. The lack of such a study in the literature makes our study valuable. Larger centered studies will be more useful in terms of the accuracy of the results. In larger studies to be conducted with the ANXA3 molecule, studies including genetic analysis must be carried out in order to accept the results as definitive.

## Acknowledgments

The authors affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. The authors declare that they have no competing interests. No funding was received.

## REFERENCES

**1**.Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. Lancet. 2018;392(10153):1147-59.

**2.** Abraham JR, Jaffe GJ, Kaiser PK, et al. Impact of Baseline Quantitative OCT Features on Response to Risuteganib for the Treatment of Dry Age-Related Macular Degeneration: The Importance of Outer Retinal Integrity. Ophthalmol Retina. 2022;6(11):1019-27.

**3.** Hobbs SD, Pierce K. Wet Age-Related Macular Degeneration (Wet AMD). In: StatPearls. Treasure Island (FL): StatPearls Publishing; November 7, 2022.

**4.** Chaudhuri M, Hassan Y, Bakka Vemana PPS, Bellary Pattanashetty MS, Abdin ZU, Siddiqui HF. Age-Related Macular Degeneration: An Exponentially Emerging Imminent Threat of Visual Impairment and Irreversible Blindness. Cureus. 2023;15(5):e39624.

**5.** Zhang H, Zhang Z, Guo T, et al. Annexin A protein family: Focusing on the occurrence, progression and treatment of cancer. Front Cell Dev Biol. 2023;11:1141331.

**6.** Shao G, Zhou H, Zhang Q, Jin Y, Fu C. Advancements of Annexin A1 in inflammation and tumorigenesis. Onco Targets Ther. 2019;12:3245-54.

**7.** Ozturk A. Role of annexin A3 in breast cancer (Review). Mol Clin Oncol. 2022;16(6):111.

**8.** Mussunoor S, Murray GI. The role of annexins in tumour development and progression. J Pathol. 2008;216(2):131-40.

**9.** Gerke V, Moss SE. Annexins: from structure to function. Physiol

Rev. 2002;82(2):331-71.

**10.** Lee SH, Lee PH, Kim BG, Hong J, Jang AS. Annexin A5 Protein as a Potential Biomarker for the Diagnosis of Asthma. Lung. 2018;196(6):681-9.

**11.** Hedhli N, Falcone DJ, Huang B, Ceserman-Maus G, Kraemer R, Zhai H, et al. The annexin A2/S100A10 system in health and disease: emerging paradigms. J Biomed Biotechnol. 2012;2012:406273.

**12.** Weiss R, Bitton A, Ben Shimon M, Goldman SE, Nahary L, Cooper I, et al. Annexin A2, autoimmunity, anxiety and depression. J Autoimmun. 2016;73:92-9.

**13.** Wu N, Liu S, Guo C, Hou Z, Sun MZ. The role of annexin A3 playing in cancers. Clin Transl Oncol. 2013;15(2):106-10.

**14.** Lessner G, Schmitt O, Haas SJ, Mikkat S, Kreutzer M, Andreas W, et al. Differential proteome of the striatum from hemiparkinsonian rats displays vivid structural remodeling processes. J Proteome Res. 2010;9(9):4671-87.

**15.** Sohma H, Imai S, Takei N, Honda H, Matsumoto K, Utsumi K, et al. Evaluation of annexin A5 as a biomarker for Alzheimer's disease and dementia with lewy bodies. Front Aging Neurosci. 2013;5:15.

**16.** André da Silva R, Moraes de Paiva Roda V, Philipe de Souza Ferreira L, Oliani SM, Paula Girol A, Gil CD. Annexins as potential targets in ocular diseases. Drug Discov Today. 2022;27(11):103367.

**17.** Schloer S, Pajonczyk D, Rescher U. Annexins in Translational Research: Hidden Treasures to Be Found. Int J Mol Sci. 2018;19(6):1781.

**18.** Grewal T, Rentero C, Enrich C, Wahba M, Raabe CA, Rescher U. Annexin Animal Models-From Fundamental Principles to Translational Research. Int J Mol Sci. 2021;22(7):3439.

**19.** Risk factors for neovascular age-related macular degeneration. The Eye Disease Case-Control Study Group. Arch Ophthalmol. 1992;110(12):1701-8.

**20.** Türker Aslan H, Ateş Ö. İnvestigaiton of level of serum interleukin 17 in age-related macular degeneration. Sabuncuoglu Serefeddin Health Sciences. 2002;4(2), 9-16.

**21.** Bandorowicz-Pikuła J, Woś M, Pikuła S. Udział aneksyn w przekazywaniu sygnałów, regulacji struktury błony komórkowej i naprawie jej uszkodzeń [Participation of annexins in signal transduction, regulation of plasma membrane structure and membrane repair mechanisms]. Postepy Biochem. 2012;58(2):135-48.

**22.** Fatimathas L, Moss SE. Annexins as disease modifiers. Histol Histopathol. 2010;25(4):527-32.

**23.** Branishte T, Arsenescu-Georgescu C, Tomescu MC, Braniste A, Mitu F. Annexins, calcium-dependent phospholipid binding proteins in irreducible heart failure. Rev Med Chir Soc Med Nat Iasi. 2013;117(3):648-53.

**24.** Bianchi C, Bombelli S, Raimondo F, Torsello B, Angeloni V, Ferrero S, et al. Primary cell cultures from human renal cortex and renal-cell carcinoma evidence a differential expression of two spliced isoforms of Annexin A3. Am J Pathol. 2010;176(4):1660-70.

**25.** Baine MJ, Chakraborty S, Smith LM, Mallya K, Sasson AR, Brand RE, et al. Transcriptional profiling of peripheral blood mononuclear cells in pancreatic cancer patients identifies novel genes with potential diagnostic utility. PLoS One. 2011;6(2):e17014.

**26.** Yip KT, Das PK, Suria D, Lim CR, Ng GH, Liew CC. A case-controlled validation study of a blood-based seven-gene biomarker panel for colorectal cancer in Malaysia. J Exp Clin Cancer Res. 2010;29(1):128.

**27.** Liu Y, Li Y, Tan BB, Zhao Q, Fan L, Zhang Z, et al. Technique appraisement of comparative proteomics and screening of differentiation-related protein in gastric carcinoma. Hepatogastroenterology. 2013;60(123):633-7.

**28.** Xie YQ, Fu D, He ZH, Tan QD. Prognostic value of Annexin A3 in human colorectal cancer and its correlation with hypoxia-inducible factor-1α. Oncol Lett. 2013;6(6):1631-35.

**29.** Yu J, Li X, Zhong C, Li D, Zhai D, Hu W, et al. High-throughput proteomics integrated with gene microarray for discovery of colorectal cancer potential biomarkers. Oncotarget. 2016;7(46):75279-92.

**30.** Tong M, Fung TM, Luk ST, Ng KY, Lee TK, Lin CH, et al. ANXA3/ JNK Signaling Promotes Self-Renewal and Tumor Growth, and Its Blockade Provides a Therapeutic Target for Hepatocellular Carcinoma. Stem Cell Reports. 2015;5(1):45-59.

**31.** Penfold PL, Killingsworth MC, Sarks SH. Senile macular degeneration. The involvement of giant cells in atrophy of the retinal pigment epithelium. Invest Ophthalmol Vis Sci. 1986;27(3):364-71.

**32.** Tso MO. Experiments on visual cells by nature and man: in search of treatment for photoreceptor degeneration. Friedenwald lecture. Invest Ophthalmol Vis Sci. 1989;30(12):2430-54.

**33.** Sarks SH. Ageing and degeneration in the macular region: a clinico-pathological study. Br J Ophthalmol. 1976;60(5):324-41.

**34.** Holz FG, Bellmann C, Margaritidis M, Schütt F, Otto TP, Völcker HE. Patterns of increased in vivo fundus autofluorescence in the junctional zone of geographic atrophy of the retinal pigment epithelium associated with age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 1999;237(2):145-52.

**35.** Park JE, Lee DH, Lee JA, Park SG, Kim NS, Park BC, et al. Annexin A3 is a potential angiogenic mediator. Biochem Biophys Res Commun. 2005;337(4):1283-7.

# ANALYSIS OF CERVICAL POSTURE IN PATIENTS WITH BENIGN PAROXYSMAL POSITIONAL VERTIGO

## Benign Paroksismal Pozisyonel Vertigolu Hastalarda Servikal Postür Analizi

Tugba OZUDOGRU CELIK[1]

[1]Department of Physical Medicine and Rehabilitation,
Ankara City Hospital,
University of Health Sciences Türkiye,
Ankara,
Türkiye

Tugba OZUDOGRU CELIK, Dr.
(0000-0003-0528-149X)

**İletişim:**
Dr. Tugba OZUDOGRU CELIK
Department of Physical Medicine and Rehabilitation, Ankara City Hospital,
University of Health Sciences Türkiye,
Ankara, Türkiye

**Geliş tarihi/Received:** 10.08.2023
**Kabul tarihi/Accepted:** 11.09.2023
**DOI:** 10.16919/bozoktip.1340752

Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

## ABSTRACT

**Objective:** Reduced cervical lordosis, frequently seen in benign paroxysmal positional vertigo (BPPV), has recently drawn attention to cervical posture disorder in the etiology. This study aimed to investigate the relationship between BPPV and cervical posture.

**Material and Methods:** Twenty-seven patients with BPPV (mean age 45.5±8.07 years) and 29 healthy volunteers without BPPV (mean age 36.0±9.11 years) were included in our study. Cervical spine range of motion (ROM) measurements, cervical lordosis angle (fleche cervicale) and posture evaluation were performed with DIERS Formetric 4D imaging device. The neck disability index (NDI) and neck pain Visual Analog Scale (VAS) of each patient was recorded.

**Results:** In cervical ROM assessment, all cervical ROMs were significantly lower in the case group ($p < 0.05$) except extension ($p > 0.05$). Neck pain VAS ($p = 0.004$) and NDI ($p < 0.01$) scores were significantly higher in the case group. There was no statistically significant difference between the groups in comparison of spinal sagittal angle parameters ($p > 0.05$). There was a significant positive correlation between fleche cervicale and thoracic kyphosis index ($r = 0.630$, $p < 0.01$).

**Conclusion:** No association was found between BPPV and cervical posture. Decreased cervical lordosis is a consequence of BPPV, not an etiologic cause. Painful cervical pathologies may accompany BPPV.

**Keywords:** *Benign Paroxysmal Positional Vertigo (BPPV), Cervical Lordosis, DIERS Formetric 4D Motion Imaging System*

## ÖZET

**Amaç:** Benign paroksismal pozisyonel vertigoda (BPPV) sıklıkla görülen azalmış servikal lordoz, son zamanlarda etiyolojide servikal postür bozukluğuna dikkat çekmektedir. Bu çalışmada BPPV ile servikal postür arasındaki ilişkinin araştırılması amaçlanmıştır.

**Gereç ve Yöntemler:** Çalışmamıza BPPV'li 27 hasta (ortalama yaş 45,5 ± 8,07 yıl) ve BPPV'si olmayan 29 sağlıklı gönüllü (ortalama yaş 36,0 ± 9,11 yıl) dahil edildi. DIERS formetric 4D görüntüleme cihazı ile servikal omurga eklem hareket açıklığı (EHA) ölçümleri, servikal lordoz açısı (fleche servikale) ve postür değerlendirmesi yapıldı. Her hastanın boyun disabilite indeksi (NDI) ve boyun ağrısı Vizüel Analog Skala (VAS) kaydedildi.

**Bulgular:** Servikal EHA değerlendirmesinde, tüm servikal EHA'lar vaka grubunda ($p < 0,05$) ekstansiyon ($p > 0,05$) dışında anlamlı olarak düşüktü. Boyun ağrısı VAS ($p = 0,004$) ve NDI ($p < 0,01$) skorları vaka grubunda anlamlı olarak yüksekti. Spinal sagittal açı parametreleri karşılaştırıldığında gruplar arasında istatistiksel olarak anlamlı fark yoktu ($p > 0,05$). Fleche servikal ile torasik kifoz indeksi arasında anlamlı bir pozitif korelasyon vardı ($r = 0,630$, $p < 0,01$).

**Sonuç:** BPPV ile servikal postür arasında ilişki bulunamadı. Azalmış servikal lordoz BPPV'nin bir sonucudur, etiyolojik bir neden değildir. Ağrılı servikal patolojiler BPPV'ye eşlik edebilir.

**Anahtar Kelimeler:** *Benign Paroksismal Pozisyonel Vertigo (BPPV), Servikal Lordoz, DIERS Formetric 4D Hareket Görüntüleme Sistemi*

Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

## INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is the most frequently occurring cause of vertigo. The lifetime prevalence rate is 2.4%. It is characterized by rotatory, short-lasting episodes of severe dizziness that occur with head movements (1, 2). BPPV occurs as a result of endolymph flow due to the free movement of otoliths separated from the utricular macula in the affected semicircular canals (3). Idiopathic BPPV occurs more frequently in women and elderly individuals. The female/male ratio is 2-3/1. The right ear is mainly affected and primarily develops in the posterior and horizontal semicircular canals (4).

The occurrence of BPPV is explained by two accepted theories: cupulolithiasis and canalolithiasis. In cupulolithiasis, the gravity of otoconia, which is higher than that of endolymph, adheres to the cupula of the semicircular canal, causing inappropriate cupula-endolymph movement with specific head movements, resulting in vertigo attacks. In canalolithiasis, it is said that the otoconia do not adhere to the cupula but circulate freely in the endolymph, and these particles settle in the endolymph because they are denser than the endolymph. It has been reported that vertigo attacks occur due to pushing and pulling the otoconia to the cupula with head movements (5). The causes of BPPV are examined in two groups primary (idiopathic) and secondary. Primary cases are idiopathic BPPV and constitute 50-70% of patients (6, 7).

Dix-Hallpike Maneuver is the gold standard for posterior canal BPPV. Other diagnostic tests include the Side Lying Test, Supine Head-Roll maneuver, Bow and Lean Test, and the Straight-Back Head Hanging Test, which is proposed as an alternative method (8). Dizziness is an umbrella term. It includes sensations such as vertigo, imbalance, dizziness, and presyncope. From this point of view, vertigo is only a part of dizziness. However, the International Society of Neurotology has declared that dizziness and vertigo are independent allelic symptoms. Dizziness and vertigo may coexist or occur one after the other. Dizziness (cervical vertigo) can also occur in cervical pathologies. Cervical degenerative disease is the most common cervical disease (9).

BPPV and cervicogenic dizziness are distinct diseases. Dizziness or vertigo is the result of vestibular or nonvestibular dysfunction. Cervicogenic vertigo belongs to the nonvestibular group, and its psychophysiology is still controversial. The central nervous system must integrate symmetrical inputs from the auditory, visual, and vestibular organs and proprioception inputs for balance and coordination. Any dysfunction that disrupts this integration results in dizziness and imbalance. Degeneration, inflammation, trauma, and mechanical dysfunction of the spine may be factors in the etiology of cervicogenic dizziness (10). Most researchers have analyzed the mechanism of cervicogenic dizziness in 3 categories: 1- Sympathetic plexus irritation, 2- Abnormal somatosensory input from the neck, and 3- Vertebrobasilar insufficiency. Among these, vertebrobasilar insufficiency is a mechanism accepted by most researchers (11). There are few studies in the literature on the relationship between abnormal head and neck posture and BPPV. Prolonged forward-facing work, increased thoracic kyphosis, and cervical degeneration results in forward head posture (FHP) (12). In particular, changes in the upper cervical spine are associated with dizziness more than in the lower cervical spine. Most cervical flexion, extension, and rotation movements occur between the atlantooccipital and atlantoaxial joints (13).

As a result of impaired upper cervical alignment and functional and structural changes in the suboccipital muscles, unnecessary stimuli persist due to instability in the facet joints and ligaments. Thus, proprioceptive inputs from the neck to the central nervous system become inconsistent with vestibular and visual inputs. As a result of the incompatibility of the information, integration is disrupted, and dizziness, and headache occur. Dizziness does not occur in every patient with abnormal head-neck posture (14).

There are different methods to measure FHP: Head tilt angle, Craniovertebral angle, Cobb angle, and cervical inclination angle measurement for cervical lordosis measurement (15). In FHP, stress increases in the posterior cervical spine, and muscle length changes. The increase in muscle length decreases joint position sensation (16).

This study aimed to investigate the relationship between BPPV and cervical posture, obtain clues to shed light on the unknown etiology and have an idea about the necessity of postural evaluation and interventions in diagnosis and treatment. For this purpose, DIERS

Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

Formetric 4D, Diers International GmbH Schlangenbad, Germany.

## MATERIAL AND METHODS

In this research, which we conducted as a case-control study, the rules of the Declaration of Helsinki were followed. The patient and control groups were verbally informed about the course and purpose of the study. In addition, a written informed consent form was obtained from each patient. Ethical approval was obtained from Ankara City Hospital local ethics committee (E2-21-93). Patients who were admitted to Ankara City Hospital Neurology and Ear, Nose and Throat (ENT) departments between September 2021 and February 2022, who were diagnosed or followed up with BPPV as a result of routine examinations performed by Neurology and ENT departments, and healthy volunteers without BPPV diagnosis were enrolled in our study. The neurologic examination consisted of a systemic examination to detect nystagmus, a gait examination, cerebellar tests, and a brief neurologic examination. ENT examination consisted of bilateral otoscopic examination to check the tympanic membrane and middle ear and audiological examination for inner and middle ear pathologies.

According to the inclusion and exclusion criteria, 27 BPPV patients and 29 healthy volunteers without BPPV were enrolled. The age range of the participants was 18-60 years. Exclusion criteria; patients with vertigo of central origin, patients with problems in the tympanic membrane or middle ear as a result of the bilateral otoscopic examination in ENT examination, patients with neurological pathology as a result of nystagmus investigation, gait examination, cerebellar tests and brief neurological examination in the systemic examination, patients with hearing loss or pressure problems indicating inner ear or middle ear pathology as a result of the audiological examination, metabolic disorders that may mimic peripheral vertigo, patients with BPPV diagnosed as a secondary cause, patients with a history of psychosomatic disorders, heart disease, hypertension, orthostatic hypotension, cerebrovascular diseases, migraine, atherosclerosis, diabetes mellitus, cervical instability, inflammatory disease, tumoral and infectious diseases, and patients with anemia, hyperglycemia and high sedimentation rate in laboratory tests.

Gender, age, body mass index, weight, height, employment status, education, marital status, comorbidity, smoking, cell phone screen time, cervical spine range of motion (ROM) measurements (measured with a goniometer) were recorded in the patient and control groups. Cervical lordosis angle (fleche cervicale) and posture evaluation were performed with DIERS formetric 4D imaging device. The neck disability index (NDI) and neck pain Visual Analog Scale (VAS) of each patient was recorded.

Posture and cervical lordosis (fleche cervicale) were measured by the DIERS Formetric 4D motion imaging system in the Posture Analysis laboratory of Ankara City Hospital Physical Therapy and Rehabilitation Hospital in the presence of a physiotherapist. The DIERS formetric 4D system provides a 3-dimensional analysis of the spine surface for assessing posture with 4D technology, which pioneered functional clinical measurement technology. A precise measurement is made, and postural variants can be eliminated. Rasterstereography analyzes the surface topography of the spine without radiation, allowing the measurement of spinal deformity in 3D. It uses triangulation points for this. The DIERS formetric 4D System uses photogrammetric video recording of the spine surface. The measurement is performed in standing, static posture. For raster stereographic measurements, a white line of light is projected parallel to the surface of the spine. Anatomical landmarks are automatically fixed by adding convex and concave regions to this light curve pattern. The system can create a 3D human spine model and calculate relevant clinical parameters. Digital recording takes approximately 3 seconds, and 12 images are acquired. Data analysis is done with in-computer software.

### In the DIERS formetric 4D System:

Kyphosis angle: Between vertebral prominence and estimated T12 position,

Lordosis angle Measured between T12 and the midpoint of the right and left dimples.

Fleche cervicale: The distance between the vertical plumb line and the cervical apex.

Fleche lombaire is the spatial distance between the vertical plumb line and the lumbar apex (17).

Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

A study of patients with idiopathic scoliosis found that measurements made with the Formetric 4D dynamic system were comparable to the current gold standard. The researchers reported that the DIERS 4D Formetric System has a high clinical value in assessing spinal curvatures. (18).

The Neck Disability Questionnaire assesses neck pain's effect on daily living activities. It consists of 10 questions about self-care, neck pain intensity, reading, headache, driving, lifting, sleep, concentration, and leisure activities. It has been reported that the Turkish version of the NDI is a reliable and valid measurement method for evaluating disability caused by problems in the neck region because patients easily understand it and have a short application time in the clinic (19).

Data were analyzed using Statistical Package for Social Sciences 23 (SPSS 23.0) (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) software. Variables were investigated using visual and analytical methods (Shapiro-Wilks test) to determine whether they were usually distributed. Descriptive statistics of normally distributed variables were presented as mean and standard deviation. In contrast, descriptive statistics of non-normally distributed and ordinal variables were presented as median, minimum-maximum values, and frequency tables. Physical and socio-demographic characteristics were compared using Mann-Whitney U tests or independent sample t-tests for numerical variables and the chi-square test for categorical variables. Fleche cervicale, thoracic kyphosis index, fleche lombaire and lumbar lordosis (LL) angle between groups were analyzed by independent sample t-test. Pearson correlation test was used to evaluate the relationship between LL angle, fleche lombaire, thoracic kyphosis index, and fleche cervicale.

## RESULTS

The socio-demographic and physical characteristics of the participants are shown in Table 1. The mean age of the subjects were 45.5 ± 8.07 years, and 23 (85.2%) of the patients were female. Except for age and parity ($p < 0.05$), there was no significant difference between the groups in demographic data ($p > 0.05$).

In the cervical ROM evaluation, all cervical ROMs were significantly less in the case group except extension ($p < 0.05$). Neck pain (VAS) ($p= 0.004$) and NDI ($p < 0.01$) scores were significantly higher in the case group. There was no statistically significant difference between the groups in comparison of spinal sagittal angle values ($p > 0.05$) (Table 2).

In the correlation study between variables, there was a significant positive correlation between fleche cervicale and thoracic kyphosis index ($r = 0.630$, $p<0.01$; Figure 1). Also, LL angle was positively correlated with thoracic kyphosis index ($r = 0.437$, $p < 0.01$).

## DISCUSSION

BPPV is the most expected diagnosis of vertigo. The most accepted explanation for its pathogenesis is that otoliths fall from the utricular macula into the semicircular canals. Thus, an abnormal movement sensation occurs due to a fluctuation in the endolymph (20). Since decreased cervical lordosis frequently accompanies BPPV. Recently, it has been suggested that cervical posture disorder may have a role in the etiology. Our study found no relation between BPPV and cervical lordosis angle. There was no significant difference between the two groups in fleche cervicale values.

Cervical vertigo is a different disease from BPPV. In its pathogenesis, confusion in proprioception caused by muscle, bone, and joint pathologies in the neck region, cervical sympathetic dysfunction, and decreased vertebral artery blood flow play a role (21). Traumatic or degenerative changes in the cervical spine and problems in the neck muscles, or sometimes just the pain itself, induce impaired sensation and lead to imbalanced symptoms. The cause of cervical dizziness is decreased vertebral artery blood flow caused by neck rotation in the degenerative cervical spine, compression of sympathetic nerve fibers, or proprioceptive receptor dysfunction in neck tissues (22).

Very few studies are on the relationship between BPPV and cervical lordosis. The fact that the etiology of BPPV cannot be found with a rate of 50-70% and postural disorders, including cervical axis straightening, are frequently observed in these patients has drawn attention to the possibility that the musculoskeletal system may be the etiologic factor. Erdem et al. investigated cervical lordosis in 40 patients with BPPV

Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

**Table 1.** Baseline demographic data of both groups.

| Characteristics | Study group (n = 27) | Control group (n = 29) | p |
|---|---|---|---|
| **Age (years, mean±SD)** | 43.5 ± 8.07 | 36.0 ± 9.11 | **.002*** |
| **Weight (median (min-max))** | 70 (52 - 106) | 59 (49 - 103) | .055 |
| **BMI (median (min-max))** | 26.1 (19.5 - 41.4) | 23.2 (19.1 - 41.3) | .079 |
| **Gender (n, %)** | | | |
| Female | 23 (85.2) | 22 7(5.9) | .380 |
| Male | 4 (14.8) | 7 (24.1) | |
| **Employment Status (n, %)** | | | |
| Not working | 13 (11.6) | 11 (37.9) | .440 |
| Working | 14 (15.4) | 18 (62.1) | |
| **Marital status (n, %)** | | | |
| Single | 2 (7.4) | 8 (27.69 | .080 |
| Married | 25 (22.2) | 21 (72.4) | |
| **Child (n, %)** | | | **.011*** |
| No | 3 (11.1) | 12 (41.4) | |
| Yes | 24 (88.9) | 17 (58.69) | |
| **Comorbidity status (n, %)** | | | |
| No | 14 (51.9) | 20 (69.0) | .190 |
| Yes | 13 (48.1) | 9 (31.0) | |
| **Cigarette smoking (n, %)** | | | |
| No | 17 (63.0) | 16 (55.2) | .554 |
| Yes | 10 (37.0) | 13 (44.8) | |
| **Screen time (n, %)** | | | |
| Less than 1 hour | 12 (44.4) | 8 (27.6) | .418 |
| 1-4 hours | 6 (22.2) | 8 (27.6) | |
| More than 4 hours | 9 (33.3) | 13 (11.4) | |

*p < 0.05, SD; standard deviation, BMI; body mass index.

and found that the angle was below average in 35 of 40 patients (87.5%). Based on this, the researchers reported that a decrease in the cervical axis may be an etiologic factor in BPPV (23).

However, there was no control group of healthy subjects in this study. Considering that decreased cervical lordosis is very common in the general population and is due to many different causes, we believe it is challenging to establish a definite link between BPPV and cervical lordosis without comparing it with healthy controls. In our study, we worked with a group of patients diagnosed with BPPV and a control group of healthy volunteers. In a study on the causes of cervical axis flattening, cervical lordosis was investigated by Cobb angle measurement. Patients with decreased cervical lordosis were diagnosed with tension-type headache, cervical spondylosis, cervical herniation, fibromyalgia, myofascial pain syndrome (MPS), and anxiety depression (24). Head position sense is influenced by proprioceptive input from the neck and vestibular system input. There is a wide anatomical connection between these two systems. If the information about the position of the head from the vestibular system is not precise or if there is an error in the integration of this information in the central nervous system, the head position may change (25).

Patients with peripheral vestibular dysfunction generally have decreased flexibility and relaxation capacity. One study pointed out that about half

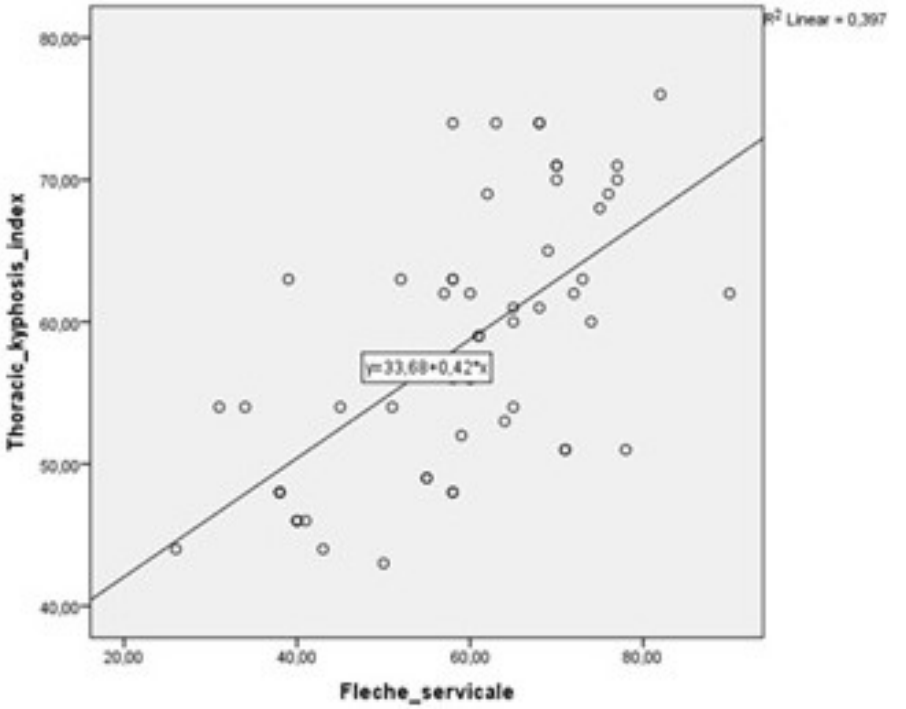
Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

**Table 2.** Comparison of spinal sagittal values and ROM parameters between groups.

| **Characteristics features** | **Study group (n = 27) X±SD** | **Control group (n = 29) X±SD** | **t values** | **p** |
|---|---|---|---|---|
| Fleche cervicale(mm) | 60.6 ± 12.39 | 57.5 ± 15.79 | -.816 | .418 |
| Thoracic kyphosis index | 60.2 ± 9.8 | 56.5 ± 8.8 | -1.500 | .139 |
| Fleche lombaire(mm) | 48.48 ± 12.6 | 46.0 ± 11.5 | -.768 | .446 |
| Lumbar lordosis angle (°) | 51.18 ± 8.3 | 48.79 ± 8.01 | -1.096 | .278 |
| **Characteristic features** | **Study group (n = 27) (Median (min-max))** | **Control group (n = 29) (Median (min-max))** | **z** | **p** |
| Neck disability index | 1 (0-3) | 0 (0-3) | -3.610 | **.000*** |
| Neck pain (VAS) | 6 (0-9) | 2 (0-9) | -2.869 | **.004*** |
| CROM_F (°) | 40 (30-45) | 45 (30-45) | -2.248 | **.025*** |
| CROM_E (°) | 40 (30-45) | 40 (30-45) | -.569 | .569 |
| CROM_LF-right (°) | 40 (30-40) | 40 (30-45) | -3.394 | **.001*** |
| CROM_LF-left (°) | 40 (25-45) | 40 (30-45) | -2.468 | **.014*** |
| CROM_R-right (°) | 60 (50-60) | 60 (50-70) | -2.396 | **.017*** |
| CROM_R_left (°) | 60 (45-70) | 60 (50-70) | -1.079 | **.0281*** |

*p < 0.05, SD; standard deviation, VAS; visual analog scale, CROM_F-; cervical range of motion-flexion, CROM_E; cervical range of motion-extension, CROM_LF-right; cervical range of motion-right lateral flexion, CROM_LF-left; cervical range of motion-left lateral flexion, CROM_R-right; cervical range of motion-right rotation, CROM_R-left; cervical range of motion-left rotation.

**Figure 1.** Correlation between fleche cervicale and thoracic kyphosis index.



Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

of such patients showed reduced ROM in the neck, temporomandibular joints, shoulders, and dorsal spine. Muscle palpation revealed upper trapezius and sternocleidomastoid muscle contractions in 70 to 94% of patients (26). Patients with untreated vestibular hypofunction may adopt a rigid head posture to avoid symptoms. They may tilt their head forward, or the patient may turn them toward the labyrinth (27). Vestibuloocular, vestibulocollic, vestibulospinal, and many other reflexes that occur with vestibular stimulation increase the tone of the neck, trunk, and extremity muscles against gravity. Since stimuli from cervical proprioceptors in BPPV will increase the patient's current complaint of dizziness, the patient can keep his/her head tilted forward to reduce the stimulation of proprioceptors in that region (28).

Based on this literature information, BPPV, a peripheral vestibular dysfunction, is one of the causes of decreased cervical lordosis. There was no significant difference between our case group and the control group regarding cervical lordosis because decreased cervical lordosis, which is already very common in society, is not specific to any disease. It is seen that decreased cervical lordosis is not a condition specific to BPPV. It can also be seen in healthy asymptomatic individuals like our control group. Therefore, decreased cervical lordosis is not an etiologic factor in BPPV but rather a consequence of BPPV. However, in the association of cervicogenic dizziness and BPPV, symptoms originating from the neck may be added to the existing picture and increase the severity of the symptoms.

The relationship between cervical lordosis and other cervical symptoms, such as pain, is also controversial. In the literature, studies show a relationship between decreased cervical lordosis and neck pain, and studies report that decreased cervical lordosis is not associated with clinical symptoms. However, the relationship between differences in cervical lordosis angles and neck pain is vague in daily practice. In a study in which cervical lordosis was measured by Cobb, Tangent, and effective cervical lordosis methods in 44 patients with chronic neck pain and its relationship with neck pain was investigated, no significant relationship was found between neck pain and cervical lordosis (29). In a study conducted with 100 participants who were chronic laptop computer users and investigated the relationship between FHP and neck pain, no relationship was found between FHP and neck pain and cervical ROMs (30). A meta-analysis study reported that although FHP leads to decreased performance-based balance and cervical proprioception, the current evidence for the relationship between FHP and static balance and postural stability control and between FHP and vestibular deficits is controversial (28).

Kültür et al. reported that musculoskeletal system disorders may be the etiologic factor in BPPV. They suggested that most BPPV patients have decreased cervical lordosis, relapses are frequent despite Epley canalith repositioning treatment being the most accepted treatment, and musculoskeletal interventions such as manipulation are effective in BPPV. He divided 72 patients into two groups and performed only Epley maneuver in one group and cervical manipulation in the other group. He reported that the results were significantly better in the cervical manipulation group (31). However, there was no control group in this study. In addition, the improvement of vertigo with cervical traction and manipulative treatments suggests that it has a cervical origin rather than a vestibular focus (22). Since BPPV and cervicogenic dizziness can coexist and one worsens the other, improving the cervical pathology most likely reduced symptom severity and may have led to a better treatment outcome. Martelucci et al. reported that the success rate of the Epley maneuver decreased in cervical ROM limitation. Because in this maneuver, the patient's neck is forced to flexion, extension, and rotation. Since cervical ROM limitation is already expected in BPPV, they thought that manipulative approaches to the cervical spine would allow practical application of the Epley maneuver by improving ROM. For this purpose, they divided the patients into two groups and found that cervical flexion and extension limitations were significantly higher in those who needed multiple maneuvers (32). In conclusion, cervical manipulation positively affects the treatment results in BPPV by two mechanisms. The first mechanism of action is that it decreases the severity of the symptom by eliminating cervical dizziness in cases where BPPV and cervical dizziness are together, and the second mechanism of action is that it makes the Epley maneuver, which is the specific treatment of BPPV, effective.

Bozok Tıp Derg 2023;13(3):58-67
Bozok Med J 2023;13(3):58-67

In this study, cervical ROM was significantly limited in the patient group compared to the control group. Cervical ROM limitation in BPPV is consistent with other reports in the literature. However, Martelucci stated that treatment failure is more strongly associated with the limitation of extension rather than the limitation of flexion. In contrast, in our study, the limitations of cervical flexion, rotation ($p < 0.05$), and lateral flexion ($p < 0.01$) were significantly different. No significant difference was found between the two groups in terms of extension. This result supports that there is no relationship between decreased cervical lordosis and BPPV.

Among cervical pathologies, cervical spondylosis is the pathology that has the most consensus about its relation with BPPV. Cervical degenerative disc disease is the most common disc pathology, and vertigo is observed in 50-60% of patients (33). Martinez et al. in their retrospective study of 493 patients, they analyzed the cervical radiographs of patients presenting with vertigo. They obtained radiographs in 281 of 493 patients. Degenerative changes were found in 74.1% of patients, osteophytes in 49.5%, and abnormal cervical lordosis in 37.1% (34). The posterior circulation is susceptible to ischemia due to the vertebral arteries' proximity to the cervical spine. This mechanism may be responsible for central and peripheral vestibular symptoms such as vertigo, dizziness, nystagmus, and imbalance. Olszewski et al. concluded that the vestibular labyrinth is selectively more sensitive to ischemia in the posterior circulation (35).

In a meta-analysis of 99 studies and 36646 patients, risk factors for recurrence in BPPV were evaluated. Although 30 risk factors were defined, 13 of them were found to be significant risk factors. The only cervical pathology among these 13 important risk factors was cervical spondylosis (36). The circulation of the inner ear is provided by the vertebrobasilar system, making the labyrinth susceptible to ischemia due to its localization in the inner ear, and labyrinth ischemia leads to the development of BPPV (37).

In the current study, NDI, and neck pain VAS scores were significantly higher in the case group compared to the control group ($p < 0.05$). Therefore, we can assume an association between BPPV and other painful cervical pathologies, but no association with decreased cervical lordosis was found. Considering that the mean age of our patient group was significantly higher than the control group ($p < 0.05$), we think that the only cervical pathology with an etiologic link to BPPV is cervical spondylosis causing vertebrobasilar insufficiency. Other cervical pathologies with vertigo are not associated with BPPV but with cervicogenic dizziness. BPPV and cervicogenic dizziness can be seen together. Therefore, other cervical pathologies, including decreased cervical lordosis, may not cause BPPV but may increase BPPV symptom severity. Musculoskeletal therapeutic approaches may be beneficial in BPPV. However, this is not directly affecting the pathophysiology of BPPV, but indirectly by relieving cervicogenic vertigo that is superimposed on BPPV or by facilitating canalith repositioning, the specific treatment for BPPV.

The limitation of this study is the small number of cases and the fact that cervical radiographs were not evaluated to detect other cervical pathologies in the participants.

## CONCLUSION

There is no relationship between BPPV and decreased cervical lordosis. Decreased cervical lordosis is a consequence rather than a cause of BPPV. Decreased cervical lordosis is not an etiologic factor in BPPV, but it may lead to aggravation of the symptoms with the addition of cervicogenic dizziness to BPPV.

## ACKNOWLEDGEMENTS

The author reports no relationship that could be construed as a conflict of interest. The study did not get any type of financial support. The author thanks Dr Ümit Görgülü and Dr Nurcan Kum for their participation in the data collection process of this study.

## REFERENCES

**1.** Kim HJ, Park J, Kim JS. Update on benign paroxysmal positional vertigo. J Neurol. 2021 May;268(5):1995-2000.

**2.** Dağkıran M, Sürmelioğlu Ö, Özlem AY. Diagnosis and Treatment Approach in Benign Paroxysmal Positional Vertigo. Arşiv Kaynak Tarama Dergisi 2015;24(4):555-64.

**3.** Hornibrook J. Benign Paroxysmal Positional Vertigo (BPPV): History, Pathophysiology, Office Treatment and Future Directions. Int J Otolaryngol. 2011;2011:835671.

**4.** von Brevern M, Radtke A, Lezius F, Feldmann M, Ziese T, Lempert T,

et al. Epidemiology of benign paroxysmal positional vertigo: a population based study. J Neurol Neurosurg Psychiatry. 2007 Jul;78(7):710-5.

**5.** Durmuş B, Fırat Y, Yıldırım T, Kalcıoğlu T, Altay Z. Benign Paroksismal Pozisyonel Vertigo Tedavisinde Semont ve Modifiye Epley Manevralarının Etkinliği ve Brandt-Daroff Egzersizlerinin Nüksleri Önlemedeki Etkisi. Fırat Tıp Dergisi. 2010;15(3): 131-6.

**6.** Parnes LS, Agrawal SK, Atlas J. Diagnosis and management of benign paroxysmal positional vertigo (BPPV). CMAJ. 2003 Sep 30;169(7):681-93.

**7.** Selçuk A, Akdoğan Ö, Özcan İ, Dere H. Benign paroksizmal pozisyonel vertigoda patofizyolojiye göre uygun tedavinin belirlenmesi. KBB-Forum. 2008; 7(1):52-8.

**8.** Burak Öztürk, Münevver Güleç, Teslime Nur Deveci, Meryem Tuğçe Güler. Benign Paroksismal Pozisyonel Vertigo: Patofizyoloji, Değerlendirme veTanılama. TJAHR. 2019;2(1):18−28.

**9.** Li Y, Yang L, Dai C, Peng B. Proprioceptive Cervicogenic Dizziness: A Narrative Review of Pathogenesis, Diagnosis, and Treatment. J Clin Med. 2022;11(21):6293.

**10.** Yacovino DA, Hain TC. Clinical characteristics of cervicogenic-related dizziness and vertigo. Semin Neurol. 2013;33(3):244-55.

**11.** Lima Neto AC, Bittar R, Gattas GS, Bor-Seng-Shu E, Oliveira ML, Monsanto RDC,et al. Pathophysiology and Diagnosis of Vertebrobasilar Insufficiency: A Review of the Literature. Int Arch Otorhinolaryngol. 2017;21(3):302-7.

**12.** Savitz SI, Caplan LR. Vertebrobasilar disease. N Engl J Med. 2005;352(25):2618-26.

**13.** Swartz EE, Floyd RT, Cendoma M. Cervical spine functional anatomy and the biomechanics of injury due to compressive loading. J Athl Train. 2005;40(3):155-61.

**14.** Yun-Hee Sung. Suboccipital Muscles, Forward Head Posture, and Cervicogenic Dizziness. Medicina (Kaunas). 2022 Dec 5;58(12):1791.

**15.** Hulse, M. Disequelibrium caused by a functional disturbance of the upper cervical spine, clinical aspects and differential diagnosis. Manual Med. 1983;1:18±23.

**16.** Sung YH. Suboccipital Muscles, Forward Head Posture, and Cervicogenic Dizziness. Medicina (Kaunas). 2022;58(12):1791.

**17.** Zurawski AL, Kiebzak WP, Kowalski IM, Sliwinski G, Sliwinski Z. Evaluation of the association between postural control and sagittal curvature of the spine. PLoS One. 2020;15(10):e0241228.

**18.** Gipsman A, Rauschert L, Daneshvar M, Knott P. Evaluating the Reproducibility of Motion Analysis Scanning of the Spine during Walking. Adv Med. 2014;2014:721829.

**19.** Aslan E, Karaduman A, Yakut Y, Aras B, Simsek IE, Yagli N. The cultural adaptation, reliability and validity of neck disability index in patients with neck pain: a Turkish version study. Spine (Phila Pa 1976). 2008;33(11):E362-5.

**20.** Wang W, Peng L, Xi Han, Xiang M, Shanshan L, Chao W, et al. New views on benign paroxysmal positional vertigo. Journal of Bio-X Research. 2020;3(2):78-82.

**21.** Sung YH. Upper cervical spine dysfunction and dizziness. J Exerc Rehabil. 2020;16(5):385-91.

**22.** Chu ECP, Chin WL, Bhaumik A. Cervicogenic dizziness. Oxf Med Case Reports. 2019;2019(11):476-8.

**23.** Erdem D, Aksoy Yıldırım G, Ulaş Erdem E. Evaluation of Cervical Lordosis in Benign Paroxysmal Positional Vertigo: Pilot Study. KBB-Forum. 2013;12(3):70-4.

**24.** Demirel A, Adak B. Servikal Vertebral Aks Düzleşmesi: Demografi ve Nedenler. Abant Med J. 2022;11(2):250-6.

**25.** Moustafa IM, Youssef A, Ahbouch A, Tamim M, Harrison DE. Is forward head posture relevant to autonomic nervous system function and cervical sensorimotor control? Cross sectional study. Gait Posture. 2020;77:29-35.

**26.** MigliareseS, Emma W. Review of forward-head posture and vestibular deficits in older adults Curr. Geriatr. Rep. 8 (3) (2019), pp. 194-201.

**27.** Mahmoud NF, Hassan KA, Abdelmajeed SF, Moustafa IM, Silva AG. The Relationship Between Forward Head Posture and Neck Pain: a Systematic Review and Meta-Analysis. Curr Rev Musculoskelet Med. 2019;12(4):562-77.

**28.** Lin G, Zhao X, Wang W, Wilkinson T. The relationship between forward head posture, postural control and gait: A systematic review. Gait Posture. 2022;98:316-29.

**29.** Soylu Boy FN, Ünlü Özkan F, Erdem S, Özdemir G, Geler Külcü D, Akpınar P, et al. Servikal lordoz açıları ve boyun ağrısı ilişkisinin değerlendirilmesi. Marmara Medical Journal. 2014; 27: 112-5.

**30.** Worlikar, Apurva Nitin, and Mayuri Rajesh Shah.Incidence of Forward Head Posture and Associated Problems in Desktop Users. International Journal of Health Sciences & Research. 2019;9(2):96-100.

**31.** Kültür T, Şimşek G, Ağır H. The Effect of Cervical Manipulation Treatment in Benign Paroxysmal Posıtional Vertigo Patients with Neck Pain. KÜ Tıp Fak Derg. 2020;22(1):113-20.

**32.** Martellucci S, Attanasio G, Ralli M, Marcelli V, de Vincentiis M, Greco A, et al. Does cervical range of motion affect the outcomes of canalith repositioning procedures for posterior canal benign positional paroxysmal vertigo? Am J Otolaryngol. 2019 Jul-Aug;40(4):494-8.

**33.** Peng B. Cervical Vertigo: Historical Reviews and Advances. World Neurosurg. 2018;109:347-50.

**34.** Becares-Martinez C, Lopez-Llames A, Martin-Pagan A, Cores-Prieto AE, Arroyo-Domingo M, Marco-Algarra J, et al. Cervical spine

radiographs in patients with vertigo and dizziness. Radiol Med. 2020;125(3):272-9.

**35.** Olszewski J, Majak J, Pietkiewicz P, Luszcz C, Repetowski M. The association between positional vertebral and basilar artery flow lesion and prevalence of vertigo in patients with cervical spondylosis. Otolaryngol Head Neck Surg. 2006 Apr;134(4):680-4.

**36.** Li S, Wang Z, Liu Y, Cao J, Zheng H, Jing Y, et al. Risk Factors for the Recurrence of Benign Paroxysmal Positional Vertigo: A Systematic Review and Meta-Analysis. Ear Nose Throat J. 2022;101(3):NP112-NP134.

**37.** Liu Y, Wang W, Gong SS. Related factors of benign paroxysmal positional vertigo: investigation of 310 patients Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2016 May 5;30(9):748-50.

# LAPAROSKOPİK ADRENALEKTOMİDE PREOPERATİF DEMOGRAFİK VE KLİNİK ÖZELLİKLERİN POSTOPERATİF KOMPLİKASYONLAR ÜZERİNDEKİ ETKİSİ

## The Effect Of Preoperative Demographic And Clinical Characteristics On Postoperative Complications In Laparoscopic Adrenalectomy

Burhan BAYLAN[1], Recep UZUN[1]

[1]Afyonkarahisar Sağlık Bilimleri Üniversitesi,
Tıp Fakültesi,
Üroloji Anabilim Dalı,
Afyonkarahisar,
Türkiye

Burhan BAYLAN, Dr. Öğr. Ü.
(0000-0002-5509-7140)
Recep UZUN, Arş. Gör.
(0000-0002-0841-8757)

**İletişim:**
Dr. Öğr. Ü. Burhan BAYLAN
Zafer Sağlık Külliyesi Dörtyol Mah.
2078 Sokak, No: 3, F Blok, Pk. 03030,
Afyonkarahisar

**Geliş tarihi/Received:** 13.08.2023
**Kabul tarihi/Accepted:** 12.09.2023
**DOI:** 10.16919/bozoktip.1342483

Bozok Tıp Derg 2023;13(3):68-72
Bozok Med J 2023;13(3):68-72

## ÖZET

**Amaç:** Laparoskopik adrenalektomi (LA), primer aldosteronizm (PA) veya Cushing sendromu (CS) ile ilişkili olanlar da dahil olmak üzere küçük benign adrenal tümörlerin cerrahi tedavisinde altın standarttır. LA'da, postoperatif dönem komplikasyonlar ile başta vücut kitle indeksi olmak üzere diğer özelliklerin ilişkisini araştırmayı planladık.

**Gereç ve Yöntemler:** Kliniğimizde adrenalektomi yapılan 47 hasta retrospektif incelendi. Hastaların tümünde preoperatif Vucut Kitle İndeksinin (VKİ) içinde bulunduğu demografik özellikler, İntraoperatif verilerde işlem yaklaşımı, kitle tarafı, kitle boyutu, operasyon süresi ve hesaplanan kan kaybı değerleri kaydedildi. Postoperatif veriler erken ve geç komplikasyonlara dair Modifiye Clavien-Dindo dereceli komplikasyonların sınıflandırılmasını içermektedir.

**Bulgular:** LA uygulanan hastaların %31,91'i erkek (n=15) idi. Ortalama yaş 53,4 idi. Ortalama VKİ 24,15(20,2-28,9) kg/m² idi. VKİ normal (18,5-24,9 kg/m2 ) olan 16 hasta, VKİ kilolu olan (25-29 kg/m² ) 31 hasta mevcuttu. Postoperatif dönem komplikasyonlar Modifiye Clavien-Dindo sınıflamasına Grade 0-1 %70,2; Grade 2 %23,4, Grade 3 %0,2, Grade 4 %0,4 olarak bulundu. Ortalama hastanede kalış süresi 2,91(1-5) gündü. VK kilolu olan hastalarda, VK normal olan hastalara göre Grade 2 komplikasyon görülme riski istatistiksel olarak daha fazlaydı.

**Sonuç:** LA endikasyonu olan ve VK kilolu (25-29 kg/m² ) grupta yer alan hastalarda Clavien Dindo Grade 2 komplikasyon gelişme riski yüksek olması nedeniyle postoperatif dönemde yakın takip edilmedir.

**Anahtar Kelimeler:** *Laparoskopi, Adrenalektomi, Komplikasyon, VKİ*

## ABSTRACT

**Objective:** Laparoscopic adrenalectomy (LA) is the gold standard in the surgical treatment of small benign adrenal tumors, including those associated with primary aldosteronism (PA) or Cushing's syndrome (CS). In LA, we aimed to investigate the relationship between postoperative complications and other characteristics, especially body mass index.

**Material and Methods:** 47 patients who underwent adrenalectomy in our clinic were retrospectively analyzed. Demographic characteristics including preoperative Body Mass Index (BMI), intraoperative data showed the procedure approach, mass side, mass size, operation time and calculated blood loss values in all patients. Postoperative data include classification of Modified Clavien-Dindo grade complications related to early and late complications.

**Results:** 31.91% of the patients who underwent LA were male (n=15). The mean age was 53.4 years. The mean BMI was 24.15 (20.2-28.9) kg/m². There were 16 patients with normal BMI (18.5-24.9 kg/m²) and 31 patients with overweight BMI (25-29 kg/m²). Postoperative period complications were classified as Grade 0-1 70.2% according to the Modified Clavien-Dindo classification; Grade 2 was 23.4%, Grade 3 was 0.2%, and Grade 4 was 0.4%. The mean length of hospital stay was 2.91 (1-5) days. Patients with overweight BMI had a statistically higher risk of Grade 2 complications than patients with normal BMI

**Conclusion:** Patients with LA indications and BMI in the overweight (25-29 kg/m²) group should be followed up closely in the postoperative period because of the high risk of developing Clavien Dindo Grade 2 complications.

**Keywords:** *Laparoscopy, Adrenalectomy, Complication, BMI*

## GİRİŞ

Laparoskopik adrenalektomi (LA), primer hiperaldosteronizm (PA) veya Cushing sendromu (CS) ile ilişkili olanlar da dahil olmak üzere küçük benign adrenal tümörlerin cerrahi tedavisinde altın standarttır (1-4). LA açık ameliyatlarla karşılaştırıldığında, daha az tahmini kan kaybı, daha az ağrı, daha hızlı iyileşme, daha az ileus insidansı, daha kısa hastanede kalış süresi ve daha küçük yara izi gibi avantajlara sahiptir (5,6). Amerika Birleşik Devletleri ulusal araştırmaları ayrıca LA'nın açık adrenalektomiden anlamlı derecede daha düşük perioperatif morbiditeye sahip olduğunu doğrulamıştır (7).

Bununla birlikte, özellikle böbrek, karaciğer ve dalak gibi organlara ilişkin batın cerrahisi geçirmiş hastalarda, adrenal gland bölgesinde yapışıklıklar gelişebilir. Bu durum transperitoneal LA sırasında perioperatif riski önemli ölçüde artırmaktadır (8,9).

Cushing sendromunun neden olduğu morbid obezite de dahil olmak üzere obezite insidansı her yıl artmaktadır (10). Obezite, yüksek tansiyon, diyabet ve kardiyovasküler hastalık ile ilişkisi olması nedeniyle de LA gibi cerrahi prosedürlerde komplikasyon riskini artırmaktadır (11). Bununla birlikte, çeşitli çalışmalar çelişkili sonuçlar vermiştir. Bazı çalışmalarda obez hastaların minimal invaziv cerrahiden fayda görebileceğine dair sonuçlar bulunmuştur (12,13).

Çalışmamızın amacı, LA yaptığımız hastalarda demografik özellikleri, cerrahi özellikleri ve postoperatif dönem sonuçlarımızı tanımlayarak tek merkezli bir deneyimi paylaşmaktır. Ayrıca, postoperatif dönem komplikasyonlar ile başta vücut kitle indeksi olmak üzere diğer demografik ve klinik özelliklerin ilişkisini araştırmayı amaçladık.

## GEREÇ VE YÖNTEMLER

Afyonkarahisar Sağlık Bilimleri Üniversitesi Klinik Araştırmalar Etik Kurulu'nun 2023/145 sayılı etik kurul onayı alınarak 2015- 2023 tarihleri arasında Uroloji Kliniğimiz'de LA yapılan 47 hasta retrospektif incelendi. Preoperatif veriler, hastaların yaş, cinsiyet, Vucut Kitle İndeksi (VKİ), komorbid hastalıklar ve sigara kullanımı gibi demografik özelliklerini içeriyordu. İntraoperatif verilerde kitle tarafı, kitle boyutu, kitle fonksiyonel aktivitesi, operasyon süresi ve hesaplanan kan kaybı yer aldı. Postoperatif veriler erken ve geç komplikasyonlara dair Modifiye Clavien-Dindo dereceli komplikasyonların sınıflandırmasını içermektedir. Hastalardan operasyon öncesi aydınlatılmış onam alındı.

### İstatistiksel Analiz:

Veri analizi, IBM SPSS Statistics ver. 25.0 yazılımı (IBM Corporation, Armonk, NY, ABD) kullanılarak gerçekleştirilmiştir. Kategorik veriler sayı (n) ve yüzde (%) olarak ifade edilirken, nicel veriler ortalama ve yüzdelik dilimler olarak verilmiştir. Demografik, klinik ve biyokimyasal değişkenler ile ana sonuç değişkeni arasındaki ilişkileri belirlemek için tek değişkenli lojistik regresyon analizleri uygulanmıştır. Her potansiyel tahminci için oran oranları ve %95 güven aralığı da hesaplandı.

## BULGULAR

LA uygulanan toplam 47 hastanın %31,91'ini (n=15) erkek hastalar oluşturdu. Ortalama yaş 53,4 idi. Ortalama VKİ 24,15 (20,2-28,9) kg/m² idi. Çalışmamızda VKİ normal (18,5-24,9 kg/m² ) olan 16 hasta, VKİ kilolu (25-29 kg/m² ) olan 31 hasta mevcuttu. 31 (%65,9) hastada hipertansiyon (HT) öyküsü ve 16 (%34) hastada Tip 2 diyabetes mellitus (DM) öyküsü mevcuttu. Hastaların 4 (%21,27)'ünde HT ve DM birlikte görülmekteydi. Adrenalektomi yapılan hastaların 20 (%42,55)'inde fonksiyonel adenom mevcuttu. Primer hiperaldosteronizm 6 olguda, Cushing Sendromu 7 ve Feokromasitoma 7 olguda cerrahi endikasyondu (Tablo 1).

Ortalama ameliyat süresi 97,65 dk idi. İntraoperatif kan kaybı ortalaması 120,93 cc idi. Ortalama tümör boyutu 59,67 (10-210) mm'di. Olguların 18 (%38,3)'ine sağ taraflı adrenalektomi uygulandı; 1 olguda medikal yanıtsız ektopik cushing hastalığı tanısı ile bilateral adrenalektomi yapıldı. Ortalama hastanede kalış süresi 2,91(1-5) gündü. Hastalarda postoperatif yoğun bakım takibi gerekli olmadı. Mortalite oranı %0 idi, Postoperatif dönem komplikasyonlar Modifiye Clavien-Dindo sınıflamasına göre değerlendirildi. (Grade 0-1 = %70,2; Grade 2 = %23,4; Grade 3 = %0,2; Grade 4 = %0,4). Grade 1 komplikasyonlu hastalara elektrolitik replasmanı yapıldı. Tip 2 komplikasyon gelişen 4 hastaya eritrosit replasmanı uygulandı. 1 hastada intraoperatif vasküler hasar gelişmesi nedenli açık operasyona geçildi. 1 hastaya komşu böbrek hasarı

Bozok Tıp Derg 2023;13(3):68-72
Bozok Med J 2023;13(3):68-72

**Tablo 1.** Demografik ve Klinik Özellikler

| Değişken Demografi | Sonuç |
|---|---|
| **Yaş** | 53,4 (26-76) |
| **VK** | 24,15 (20,2-28,9) |
| **VK değerlerine göre kişi sayısı** | **N: 47** |
| Normal Kilo (18,5-24,9 kg/m$^2$) | 16 |
| Kilolu (25-29 kg/m$^2$) | 31 |
| **Cinsiyet** | **N:47** |
| **Erkek** | 15 |
| **Kadın** | 32 |
| **Diyabet** | 16 |
| **Hipertansiyon** | 31 |
| **Sigara kullanımı** | 9 |
| **Kitle taraf** | **N:47** |
| **Sağ** | **18** |
| **Sol** | **29** |
| **Kitle boyut (mm)** | **59,67 (10-210)** |
| **Hormonal aktivite** | **N:47** |
| **Nonfonksiyone** | **27** |
| **Fonksiyone** | **20** |
| **Hiperaldosteronizm** | **6** |
| **Cushing sendromu** | **7** |
| **Feokromasitoma** | **7** |
| **Intraoperatif kan kaybı (cc)** | **120,93 (40-300)** |
| **Ameliyat süresi (dk)** | **97,65 (40-180)** |
| **Postoperatif dren çekilme süresi (gün)** | **1,87 (1-4)** |
| **Clavien Dindo Komplikasyon** | **N:47** |
| **Grade 0** | **18** |
| **Grade 1** | **15** |
| **Grade 2** | **11** |
| **Grade 3b** | **1** |
| **Grade 4a** | **2** |
| **Patolojik sonuç** | **N:47** |
| **Adenoma** | **37** |
| **Neoplazi** | **10** |
| **Hastanede kalış süresi(gün)** | **2,91 (1-5)** |

VK: Vücut kitle

nedenli nefrektomi ve 1 hastada komşu dalak hasarı nedenli splenektomi yapılması gerekti. Hastalarda postoperatif dönem komplikasyonlar ile demografik özellikler arasındaki ilişki istatistiksel olarak değerlendirildi. Postoperatif dönem komplikasyonlarla demografik verilerden yaş, cinsiyet, tümör tarafı, tümörün fonksiyonel aktivitesi ile istatistiksel anlamlı ilişki saptanmadı. VK normal olan ve VK kilolu olan hasta gruplarının demografik özellikleri ve komorbiteleri açısından karşılaştırıldıklarında istatistiksel anlamlı farklılık olmadığı gözlendi. VK kilolu olan hastalarda, VK normal olan hastalara göre Grade 2 komplikasyon görülme riski istatistiksel olarak daha fazlaydı (Tablo 2). Her ne kadar istatistiksel olarak anlamlı görülmese

Bozok Tıp Derg 2023;13(3):68-72
Bozok Med J 2023;13(3):68-72

**Tablo 2.** VK ile Modifiye Clavien Dindo komplikasyon derecelerine ilişkin lojistik regresyon analizleri

| | Normal Kilo hasta (n=16) | Kilolu hasta (n=31) | OR (95%CI) | p-value |
|---|---|---|---|---|
| **Grade 1** | 6 | 9 | 1.095 (0.863-1.389) | 0.455 |
| **Grade 2** | 1 | 10 | 0.884 (0.808-0.968) | **0,008** |
| **Grade 3b** | 0 | 1 | 2.314 (0.571-9.383) | 0.240 |
| **Grade 4** | 0 | 2 | 1.071 (0.236-4.854) | 0.929 |

de Grade 3b ve Grade 4 komplikasyon görülen hastaların VK kiloluydu. Grade 1 ve grade 1'den yüksek komplikasyon gelişen hastalar ayrı gruplar halinde karşılaştırıldığında; grade 1 üzeri komplikasyon gelişen grubun tümör boyutu ile Grade 1 komplikasyon gelişen grubun tümör boyutları arasında istatistiksel anlamlı fark tespit edilmedi.

## TARTIŞMA

Günümüzde LA, açık yaklaşıma göre daha düşük morbidite, mortalite, hastanede kalış süresinin azalması ve daha düşük intraoperatif kan kaybı nedeniyle adrenal kitlelerin tedavisinde altın standart yaklaşım olarak kabul edilmektedir. Bununla birlikte, bildirilen veriler perioperatif özellikler veya postoperatif sonuçlar açısından heterojendir (14). Özellikle yara ve septik komplikasyonlar olmak üzere komplikasyon artışı için önemli bir faktör olarak kabul edilen obezite insidansındaki artış LA için yeni zorluklar ortaya çıkarmaktadır (15).

Obezite, artmış morbidite ve mortalite ile ilişkili olarak dünya çapında bir endişe kaynağı haline gelmiştir (13). Artmış VKİ ile operatif ve postoperatif komplikasyonlar arasındaki ilişki halen araştırma konusudur. Danwang ve ark. gibi bazı yazarlar obez hastalarda postoperatif sonuçların artmadığını öne sürmektedir. Bununla birlikte, bildirilen çalışmalar sınırlıdır (13, 16-18). Buna karşılık, cerrahi komplikasyonların değerlendirme yöntemleri sürekli olarak değiştirilmiş ve endikasyon noktaları da gözden geçirilmiştir. Bu faktörler obezitenin etkisini gizleyebilir. Bununla birlikte, Dancea ve ark. obez hastaların postoperatif komplikasyon oranlarının nispeten yüksek olduğunu bulmuşlardır (17). Obez hastalarda daha büyük omentum üzerindeki ağır yük nedeniyle, cerrahlar dalağa kolayca zarar verebilecek sol adrenal beze ulaşmak için dalak fleksini harekete geçirmeyi tercih ederler. Sol taraflı transperitoneal LA sırasında ve bu kohortta 4 dalak hasarı vakası gözlenmiştir (17).

Giron ve ark yaptığı çalışmada, artmış VKİ, dönüşüm oranı, morbidite veya yeniden kabul oranları ile ilişkili saptanmamıştır (19). Bu mevcut çalışmaların sonuçlarından farklı olarak çalışmamızda VK ile değerlendirildiğinde kilolu olan hastalarda, VK normal olan hastalara göre Grade 2 komplikasyon görülme riski istatistiksel olarak anlamlı daha fazlaydı. Çalışmamızda her ne kadar istatistiksel olarak anlamlı görülmese de Grade 3 ve Grade 4 komplikasyon görülen hastalarda VK kiloluydu.

LA'de tümör boyutunun morbidite ile anlamlı ilişkili olduğunu gösteren çalışmalar mevcuttur (20,21). Bu çalışmaların aksine, çalışmamızda tümör boyutunun morbidite üzerindeki etkili olmadığı görülmüştür. Bu küçük örneklem büyüklüğü ile ilişkili olabilir.

Çalışmamızın kısıtlılıkları arasında retrospektif yapısı ve örneklem büyüklüğünün küçük olması yer almaktadır. Çalışmamızda tümör hacmi ile morbidite arasında bir ilişki olmamasına rağmen, p değeri, örneklem büyüklüğünün artmasıyla verilerin istatistiksel olarak anlamlı bir değere ulaşabileceğini düşündürmektedir.

## SONUÇ

LA gibi minimal invaziv teknikler, kabul edilebilir morbidite oranları ve hastane yatış süreleri ile güvenli ve uygulanabilir yaklaşımlardır. LA yapılan hastalarda VK kilolu (25-29 kg/m² ) grupta yer alan hastalarda Clavien Dindo Grade 2 komplikasyon gelişme riski yüksek olması nedeniyle postoperative dönem takiplerde bu açıdan dikkatli olunmalıdır.

## TASDİK VE TEŞEKKÜR

Bu çalışma için finansal destek alınmamıştır. Yazarlar, birbirleri arasında herhangi bir çıkar çatışması bulunmadığını beyan ederler.

## KAYNAKLAR

**1.** Gagner M, Lacroix A, Bolté E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med. 1992 Oct 1;327(14):1033.

**2.** Ball MW, Hemal AK, Allaf ME. International Consultation on Urological Diseases and European Association of Urology International Consultation on Minimally Invasive Surgery in Urology: laparoscopic and robotic adrenalectomy. BJU Int. 2017 Jan;119(1):13-21.

**3.** Go H, Takeda M, Takahashi H, Imai T, Tsutsui T, Mizusawa T et al. Laparoscopic adrenalectomy for primary aldosteronism: a new operative method. J Laparoendosc Surg. 1993 Oct;3(5):455-9.

**4.** Smith CD, Weber CJ, Amerson JR. Laparoscopic adrenalectomy: new gold standard. World J Surg. 1999 Apr;23(4):389-96.

**5.** Hallfeldt KK, Mussack T, Trupka A, Hohenbleicher F, Schmidbauer S. Laparoscopic lateral adrenalectomy versus open posterior adrenalectomy for the treatment of benign adrenal tumors. Surg Endosc. 2003 Feb;17(2):264-7.

**6.** Kim HH, Kim GH, Sung GT. Laparoscopic adrenalectomy for pheochromocytoma: comparison with conventional open adrenalectomy. J Endourol. 2004 Apr;18(3):251-5.

**7.** Lee J, El-Tamer M, Schifftner T, Turrentine FE, Henderson WG, Khuri S et al. Open and laparoscopic adrenalectomy: analysis of the National Surgical Quality Improvement Program. J Am Coll Surg. 2008 May;206(5):953-9; discussion 959-61.

**8.** Economopoulos KP, Phitayakorn R, Lubitz CC, Sadow PM, Parangi S, Stephen AE et al. Should specific patient clinical characteristics discourage adrenal surgeons from performing laparoscopic transperitoneal adrenalectomy? Surgery. 2016 Jan;159(1):240-8.

**9.** Raffaelli M, De Crea C, Bellantone R. Laparoscopic adrenalectomy. Gland Surg. 2019 Jul;8(Suppl 1):S41-S52.

**10.** Hu Q, Hang Z, Ho Y, Sun C, Xu K, Xia G et al. Impact of Obesity on Perioperative Outcomes of Retroperitoneal Laparoscopic Adrenalectomy. Urol Int. 2015;95(3):361-6.

**11.** Feder MT, Patel MB, Melman A, Ghavamian R, Hoenig DM. Comparison of open and laparoscopic nephrectomy in obese and nonobese patients: outcomes stratified by body mass index. J Urol. 2008 Jul;180(1):79-83.

**12.** Rizvi SJ, Garg N, Khemchandani S, Modi PR. Donor and Recipient Outcomes of Retroperitoneal Laparoscopic Donor Nephrectomy in Obese Versus Nonobese Donors: A Prospective Study. Transplant Proc. 2020 Jul-Aug;52(6):1661-4.

**13.** Danwang C, Agbor VN, Bigna JJ. Obesity and postoperative outcomes of the patients with laparoscopic adrenalectomy: a systematic review and meta-analysis. BMC Surg. 2020 Aug 31;20(1):194.

**14.** Materazzi G, Rossi L. Robot-assisted adrenalectomy: state of the art. Updates Surg. 2021 Jun;73(3):1131-46.

**15.** Zonča P, Bužga M, Ihnát P, Martínek L. Retroperitoneoscopic Adrenalectomy in Obese Patients: Is It Suitable? Obes Surg. 2015 Jul;25(7):1203-8.

**16.** Kazaryan AM, Marangos IP, Røsok BI, Rosseland AR, Edwin B. Impact of body mass index on outcomes of laparoscopic adrenal surgery. Surg Innov. 2011;18(4):358–67.

**17.** Dancea HC, Obradovic V, Sartorius J, Woll N, Blansfield JA. Increased complication rate in obese patients undergoing laparoscopic adrenalectomy. JSLS. 2012 Jan-Mar;16(1):45-9.

**18.** Inaishi T, Kikumori T, Takeuchi D, Ishihara H, Miyajima N, Shibata M et al. Obesity does not affect peri- and postoperative outcomes of transabdominal laparoscopic adrenalectomy. Nagoya J Med Sci. 2018 Feb;80(1):21-8.

**19.** Girón F, Rey Chaves CE, Rodríguez L, Rueda-Esteban RJ, Núñez-Rocha RE, Toledo S et el. Postoperative outcomes of minimally invasive adrenalectomy: do body mass index and tumor size matter? A single-center experience. BMC Surg. 2022 Jul 19;22(1):280.

**20.** Van der Linden P, Steichen O, Zinzindohoué F, Plouin PF. Blood pressure and medication changes following adrenalectomy for unilateral primary aldosteronism: a follow-up study. J Hypertens. 2012 Apr;30(4):761-9.

**21.** Morelli L, Tartaglia D, Bronzoni J, Palmeri M, Guadagni S, Di Franco G et al. Robotic assisted versus pure laparoscopic surgery of the adrenal glands: a case-control study comparing surgical techniques. Langenbecks Arch Surg. 2016 Nov;401(7):999-1006.

# MİKROVASKÜLER ANGİNASI OLAN BİREYLERDE EOZİNOFİL/LENFOSİT ORANININ ÖNEMİ

## Understanding the Significance of the Eosinophil to Lymphocyte Ratio in Individuals With Microvascular Angina

Zehra GÜVEN ÇETIN[1], Bekir DEMIRTAŞ[2]

[1]Ankara Bilkent Şehir Hastanesi,
Kardiyoloji Kliniği,
Ankara,
Türkiye
[2]Ankara Etlik Şehir Hastanesi,
Kardiyoloji Kliniği,
Ankara,
Türkiye

Zehra GÜVEN ÇETİN, Dr.
(0000-0001-7140-1010)
Bekir DEMİRTAŞ, Dr.
(0000-0002-6266-2291)

**İletişim:**
Dr. Zehra GÜVEN ÇETİN
Ankara Bilkent Şehir Hastanesi,
Kardiyoloji Kliniği, Üniversiteler
Mahallesi 1604. Cadde No: 9 Bilkent/
Çankaya/Ankara

**Geliş tarihi/Received:** 14.08.2023
**Kabul tarihi/Accepted:** 11.09.2023
**DOI:** 10.16919/bozoktip.1341814

Bozok Tıp Derg 2023;13(3):73-80
Bozok Med J 2023;13(3):73-80

## ÖZET

**Amaç:** Mikrovasküler anjina, epikardiyal koroner arterlerde tıkayıcı lezyon olmaksızın, eforla göğüs ağrısı, elektrokardiyografik değişiklikler, miyokardiyal iskeminin objektif olarak gösterilmesi ve koroner epikardiyal spazmın ekarte edilmesi ile tanı konan klinik bir durumdur. Etiyoloji tam olarak aydınlatılmamış olsa da kronik inflamasyon ile ilişkisi ortaya konmuştur. Eozinofil/lenfosit oranı nispeten yeni bir inflamatuar belirteçtir ve sistemik hastalıklarda prognoz ve advers etkiler ile ilişkisi gösterilmiştir. Biz bu çalışmamızda mikrovasküler anjina tanısı alış hastalarda eozinofil/lenfosit oranını araştırıp koroner arter hastalığı olmayan bireyler ile karşılaştırmayı amaçladık.

**Gereç ve Yöntemler:** Çalışmamıza göğüs ağrısı şikâyeti ile kardiyoloji polikliniğine başvurup, miyokard perfüzyon sintigrafisinde miyokardiyal iskemi tespit edilen ve yapılan koroner anjiografide tıkayıcı koroner arter lezyonu saptanmayan 96 hasta alındı. Kontrol grubuna ise genel kontrol için başvurmuş, anjinal yakınması ve elektrokardiyografik değişikliği olmayan 80 hasta dahil edildi.

**Bulgular:** Her iki gruptaki hastalar bazal karakteristik özellikler açısından benzerdi. Mikrovasküler anjina grubunda eozinofil/lenfosit oranı 0,108 ± 0,102; kontrol grubunda ise 0,068 ± 0,048 idi ve gruplar arasındaki fark istatistiksel olarak anlamlı idi (p = 0,02). Her iki grup arasında diğer kan parametreleri açısından fark tespit edilmedi.

**Sonuç:** Bu çalışmamızda mikrovasküler anjina tanısı almış hastalarda eozinofil/lenfosit oranının sağlıklı bireylere göre anlamlı olarak daha yüksek olduğunu tespit ettik. Bulgularımız kronik inflamasyonun özellikle de eozinofillerin mikrovasküler anjina patogenezinde önemli rol oynadığını göstermiş olup daha önce yapılan çalışmaları desteklemektedir. Bununla birlikte çalışmamız bu hasta popülasyonunda eozinofil/lenfosit oranını değerlendiren ilk çalışma olma özelliği taşımaktadır.

**Anahtar Kelimeler:** *Eozinofil/Lenfosit Oranı, Mikrovasküler Angina, Koroner Mikrovasküler Disfonksiyon, İnflamasyon*

## ABSTRACT

**Objective:** Microvascular angina is diagnosed by chest pain on exertion, electrocardiographic changes, objective demonstration of myocardial ischemia, and exclusion of coronary epicardial spasm without occlusive lesions in the epicardial coronary arteries. Chronic inflammation has been associated with the disease, although the exact cause remains uncertain. The eosinophil to lymphocyte ratio, a recently discovered inflammatory marker, has demonstrated a correlation with prognosis and negative outcomes in systemic diseases. In this study, we aimed to investigate the eosinophil-to-lymphocyte ratio in patients diagnosed with microvascular angina and compare it with individuals without coronary artery disease.

**Material and Methods:** We conducted a study that involved 96 patients with chest pain and myocardial ischemia detected on myocardial perfusion scintigraphy but with no occlusive coronary artery lesion on coronary angiography. The control group comprised 80 patients who were admitted for general control without anginal complaints or electrocardiographic changes.

**Results:** Baseline characteristics were similar in both groups. The microvascular angina group had a significantly higher eosinophil-to-lymphocyte ratio (0.108 ± 0.102) compared to the control group (0.068 ± 0.048) (p=0.02). No differences in other blood parameters were observed.

**Conclusion:** Our study has revealed that patients diagnosed with microvascular angina exhibit a significantly higher eosinophil to lymphocyte ratio compared to healthy individuals. These findings substantiate prior research and strongly indicate that chronic inflammation, particularly eosinophils, is a vital factor in the development of microvascular angina. Additionally, this is the first study to examine the eosinophil-to-lymphocyte ratio in this patient population, providing valuable insight into the pathogenesis of the disease.

**Keywords:** *Eosinophil To Lymphocyte Ratio; Microvascular Angina, Coronary Microvascular Disease, İnflammation*

Bozok Tıp Derg 2023;13(3):73-80
Bozok Med J 2023;13(3):73-80

## GİRİŞ

Miyokardiyal iskeminin geleneksel olarak epikardiyal koroner arterlerdeki ateroskleroz ve buna bağlı koroner arter darlığı/tıkanıklığına bağlı olduğu düşünülse de yapılan koroner anjiografilerin yaklaşık yarısında tıkayıcı koroner arter lezyonu saptanmamaktadır (1, 2). Koroner anjiyografide tıkayıcı koroner lezyon ya da koroner anomali olmaksızın göğüs ağrısı ve istirahatte elektrokardiyografi (EKG) değişikliği olması ilk olarak 1967 yılında Likoff ve ark. tarafından 15 kadın hastada raporlanmıştır (3). Daha sonra 1973 de Kemp ve ark bu klinik durumu sebebi anlaşılamayan göğüs ağrısı anlamında 'Sendrom X' olarak adlandırmıştır (4). Eforla gelişen göğüs ağrısı, göğüs ağrısı sırasında elektrokardiyografik değişikliklerin gösterilmesi, epikardiyal koroner arterlerin normal ya da normale yakın olması ve koroner vazospazmın ekarte edilmesi kardiyak sendrom X'in tanı kriterleridir (5-7). Son zamanlarda yapılan çalışmalar sonucunda bu hastalarda koroner mikrovasküler disfonksiyonunun miyokardiyal iskemiye sebep olduğu ortaya konmuş ve 'Sendrom X' yerine 'Mikrovasküler Anjina (MVA)' terimi kullanılır hale gelmiştir (8, 9).

Epikardiyal damarlardan miyokarda kadar koroner dolaşım üç komponentten oluşur. İlk kısım çapı 500µ -5 mm arasında olan epikardiyal koroner damarlardır ki anjiografi ile olarak kolaylıkla görüntülenebilir ve tedavi edilebilir. Normal fizyolojik koşullarda epikardiyal koroner arterler düşük dirençlidir ve endotel aracılı vazodilatasyon ile metabolik ihtiyacın artması durumunda kan akımını arttırabilir. Koroner dolaşımın ancak %5-10'unu oluşturur. Koroner dolaşımın ikinci komponentini ekstra miyokardiyal prearteriolar damarlar oluşturur, çapları 100-500 µ'dur. Akım ve basınç ilişkili vazodilatasyon ile arteriolar basıncı sabit tutarlar. Son olarak çapları <100 µ olan intramural arterioller gelir ve miyokardiyal kapiller yatakta sonlanırlar. Bu damarların istirahatte tonusu yüksektir ve adenozin, nitrik oksit ve prostaglandinler gibi lokal metabolite yanıt olarak dilate olurlar (10). Normal mikrosirkülasyon, hem mikrovasküler ağının yapısal bütünlüğünü hem de miyokardiyal oksijen taleplerine yanıt olarak yeterli ve hızlı arteriolar direnç değişimlerini sağlayan sinyal yollarının korunmasını gerektirir. Mikrovasküler disfonksiyonun etyopatogenezde en çok üzerinde durulan mekanizmalar arasında arteriolar yeniden şekillenme ve vazomotor disregülasyon yer alır (11). Mikrovasküler anjina sıklığı kadınlarda daha fazla görülmekle birlikte, hipertansiyon, diyabet, sigara kullanımı, dislipidemi gibi klasik aterosklerotik risk faktörlerinin mikrovasküler anjina hastaları için de risk faktörü olduğu gösterilmiştir (12, 13). İnflamasyon ateroskleroz gelişiminde ve klinik yansımalarında en önemli mekanizmadır, koroner mikrovasküler disfonksiyonun altında yatan ana mekanizmanın da kronik inflamasyon olduğu düşünülmektedir (14).

İnflamatuar belirteçlerin geliştirilmesi koroner hastalıklarda hem tanısal hem de prognostik açıdan önemlidir. Yakın zamanlarda lökosit sayımlarından türetilen belirteçler inflamasyon göstergesi olarak klinik pratikte yaygın olarak kullanılmaya başlanmıştır. Akut koroner sendromlarda, perkütan koroner işlemlerde ve kalp yetmezliğinde nötrofil, lenfosit, monosit ve eozinofil sayımlarının advers kardiyak olaylarla ilişkileri yapılan çalışmalarda kanıtlanmıştır (15). Eozinofiller inflamasyonda önemli rol oynayan hücrelerdir. Özellikle endotel disfonksiyonu ve vazokonstriksiyon yapıcı özellikleri belirgindir. Trombositlerin aktivasyonunu ve agregasyonunu stimüle ederler, trombomodülini inhibe ederek trombüs oluşumunu sağlarlar (16). Lenfosit sayısının düşüklüğü ise ateroskleroz gelişimi ve progresyonu ile ilişkilidir (17). Eozinofil/lenfosit oranı (ELR) nispeten yeni bir inflamatuar belirteçtir ve sistemik hastalıklarda prognoz ve advers etkiler ile ilişkisi gösterilmiştir (18). Akut kalp yetmezliği, koroner ektazi ve koroner yavaş akımın ELR ile ilişkileri yapılan çalışmalarda gösterilmiştir (15, 19, 20).

Biz de bu çalışmamızda miyokardiyal iskemisi dokümante edilmiş, koroner anjiografide tıkayıcı lezyonu olmayan mikrovasküler anjina hastalarında yeni bir inflamatuar belirteç olan eozinofil/lenfosit oranını araştırıp koroner arter hastalığı olmayan bireyler ile karşılaştırmayı amaçladık.

## GEREÇ VE YÖNTEMLER

Çalışmamıza Ocak 2021– Ekim 2022 tarihleri arasında Ankara Şehir Hastanesi Kardiyoloji Kliniğine göğüs ağrısı şikâyeti ile gelip mikrovasküler anjina tanısı alan 96 hasta randomize edilmiştir. Anjinal yakınması ve iskemik EKG değişikliği olmayan genel kontrol için gelmiş 80 hasta kontrol grubuna dahil edilmiştir. Helsinki Bildirgesi'ne göre, Ankara Bilkent Şehir

Bozok Tıp Derg 2023;13(3):73-80
Bozok Med J 2023;13(3):73-80

Hastanesi 2 No'lu Etik Kurulu çalışma protokolünü incelemiş ve onaylamıştır (18/01/2023 Protokol No: E2-23-3206).

Çalışmamızda kardiyoloji polikliniğe göğüs ağrısı şikâyeti ile başvuran, miyokardiyal perfüzyon sintigrafisi (MPS) ile miyokardiyal iskemisi dokümante edilip, elektif koroner anjiografi (KAG) yapılan 18-85 yaş arasındaki hastalar retrospektif olarak taranmıştır. Hastaların anjiyografi filmleri izlenip koroner arterleri normal ve hiperventilasyon testi ile vazospazmın ekarte edildiği hastalar çalışmaya randomize edilmiştir. Rutin kontrol için polikliniğime başvuran, anjinal yakınması ve EKG değişikliği olmayan hastalar kontrol grubu için seçilmiştir. Çalışmamıza tıkayıcı koroner arter hastalığı olan, daha önce perkütan ya da cerrahi yöntemler ile revaskülarizasyon yapılmış olan, koroner anjiyografide hiperventilasyon testi ile koroner arter spazmı tespit edilen hastalar ile koroner yavaş akım saptanan hastalar alınmamıştır. Sol ventrikül sistolik disfonksiyonu (sol ventrikül ejeksiyon fraksiyonu <%50, kalp kapak hastalığı (herhangi bir kalp kapağında herhangi bir seviyede darlık ya da orta-ciddi yetmezlik), konjenital kalp hastalığı, kardiyomiyopati tanısı olan hastalar çalışmamıza dahil edilmemiştir. Periferik arter hastalığı, kronik obstrüktif akciğer hastalığı, otoimmün hastalık, kronik karaciğer ya da böbrek yetmezliği, aktif ya da kronik enfeksiyon varlığı, non-steroidal anti-inflamatuar ilaç kullanımı, herhangi bir sebeple steroid ya da immünsupresan/immünmodülatör tedavi kullanımı ve aktif malignite varlığı çalışmamız için dışlama kriteridir. Hastalardan onam formu alınmıştır.

Hastalara Türk Nükleer Derneği Çalışma Grubu tarafından belirlenen standartlara göre MPS için günlük egzersiz yaklaşımı veya stres testi (dipiridamol Tc-99 m MIBI protokolü) uygulandı. Stres testi için en az 4 saat 'yiyecek ve içecek almama' koşulu belirlendi. Herhangi bir kalsiyum kanal bloker veya beta bloker ilaç varsa kalp hızı veya kan basıncında farklılığa neden olmaması ve herhangi bir kontrendikasyon yaratmaması için 48 saat önce kesildi. Modifiye Bruce protokolüne göre stres/dinlenme testinde önce 8-10 mCi, ardından 22-25 mCi Tc99m sestamibi uygulandı. Hedef kalp hızı (220-yaş) × 0,85 formülü ile hesaplandı. Efor sırasında hastada testin devamı için kontrendikasyon oluşturacak bir durum geliştiğinde işlem sonlandırıldı. İntravenöz dipiridamol (0,14 mg/kg/dk × 4 dk) uygulamasını takiben Tc99m sestamibi (stres dozu olarak 8-10 mCi) uygulaması, hasta kalp hızına (0,85 × pik) ve üzerine ulaştığında ve koşu bandı için klinik güçsüzlük geliştiğinde gerçekleştirildi. Protokolün 30. dakikasından itibaren 22 ila 25 mCi Tc99m sestamibi (yaklaşık 3 × 8-10 mCi) uygulandı; Tc 99 m sestamibi uygulaması dinlenme fazının sonunda, yaklaşık üç saat sonra tekrarlandı. Son olarak, MPS 45-60 dakika sonra gerçekleştirildi.

Çalışma grubundaki tüm hastalara deneyimli girişimsel kardiyologlar tarafından radyal arter yolu; radyal arter girişime uygun değil ise femoral arter yolu ile standart Judkins yöntemi ile koroner anjiyografi yapılmıştır. Anjiografi görüntülerinde herhangi bir lüminal daralma veya düzensizlik olmaması durumunda koroner arterler normal olarak kabul edilmiştir. Vazospazmı ekarte etmek için hastalara hiperventilasyon testi yapılmıştır.

Hastalardan koroner anjiografi öncesinde bir gecelik açlık sonrası periferik venöz kan örnekleri alınmıştır. Hastaların açlık kan şekerleri, HbA1c değerleri, lipid profilleri, karaciğer ve böbrek fonksiyon testleri ile tam kan sayımları yapılmıştır. Total ve diferansiyel lökosit ölçümleri hematolojik analizör ile otomatik yapılmıştır. ELR mutlak eozinofil sayısının mutlak lenfosit sayısına bölümü ile elde edilmiştir.

Tüm istatistiksel analizler için IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. kullanılmıştır. Sayısal değişkenlerin normal olasılık dağılımına uyum gösterip göstermedikleri Kolmogorov Smirnov testi ile sınanmıştır. Tüm sayısal değişkenler ortalama ± standart sapma ve kategorik değişkenler ise frekans (n) ve yüzde olarak gösterilmiştir.

Sayısal verilerin homojenitesinin saptanmasında Levene testi kullanılmıştır. Parametrik test koşullarını sağlayan (normal dağılım ve homojenite) değişkenler bağımız örneklem t testi, parametrik test koşullarını sağlamayan değişkenler ise Mann-Whitney U testi ile analiz edilmiştir. Kategorik değişkenlerin analizinde Pearson ki-kare testi kullanılmıştır. ELR' nin optimum sınır değerini belirlemek için Receiver operating characteristic curve (ROC) analizi kullanılmıştır. $p<0.05$ olması istatistiksel olarak anlamlı kabul edilmiştir.

## BULGULAR

Çalışmamıza dışlama kriterleri uygulandıktan sonra

Bozok Tıp Derg 2023;13(3):73-80
Bozok Med J 2023;13(3):73-80

mikrovasküler anjina grubunda 96; kontrol grubunda 80 hasta olmak üzere toplam 176 hasta dahil edilmiştir. Hastaların ortalama yaşı 61,1 idi ve yaklaşık yarısı kadındı (%51,1). Her iki gruptaki hastalar bazal karakteristik özellikler açısından benzerdi (Tablo 1). Mikrovasküler anjina grubunda ELR 0,108 ± 0,102; kontrol grubunda ise 0,068 ± 0,048 idi ve gruplar arasındaki fark istatistiksel olarak anlamlı idi (p=0,02). Her iki grup arasında diğer kan parametreleri açısından fark tespit edilmedi (Tablo1).

ROC analizi ile ELR'nin mikrovasküler anjinayı tespit etmedeki gücü test edildi. ELR > 0,0690 ile %64,6 sensitivite ve %61,3 spesifisite (Eğri altındaki alan 0,645; 0,570-0,732; p=0,01) ile mikrovasküler anjinayı tespit ettiğini saptadık.

## TARTIŞMA

Biz bu çalışmamızda mikrovasküler anjina hastalarında başka bir deyiş ile kardiyak sendrom X hastalarında ELR'nin koroner arter hastalığı olmayan bireylere göre daha yüksek olduğunu tespit ettik. Bildiğimiz kadarıyla çalışmamız literatürde mikrovasküler anjina hastalarında ELR'nin çalışıldığı ilk çalışmadır.

Epikardiyal damarları takip eden prearterioller, arterioller ve kapiller damarlar koroner mikro dolaşımı oluşturur. Koroner dolaşım, miyojenik tonus, metabolik sinyaller ve dolaşımdaki hormonlar arasındaki etkileşim ile miyokardiyal oksijen arz ve talebini dengede tutar (21). Yakın zamanda yapılan çalışmalarda koroner mikrovasküler disfonksiyonun patofizyolojisini açıklayan endotipler tanımlanmıştır (22, 23). Yapısal ve fonksiyonel olarak adlandırılan bu endotiplerin tıkayıcı koroner arter lezyonu olmayan hastalarda miyokardiyal iskemiden sorumlu olduğu düşünülmektedir. Yapısal mikrovasküler disfonksiyonda istirahatte koroner kan akımı normaldir fakat fizyolojik

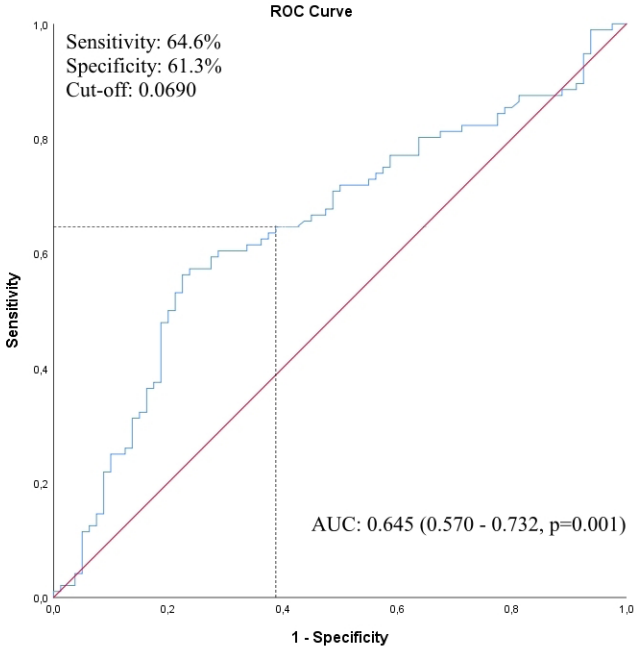
**Tablo 1.** Hastaların demografik, klinik ve laboratuvar özellikleri

| Değişkenler | Toplam (121) | Kontrol (75) | MVA (46) | p |
|---|---|---|---|---|
| Yaş | 61.1 ± 8.9 | 62.2 ± 8.8 | 60.2 ± 9.0 | 0.136 |
| Kadın cinsiyet, n (%) | 90 (51.1) | 46 (57.5) | 44 (45.8) | 0.123 |
| Hipertansiyon, n (%) | 109 (61.9) | 55 (68.8) | 54 (56.3) | 0.089 |
| Diabetes mellitus, n (%) | 67 (38.1) | 30 (37.5) | 37 (38.5) | 0.887 |
| Sigara, n (%) | 56 (32.5) | 26 (32.5) | 30 (31.3) | 0.859 |
| ACEi, n (%) | 103 (58.5) | 53 (66.3) | 50 (52.1) | 0.058 |
| Beta bloker, n (%) | 116 (65.9) | 56 (70.0) | 60 (62.5) | 0.296 |
| Statin, n (%) | 51 (29) | 29 (36.3) | 22 (22.9) | 0.052 |
| Lökosit x1000/uL | 7.38 ± 1.85 | 7.40 ± 2.01 | 7.36 ± 1.71 | 0.895 |
| Lenfosit, x1000/uL | 2.15 ± 0.68 | 2.25 ± 0.76 | 2.07 ± 0.61 | 0.079 |
| Nötrofil x1000/uL | 4.63 ± 1.56 | 4.57 ± 1.72 | 4.68 ± 1.43 | 0.653 |
| Monosit x1000/uL | 0.42 ± 0.14 | 0.43 ± 0.14 | 0.41 ± 0.14 | 0.451 |
| Eozinofil x1000/uL | 0.17 ± 0.12 | 0.14 ± 0.09 | 0.20 ± 0.14 | 0.004 |
| Trombosit, x1000/uL | 271.7 ± 78.0 | 283.4 ± 85.1 | 261.9 ± 70.6 | 0.068 |
| Kreatinine, mg/dL | 0.85 ± 0.19 | 0.85 ± 0.19 | 0.84 ± 0.19 | 0.964 |
| Total Kolesterol mg/dl | 182.9 ± 39.5 | 181.3 ± 43.4 | 184.2 ± 36.1 | 0.639 |
| Trigliserid mg/dl | 175.3 ± 102.8 | 171.6 ± 95.5 | 178.4 ± 108 | 0.667 |
| LDL mg/dl | 105.7 ± 33.6 | 104.9 ± 35.0 | 106.4 ± 32.5 | 0.769 |
| HDL mg/dl | 44.1 ± 11.6 | 44.2 ± 13.2 | 44.1 ± 10.1 | 0.970 |
| Ürik asit mg/dl | 5.4 ± 1.4 | 5.4 ± 1.5 | 5.4 ± 1.4 | 0.969 |
| ELR | 0.090 ± 0.080 | 0.068 ± 0.048 | 0.108 ± 0.102 | **0.002** |

ELR: Eozinofil/lenfosit oranı, ACE: Anjiotensin dönüştürücü enzim, uL: Unit load, mg/dL: miligram desilitre, LDL: düşük yoğunluklu lipoprotein, HDL: yüksek yoğunluklu lipoprotein

Bozok Tıp Derg 2023;13(3):73-80
Bozok Med J 2023;13(3):73-80

**Şekil 1.** Mikrovasküler anjina ile eozinofil/lenfosit oranı (ELR) arasındaki ilişkiyi gösteren ROC eğrisi




strese yanıt olarak koroner kan akımı yeterli oranda artmaz ve iskemiye sebep olur. Bunun mikrovasküler hipertrofi, fibrozis ve kapiller yatakta seyrekleşme gibi yapısal değişikler nedeniyle olduğu düşünülmektedir. Bu hastalarda adenozin gibi endotel aracılı olmayan vazodilatörler ile koroner akım rezervi (CFR) azalma ve mikrovasküler rezistansta artış izlenir. Ayrıca vazokonstriktör ajanlara karşı hipersensitivite tespit edilmiştir. Bu hastalar daha çok kontrolsüz hipertansiyon, tip 2 Diyabetes Mellitus, efor ilişkili hipertansiyon gibi aterosklerotik risk faktörlerine sahiptir. Fonksiyonel mikrovasküler disfonksiyon ise daha çok akım aracılı vazodilatasyonun baskın olduğu orta-geniş çaplı arteriollerde görülür. Fizyolojik şartlarda metabolik ihtiyaç arttığında öncelikli olarak distal arteriollerde vazodilatasyon başlar ve epikardiyal koroner arterlere doğru yukarı yönlü devam eder. Fonksiyonel tip mikrovasküler disfonksiyonda akım aracılı vazodilatasyon endotel disfonksiyonu nedeniyle bozulur ve yetersiz vazodilatasyon ya da paradoks vazokonstriksiyona neden olur. Bu hastalara intrakoroner asetilkolin verildiğinde vazodilatör cevapta azalma (istirahat akımdan <1,5 kat artış), epikardiyal vazospazm olmaksızın no-reflow'a benzer kan akımında belirgin azalma, yine spazm olmaksızın distal epikardiyal damarlarda diffüz daralma tespit edilmiştir (9, 22, 23). Patofizyolojik olarak birçok nokta aydınlatılmış gibi görülse de koroner mikro-sirkülasyonda bu yapısal ve fonksiyonel değişikliklere sebep olan faktörler halen tam olarak tespit edilememiştir. Ancak hiperglisemi, insulin direnci, oksidatif stres ve kronik inflamasyon; sigara, yaş, hiperlipidemi, hipertansiyon gibi geleneksel aterosklerotik risk faktörlerinden sonra en önemli risk faktörleri olarak görünmektedir (9, 24). Recio-mayoral ve ark. yaptığı çalışmada aterosklerotik risk faktörü olmayan ve kronik inflamatuar hastalık (sistemik lupus eritematozus ve romatoid artrit) tanısı ile takip edilen, KAG normal ya da normale yakın olan hastalarda pozitron emisyon tomografisi (PET) ile miyokard kan akımı (MBF) ölçülmüş ve koroner akım rezervinde (CFR) anlamlı azalma tespit edilmiş. Bu hastalarda CFR'daki azalmanın hastalık aktivitesi ve hastalık süresi ile ilişkili olduğu gösterilmiştir (25). Çeşitli inflamatuar belirteçler mikrovasküler anjina tanısı alan hastalarda çalışılmıştır ve normal popülasyon ile karşılaştırıldığında bu hastalarda daha yüksek olduğu tespit edilmiştir.

Bozok Tıp Derg 2023;13(3):73-80
Bozok Med J 2023;13(3):73-80

Lanza ve ark. yaptığı çalışmada kardiyak sendrom X tanısı almış hastalarda C- reaktif protein (CRP) ve interlökin-1 seviyelerinin normal sağlıklı bireylere göre daha yüksek olduğunu göstermiştir (26). Bu çalışma sistemik inflamasyonun bu hastalarda patogenezde bir rol oynadığı hipotezini desteklemektedir. Yine yakın zamanda yapılan çalışmalarda interlökin-6, tümör nekrozis faktör alfa, pentraksin-3 gibi inflamatuar belirteçlerin mikrovasküler anjina hastalarında normal popülasyondan daha yüksek olduğu tespit edilmiş ve kronik inflamasyonun koroner mikrovasküler disfonksiyon etyopatogenezindeki önemi daha da iyi anlaşılmıştır (27-29).

Son yıllarda rutin biyokimya ve tam kan analizlerinden türetilen inflamatuar belirteçler popülerlik kazanmıştır. Ek maliyet yükü olmaksızın, kolay hesaplanabilir parametreler olduğundan ve kullanım kolaylığı sağladığından birçok alanda klinik olarak hem tanısal hem de prognostik önemi kanıtlandığından yaygın olarak kullanılmaktadırlar. Bu parametrelerden nötrofil/lenfosit oranı, monosit/yüksek dansiteli lipoprotein oranı ve sistemik immün inflamatuar indeks koroner mikrovasküler disfonksiyonu olan hastalarında çalışılmış ve normal sağlıklı bireyler ile karşılaştırıldığında anlamlı olarak yüksek bulunmuştur (30-32). Bizim çalışmamızda da daha önceki çalışmalara benzer olarak mikrovasküler anjina hastalarında inflamatuar bir belirteç olan ELR normal sağlıklı bireyler ile karşılaştırıldığında anlamlı olarak yüksek tespit edilmiştir (p = 0,002).

Eozinofiller, alerjik hastalıklar, tümör bağışıklığı doku hasarı, bakteriyel, viral ve parazitik enfeksiyonlar dahil olmak üzere çok sayıda inflamatuar sürecin patogenezinde rol oynayan çok işlevli lökositlerdir (15). Özellikle kardiyovasküler sistem üzerinde önemli etkileri olduğu bilinmektedir. Yapılan çalışmalarda endotel disfonksiyonu, vazospazm ve artmış trombojenite ile ilişkili olduğu gösterilmiştir (16, 33). Eozinofillerin salgıladıkları sitotoksik granül proteinler vasküler hasardan sorumludur. Major basic protein-1 eozinofil granüllerinin temel proteinidir, eozinofilik katyonik protein (ECP), eozinofilik peroksidaz (EPO) ve eozinofil derive nörotoksin (EDN) diğer önemli granül proteinleridir. Eozinofiller ayrıca lökotrienler (LTB4 ve LTC4) ve platelet aktive faktör (PAF) gibi lipid mediatörler salgılarlar. Ayrıca çok çeşitli sitokin ve kemokinleri de üretebilirler. Eozinofiller doku faktörü salgılayarak, trombosit ve diğer lökositleri uyararak tromboza meyil yaratır ayrıca majör basic protein1 (MBP-1) ve ECP trombositleri aktive eder, trombomodulini inhibe eder ve trombüs oluşumunu destekler(16). ECP seviyesinin hem çıplak hem de ilaç kaplı stentlerde tromboz ve advers kardiyak olaylarla ile ilişkili olduğu yapılan çalışmalarda gösterilmiştir (34, 35). Umemoto ve ark. yaptığı çalışmada vazospastik anjina pektorisi olan hastalarda eozinofil seviyesinin hem stabil anjina pektorisi olan hem de normal sağlıklı bireylere göre daha yüksek olduğu ortaya konmuştur (33). Yine Erdoğan ve ark. yaptığı çalışmada anjina pektorisli hastalarda eozinofil seviyelerinin normal kontrol grubuna göre anlamlı olarak yüksek tespit edilmiştir (36).

Tüm bu veriler ışında koroner mikrovasküler disfonksiyon patogenezinde eozinofillerin de rolü olduğu tahmin edilebilir. Demir ve ark yaptıkları çalışmada sendrom X hastalarında eozinofil seviyesinin normal popülasyona göre yüksek olduğunu göstermiştir ki bizim çalışmamız da bunu desteklemektedir (37).

Sistemik dolaşımda polimorfonükleer lökosit artışı ile birlikte mononükleer lökosit (monosit ve lenfosit) sayısında azalma artmış kardiyovasküler riski ile ilişkili bulunmuştur (17, 38). Artmış eozinofil seviyesi ile birlikte azalmış lenfosit seviyesi sistemik inflamasyonun bir göstergesidir ve yine endotel disfonksiyonu ile birlikte seyreden koroner yavaş akım, koroner ektazi ile ilişkisi gösterilmiştir (20, 39).

## SONUÇ

Bu çalışmamızda mikrovasküler anjina tanısı almış hastalarda ELR'nın sağlıklı bireylere göre anlamlı olarak daha yüksek olduğunu tespit ettik. Daha önce yapılan çalışmalarda mikrovasküler anjinanın kronik inflamasyon ile ilişkisi gösterilmiştir. Eozinofiller karmaşık hücrelerdir klasik inflamatuar yanıtın yansıra hipersensitivite ve şiddetli protrombotik etkileri vardır. Mikrovasküler disfonksiyonda her iki endotipin patofizyolojisini incelediğimizde eozinofillerin bu mekanizma içinde önemli rolü olabileceği hipotezimizin çıkış noktası olmuştur. Sonuçlarımız hipotezimizi desteklemekle birlikte çalışmamızın kısıtlılıkları da mevcuttur. Koroner akım rezervinin kantitatif olarak ölçülmemesi çalışmamızın en önemli kısıtlılığıdır.

Retrospektif tasarım ve hasta sayısının az olması diğer önemli kısıtlılıklardır. Mikrovasküler disfonksiyon hastalarının tedavi sonrası takibinin yapılması, tedaviden fayda gören ve görmeyen hastaların kontrol kan parametrelerinin incelenmesi, daha büyük çaplı randomize çalışmalar ile hipotezimizin desteklenmesi gerekmektedir.

## TASDİK VE TEŞEKKÜR

Yazarlar arasında herhangi bir çıkar çatışmamız bulunmamaktadır.
Çalışmamız için herhangi bir finansal destek alınmamıştır.

## KAYNAKLAR

**1**. Shaw LJ, Shaw RE, Merz CNB, Brindis RG, Klein LW, Nallamothu B, et al. Impact of Ethnicity and Gender Differences on Angiographic Coronary Artery Disease Prevalence and In-Hospital Mortality in the American College of Cardiology–National Cardiovascular Data Registry. Circulation. 2008;117:1787-801.

**2.** Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, et al. Low Diagnostic Yield of Elective Coronary Angiography. New England Journal of Medicine. 2010;362:886-95.

**3.** Likoff W, Segal BL, Kasparian H. Paradox of Normal Selective Coronary Arteriograms in Patients Considered to Have Unmistakable Coronary Heart Disease. New England Journal of Medicine. 1967;276:1063-6.

**4.** Kemp HG, Elliott WC, Gorlin R. The anginal syndrome with normal coronary arteriography. Trans Assoc Am Physicians. 1967;80:59-70.

**5.** Ong P, Camici PG, Beltrame JF, Crea F, Shimokawa H, Sechtem U, et al. International standardization of diagnostic criteria for microvascular angina. International Journal of Cardiology. 2018;250:16-20.

**6.** Parsyan A, Pilote L. Cardiac Syndrome X: Mystery Continues. Canadian Journal of Cardiology. 2012;28:S3-S6.

**7.** Melikian N, De Bruyne B, Fearon WF, MacCarthy PA. The Pathophysiology and Clinical Course of the Normal Coronary Angina Syndrome (Cardiac Syndrome X). Progress in Cardiovascular Diseases. 2008;50:294-310.

**8.** Camici PG, Crea F. Coronary Microvascular Dysfunction. New England Journal of Medicine. 2007;356:830-40.

**9.** Kunadian V, Chieffo A, Camici PG, Berry C, Escaned J, Maas AHEM, et al. An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. European Heart Journal. 2020;41:3504-20.

**10.** Pruthi S, Siddiqui E, Smilowitz NR. Beyond Coronary Artery Disease: Assessing the Microcirculation. Interventional Cardiology Clinics. 2023;12:119-29.

**11.** Mejía-Rentería H, van der Hoeven N, van de Hoef TP, Heemelaar J, Ryan N, Lerman A, et al. Targeting the dominant mechanism of coronary microvascular dysfunction with intracoronary physiology tests. The International Journal of Cardiovascular Imaging. 2017;33:1041-59.

**12.** Sara JD, Widmer RJ, Matsuzawa Y, Lennon RJ, Lerman LO, Lerman A. Prevalence of Coronary Microvascular Dysfunction Among Patients With Chest Pain and Nonobstructive Coronary Artery Disease. JACC: Cardiovascular Interventions. 2015;8:1445-53.

**13.** Konst RE, Elias-Smale SE, Lier A, Bode C, Maas AH. Different cardiovascular risk factors and psychosocial burden in symptomatic women with and without obstructive coronary artery disease. European Journal of Preventive Cardiology. 2020;26:657-9.

**14.** Zanatta E, Colombo C, D'Amico G, d'Humières T, Dal Lin C, Tona F. Inflammation and Coronary Microvascular Dysfunction in Autoimmune Rheumatic Diseases. International Journal of Molecular Sciences. 2019;20:5563.

**15.** Kounis NG, Soufras GD, Tsigkas G, Hahalis G. White Blood Cell Counts, Leukocyte Ratios, and Eosinophils as Inflammatory Markers in Patients With Coronary Artery Disease. Clinical and Applied Thrombosis/Hemostasis. 2015;21:139-43.

**16.** Wang J-G, Mahmud SA, Thompson JA, Geng J-G, Key NS, Slungaard A. The principal eosinophil peroxidase product, HOSCN, is a uniquely potent phagocyte oxidant inducer of endothelial cell tissue factor activity: a potential mechanism for thrombosis in eosinophilic inflammatory states. Blood. 2006;107:558-65.

**17.** Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which White Blood Cell Subtypes Predict Increased Cardiovascular Risk? Journal of the American College of Cardiology. 2005;45:1638-43.

**18.** Holub K, Biete A. New pre-treatment eosinophil-related ratios as prognostic biomarkers for survival outcomes in endometrial cancer. BMC Cancer. 2018;18:1280.

**19.** Vural A, Aydın E. The Predictive Value of Eosinophil Indices for Major Cardiovascular Events in Patients with Acute Decompensated HFrEF. Medicina. 2022;58:1455.

**20.** Tosu AR, Kalyoncuoğlu M, Biter Hİ, Çakal S, Çakal B, Selçuk M, et al. Association of eosinophil-to-lymphocyte ratio with coronary slow-flow phenomenon in patients undergoing coronary angiography. Archives of Medical Science – Atherosclerotic Diseases. 2022;7:29-35.

**21.** Duncker DJ, Koller A, Merkus D, Canty JM. Regulation of Coronary Blood Flow in Health and Ischemic Heart Disease. Progress in

Cardiovascular Diseases. 2015;57:409-22.

**22.** Rahman H, Ryan M, Lumley M, Modi B, McConkey H, Ellis H, et al. Coronary Microvascular Dysfunction Is Associated With Myocardial Ischemia and Abnormal Coronary Perfusion During Exercise. Circulation. 2019;140:1805-16.

**23.** Rahman H, Demir OM, Khan F, Ryan M, Ellis H, Mills MT, et al. Physiological Stratification of Patients With Angina Due to Coronary Microvascular Dysfunction. Journal of the American College of Cardiology. 2020;75:2538-49.

**24.** Sinha A, Rahman H, Perera D. Coronary microvascular disease: current concepts of pathophysiology, diagnosis and management. Cardiovascular Endocrinology & Metabolism. 2021;10:22-30.

**25.** Recio-Mayoral A, Mason JC, Kaski JC, Rubens MB, Harari OA, Camici PG. Chronic inflammation and coronary microvascular dysfunction in patients without risk factors for coronary artery disease. European Heart Journal. 2009;30:1837-43.

**26.** Lanza GA, Sestito A, Cammarota G, Grillo RL, Vecile E, Cianci R, et al. Assessment of systemic inflammation and infective pathogen burden in patients with cardiac syndrome X. The American Journal of Cardiology. 2004;94:40-4.

**27.** Wöhrle J, Nusser T, Merkle N, Kestler HA, Grebe OC, Marx N, et al. Myocardial perfusion reserve in cardiovascular magnetic resonance: Correlation to coronary microvascular dysfunction. J Cardiovasc Magn Reson. 2006;8:781-7.

**28.** Tona F, Serra R, Di Ascenzo L, Osto E, Scarda A, Fabris R, et al. Systemic inflammation is related to coronary microvascular dysfunction in obese patients without obstructive coronary disease. Nutrition, Metabolism and Cardiovascular Diseases. 2014;24:447-53.

**29.** AlBadri A, Lai K, Wei J, Landes S, Mehta PK, Li Q, et al. Inflammatory biomarkers as predictors of heart failure in women without obstructive coronary artery disease: A report from the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE). PLOS ONE. 2017;12:e0177684.

**30.** Demirkol S, Balta S, Unlu M, Arslan Z, Cakar M, Kucuk U, et al. Neutrophils/Lymphocytes Ratio in Patients With Cardiac Syndrome X and Its Association With Carotid Intima–Media Thickness. Clinical and Applied Thrombosis/Hemostasis. 2014;20:250-5.

**31.** Dogan A, Oylumlu M. Increased monocyte-to-HDL cholesterol ratio is related to cardiac syndrome X. Acta Cardiologica. 2017;72:516-21.

**32.** Akın Y, Karasu M, Deniz A, Mirzaoğlu Ç, Bolayır HA. Predictive value of the systemic immune inflammatory index in cardiac syndrome x. BMC Cardiovascular Disorders. 2023;23:146.

**33.** Umemoto S, Suzuki N, Fujii K, Fujii A, Fujii T, Iwami T, et al. Eosinophil counts and plasma fibrinogen in patients with vasospastic angina pectoris. American Journal of Cardiology. 2000;85:715-9.

**34.** Niccoli G, Schiavino D, Belloni F, Ferrante G, La Torre G, Conte M, et al. Pre-intervention eosinophil cationic protein serum levels predict clinical outcomes following implantation of drug-eluting stents. European Heart Journal. 2009;30:1340-7.

**35.** Niccoli G, Sgueglia GA, Conte M, Cosentino N, Minelli S, Belloni F, et al. Eosinophil cationic protein and clinical outcome after bare metal stent implantation. Atherosclerosis. 2011;215:166-9.

**36.** Erdogan O, Gul C, Altun A, Ozbay G. Increased Immunoglobulin E Response in Acute Coronary Syndromes. Angiology. 2003;54:73-9.

**37.** Demir M, Şentürk M, Kuzeytemiz M. The Relationship Between Eosinophil and Cardiac Syndrome X. Clinical and Applied Thrombosis/Hemostasis. 2015;21:325-8.

**38.** Ommen SR, Gibbons RJ, Hodge DO, Thomson SP. Usefulness of the Lymphocyte Concentration as a Prognostic Marker in Coronary Artery Disease. The American Journal of Cardiology. 1997;79:812-4.

**39.** Gözel N, Korkmaz H, Eroğlu O, Uku Ö, Ertuğrul K, Bilen MN, et al. A new inflammatory marker : elevated eosinophil-to-lymphocyte ratio associated with presence and severity of isolated coronary artery ectasia. Cardiovascular Journal of Africa. 2020;31:227-35.

# THE EFFECT OF IMAGERY TECHNIQUE ON SELF - EFFECTIVENESS – EFFICACY AND ANXIETY LEVELS OF NURSING STUDENTS

## İmgeleme Tekniğinin Hemşirelik Öğrencilerinin Öz Yeterlilik - Yeterlilik ve Kaygı Düzeylerine Etkisi

Betul KUS[1], Ozlem SAHIN AKBOGA[1], Gulay YILMAZ[1]

[1]Department of Nursing, Faculty of Health Sciences, Yozgat Bozok University, Yozgat, Türkiye

Betul KUS, Dr. Öğr. Ü. (0000-0001-7828-2050)
Ozlem SAHIN AKBOGA, Öğr. Gör. (0000-0002-6767-4195)
Gulay YILMAZ, Dr. Öğr. Ü. (0000-0002-1386-9018)

**İletişim:**
Dr. Öğr. Ü. Betul KUS
Department of Nursing, Faculty of Health Sciences, Yozgat Bozok University, Yozgat, Türkiye.

**Geliş tarihi/Received:** 07.08.2023
**Kabul tarihi/Accepted:** 12.09.2023
**DOI:** 10.16919/bozoktip.1339226

Bozok Tıp Derg 2023;13(3):81-89
Bozok Med J 2023;13(3):81-89

## ABSTRACT

**Objective:** To determine the effect of the imagery technique used in the Nursing Fundamentals course on the self-effectiveness–efficacy and anxiety levels of students.

**Material and Methods:** This study was designed as a randomized controlled trial. The research was completed with a total of 85 students, 40 of whom were in the intervention group and 45 in the control group. The imagery technique was applied to the intervention group once a week for 4 weeks before the laboratory practice lesson. This study are self-efficacy-sufficiecy and state and trait anxiety levels obtained from the questionnaire before and after the application.

**Results:** While there was no difference in the mean scores of self-efficacy-sufficiecy and trait anxiety of the students before and after the application of the imagery technique (p=0.515, p=0.456), it was determined that the mean score of state anxiety of the students in the intervention group decreased significantly after the application (p=0.044).

**Conclusion:** Academic nurses should work on increasing self-efficacy and reducing the level of trait anxiety, in addition to the supportive imagery technique during training.

**Keywords:** *Anxiety; Imagery; Nursing; Student; Self - Efficacy - Sufficiecy*

## ÖZET

**Amaç:** Hemşirelik Esasları dersi laboratuvar uygulamasında kullanılan imgeleme tekniğinin hemşirelik bölümü ikinci sınıf öğrencilerinin öz etkililik-yeterlik ve anksiyete düzeyine etkisini belirlemektir.

**Gereç ve Yöntemler:** Bu araştırma, müdahale (40 öğrenci) ve kontrol gruplu (45 öğrenci), ön-test ve son-test uygulamalı, randomize kontrollü çalışma olarak tasarlandı. Veriler, "Kişisel Bilgi Formu" ve "Öz Etkililik-Yeterlik Ölçeği, Durumluk ve Sürekli Kaygı Ölçeği" ile toplandı.

**Bulgular:** İmgeleme tekniği uygulaması sonrası öğrencilerin öz etkililik-yeterlik ile sürekli kaygı puan ortalamaları açısından gruplar arasında farklılık saptanmadı (p=0,515, p=0,456). İmgeleme tekniği uygulaması sonrasında ise öğrencilerin durumluk kaygı puan ortalamaları incelendiğinde gruplar arasında farklılık olduğu ve bu farkın istatiksel olarak anlamlı olduğu saptandı (p<0,05).

**Sonuç:** Uzun süren psikomotor beceri öğretiminde yaşanan kaygı, hemşirelik öğrencilerinin öğrenme düzeyini ve performansı etkilemektedir. Akademisyen hemşireler, hemşirelik öğrencisinin yaşadığı kaygının farkında olmalıdır. Öz etkililiği-yeterliliği arttırmak ve sürekli kaygı düzeyini azaltmak için destekleyici tekniklere yönelik çalışmalar yapılmalıdır.

**Anahtar Kelimeler:** *Kaygı; İmgeleme; Hemşirelik; Öğrenci; Öz Etkililik; Yeterlilik*

## INTRODUCTION

Nursing is a profession that deals with all kinds of care, treatment and rehabilitation services of healthy/sick individuals and their families. Nurses have comprehensive roles within the healthcare system, and they can identify various physical, psychological and social problems in the groups they serve (1). To overcome these problems, nurses need to be prepared during their education and supported in their working life.

During their education, nurses undergo a challenging process of theory and skill applications (2-4).

Besides their general concerns about life, this process is another stressor for the nursing students. They are expected to acquire, develop and use high-level skills such as communication, observation, situation-specific care, critical thinking, problem solving, critical decision making, emergency response and coping with stress. Nursing skills are gained through practice, trial and experience. Many of these skills should be acquired by nurses during their education. However, studies have shown that nursing students face many problems while developing their clinical skills. It has been found that people (such as nurses/educators/patients/patient relatives), educational environment, personal characteristics of the students, quality of education and students' perceptions of clinical learning are effective in acquiring the clinical skills (5). However, nursing students face many issues such as feeling inadequate, having anxiety about making mistakes, insufficient focus, decrease in clinical performance, decrease in professional values, exposure to stressors in clinical settings, burnout, difficulty in coping, difficulty in combining theoretical knowledge with practical skills and lack of clinical support (6-10). It has been found that nursing students experience above-average stress. Furthermore, academic and practice stress levels have been found to be associated with professional development and professional satisfaction (11). A similar relationship has also been found between the following: educational programmes and self-confidence and anxiety, healthy life behaviours and self-efficacy, self-efficacy, hope and learned resourcefulness, emotional intelligence, clinical communication and self-efficacy, and well-being and self-efficacy (12-16). In this context, individuals with self-efficacy and self-effectiveness believe that they can create change in various events in life, cope with events effectively, initiate the necessary actions to bring about change and obtain positive results from these actions. Nursing education includes hands-on learning experiences. Therefore, students need to develop self-effectiveness–efficacy so that they can create a roadmap during nursing education and use cognitive strategies correctly during skill training (17). Such an approach will help reduce perceived anxiety during acquiring and developing new skills.

Many methods can be used when teaching a new professional skill and when supporting individuals in newly encountered and difficult situations. One of these methods is imagery. Imagination is linked to human creativity. Imagery is how we animate and design an object, situation and/or entity by redefining it and concretising it in our minds. In other words, imagery is the ability to create an idea or image in our minds (18). Imagery supports the development of physical skills as well as mental skills. In terms of ease of use, imagery can be applied at any point of time by a group or an individual in various contexts, such as lessons, sports, home–school–work environment and illness, to increase motivation, change behaviour and strengthen areas of shortcoming (19). Imagery contributes positively to increasing concentration, building self-confidence, improving learning skills, changing behaviour, controlling emotional reactions, success, learning and developing the ability to make the right decision, teamwork and cooperation (20). No studies in the literature have applied the imagery technique on nursing students to increase self-effectiveness and efficacy and decrease stress.

Nursing students need to be prepared and supported to tackle problems they will likely experience in the future. With this in mind, this research was conducted to determine the effect of imagery technique applied in practical courses on the self-effectiveness–efficacy and anxiety levels of the nursing students.

Research Hypotheses: H1: Imagery technique is effective in increasing the students' self-effectiveness–efficacy levels.

H2: Imagery technique is effective in reducing the anxiety level of the students.

Bozok Tıp Derg 2023;13(3):81-89
Bozok Med J 2023;13(3):81-89

## MATERIALS AND METHODS

This research was designed as a randomised controlled experimental study. The research included intervention (45 students) and control (45 students) groups, and a pre-test and post-test were applied.

The research population consisted of 90 second-year nursing students taking the 'Fundamentals of Nursing' course. Sample selection was not performed, and all students voluntarily participated in the study. In this study, 45 students were included in the intervention group and 45 students were included in the control group. In the intervention group, five students left the study because of insufficient participation in interventions. The study was completed with 40 students in the intervention group and 45 students in the control group (n = 85) (Figure 1).

The research was conducted between February 2021 and May 2022 with second-year students in the Nursing Department of the Faculty of Health Sciences of a state university in Türkiye. All students were taking the 'Fundamentals of Nursing' course. The course consisted of 6 hours of theory and 12 hours of practice, of which 8 hours of professional skill practices were performed in a clinical setting and the remaining 4 hours in a practice laboratory. In the skill practice laboratory, the students practised in groups of 8–12 covering the theoretical topic of the week. During this time, an instructor accompanied the students and demonstrated the application. The students were then asked to repeat the application until they could perform it without mistakes. In the fall semester of the 2021–2022 academic year, the 'Fundamentals of Nursing' course consisted of 6 hours of theoretical lectures on Wednesday, 8 hours of clinical practice on Thursday and 4 hours of laboratory practice on Friday.

To avoid bias and ensure homogeneity, male:female ratio was kept as close as possible between the groups and the students were assigned to groups by tossing a coin according to sex.

The students were informed about the purpose and scope of the study and the intervention. Students who volunteered to participate in the study were randomised into groups. Afterwards, 'Personal Information Form', 'Self-Effectiveness–Efficacy Scale' and 'State–Trait Anxiety Inventory' were distributed to all students as the pre-test.

Intervention group: The imagery technique was applied to the students in this group on the day of the laboratory practice, before the lesson, once a week for 4 weeks. The laboratory practice consisted of 6 weeks. Pre-test was performed on the first week, followed by 4 weeks of imagery technique, and the pre-test was performed on the final week. In each application of the imagery technique, four scenarios that could be encountered in clinical practice that required skill practice were used for 30 minutes (Table 1). The imagery technique was applied by the author who had expertise and training in nursing and imagery technique. The stages of the imagery technique included preparation of a suitable environment, preparation of the students, setting the background music (ney sound), relaxation, focusing on the technique, visualising the situation to be imagined, loading positive and constructive expressions on the individual, distracting the student from the imagined situation, relaxation and ending the session.

Control group: No intervention was performed on the students in this group. After the post-test, students in the control group were shown a video on imagery technique so that they would not feel excluded and less competent and also to reduce the possible bias among the students.

The data were collected twice, before and after the application of the imagery technique, using the 'Personal Information Form' prepared by the researchers in line with the relevant literature, 'Self-Effectiveness–Efficacy Scale'and 'State and Trait Anxiety Inventory'. (5, 13, 14, 21-24).

Personal Information Form: This form consisted of eight questions on age, sex, satisfaction with nursing, adequacy of training applications and causes of anxiety (5, 13, 14).

Self-Effectiveness–Efficacy Scale (SEES): SEES was developed by Sherer et al. and adapted to Turkish by Gözüm and Aksayan (21, 22). SEES is a 5-point Likert-type self-assessment scale that consists of 23 items (1=Does not describe me at all, 2=Describes me a little, 3=I am undecided, 4=Describes me well, 5=Describes me very well). SEES has four sub-dimensions: Initiating the behaviour (items 2, 11, 12, 14, 17, 18, 20 and 22), maintaining the behaviour (items 4, 5, 6, 7, 10, 16 and 19), completing the behaviour (CB, items 3, 8, 9, 15 and 23) and coping with obstacles

Bozok Tıp Derg 2023;13(3):81-89
Bozok Med J 2023;13(3):81-89

**Figure 1.** Flowchart of the randomized controlled trial

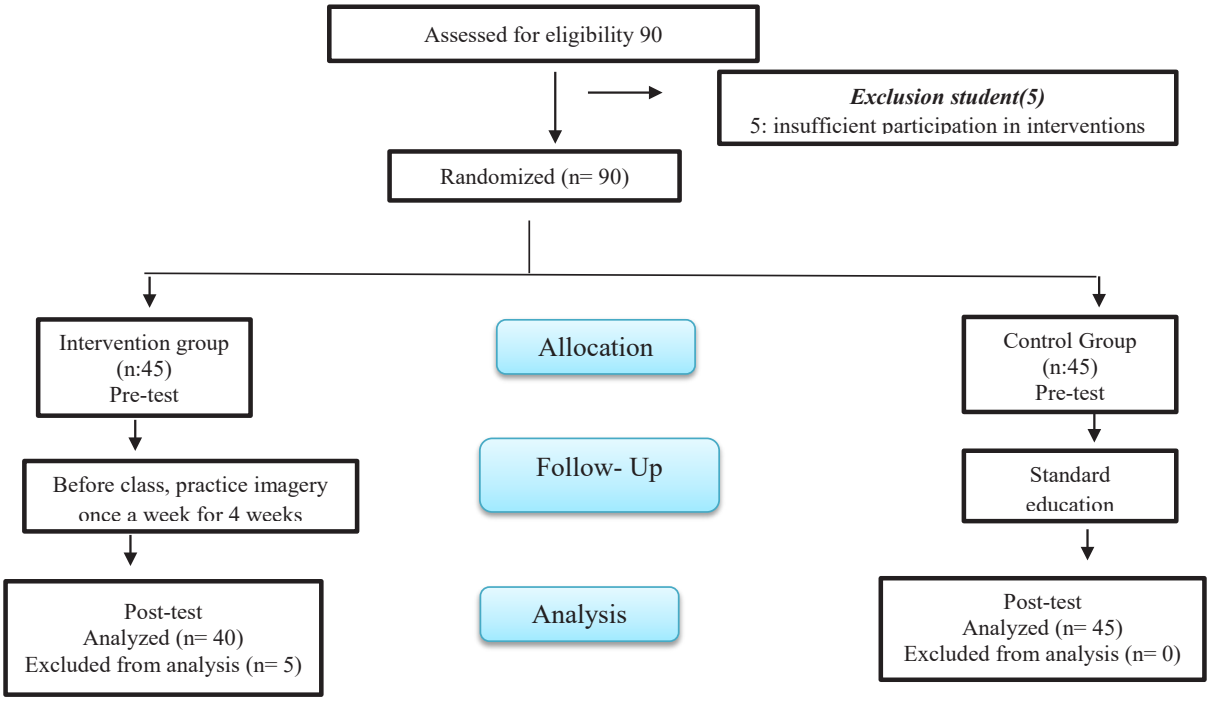



**Table 1.** Imagery Technique Session Topics

| Number of Sessions | Session Topic | Session Content |
|---|---|---|
| 1st session | Patient admission and measurement of vitals | The student initiates first communication with the patient and/or healthy individual, introduces himself/herself, meets the patient and performs the measurement of vitals by explaining it the individual. |
| 2nd session | Caring for a bedridden individual | The student gives information to a bedridden individual, explains something/interviews the individual while empathising with them and provides nursing care specific to the bedridden individual. |
| 3rd session | Interviewing an individual who is anxious due to respiratory distress and providing nursing care | The student becomes aware of the anxiety experienced by the individual suffering from respiratory distress due to chronic obstructive pulmonary disease, communicates with the patient and provides nursing care for respiratory distress. |
| 4th session | Providing nursing care to an individual with pain | The student evaluates the pain of the patient, prepares the treatment, informs the individual about pain and treatment, applies the treatment for pain and provides nursing care. |

(CO, items 1, 13 and 21). Items 2, 4, 5, 6, 7, 10, 11, 12, 14, 16, 17, 18, 20 and 22 are scored in reverse. A minimum of 23 and a maximum of 115 points can be obtained from the scale. A high total score indicates that the individual's self-effectiveness–efficacy perception is at a good level. The Cronbach's alpha value of the scale was 0.81 in the original study (21, 22). In the present research, the value was found to be 0.84 and 0.85 before and after the application, respectively.

State–Trait Anxiety Inventory (STAI): STAI was developed by Spielberger et al. and adapted to Turkish by Öner and Le Compte (25). STAI consists of 40 items and two sub-dimensions: state anxiety (items 1–20) and trait anxiety level (items 21–40). While the State Anxiety Inventory determines how the individual feels at a certain moment and under certain conditions, the Trait Anxiety Inventory determines how the individual generally feels. Both sub-dimensions are 4-point Likert-type scales. State Anxiety Inventory is scored according to the severity of experiences, as follows: 1=not at all, 2=somewhat, 3=moderately so and 4=very much so. Trait Anxiety Inventory, on the other hand, is scored according to the frequency of experiences, as follows: 1=almost never, 2=sometimes, 3=often and 4=almost always. Furthermore, 10 items (items 1, 2, 5, 8, 10, 11, 15, 16, 19 and 20) of the State Anxiety Inventory and 7 items (items 21, 26, 27, 30, 33, 36 and 39) of the Trait Anxiety Inventory are scored in reverse. The score that can be obtained from both scales ranges between 20 and 80. Higher scores indicate higher level of anxiety. The internal reliability coefficient of State Anxiety Inventory is between 0.94 and 0.96, while that of Trait Anxiety Inventory is between 0.83 and 0.87 (23, 24). In the present research, the Cronbach alpha value was found to be 0.92 and 0.89 for the State Anxiety Inventory before and after the application, respectively, and 0.81 for the Trait Anxiety Inventory before as well as after the application.

Data were analyzed using statistics software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0 Armonk, NY: IBM Corp). While evaluating the study data, the normal distribution of the data of numerical variables was evaluated with the Shapiro Wilk test of normality, as well as descriptive statistical methods (ratio, mean, standard deviation, median). Chi-square test was used to compare groups according to gender, and Mann-Whitney U test was used to compare groups according to age. Two-way analysis of variance was used in repeated measurements in the comparison of pretest-posttest scale scores between and within groups. Bonferroni correction was applied for multiple comparisons in two-way analysis of variance in repeated measures. The results were evaluated at the 95% confidence interval and the significance level was $p<0.05$. Institutional permission was obtained from the relevant health sciences faculty to conduct the study (Date: 11.11.2020). Ethical approval was obtained from the local ethics committee (Date: 11.11.2020 Decision No: 2017-KAEK-189_2020.11.11_03). Written consent was obtained from all participants in the study. The research was conducted in accordance with the Declaration of Helsinki.

## RESULTS

As shown in Table 2, 70.5% of the participants were women and the mean age was 19.89 ± 1.41 years. No significant difference was found between the groups in terms of age and sex (χ^2=0.202 p=0.653, t=1.555 p=0.538). The groups were similar in terms of descriptive characteristics (Table 2).

The mean SEES scores of the students in the intervention and control groups were 86.93 ± 13.18 and 88.93 ± 12.07, respectively, while the mean SEES scores of the students in the intervention and control groups after the application were 86.06 ± 12.18 and 88.15 ± 12.93, respectively. Accordingly, no significant difference was found between the SEES scores of the groups before and after the application (p=0.472, p=0.515). Furthermore, no significant difference was found in the intra-group comparisons before and after the application (p=0.788 for the intervention group, and p=0.272 for the control group) (Table 3).

The mean state anxiety scores of the intervention and control group were 40.09 ± 11.72 and 40.2 ± 11.87, respectively, while the mean trait anxiety scores were 45.16 ± 9.97 and 44.73 ± 12.57, respectively. No significant difference was found between the state and trait anxiety scores before the application (p=0.933, p=0.996), and the anxiety level of the students before the application was moderate.

After the application, the mean state anxiety scores

of the intervention and control groups were found to be 37.53 ± 9.28 and 41.75 ± 9.74, respectively. A statistically significant difference was found between the groups (p=0.044). In addition, no significant difference was found in the intra-group comparison of the state anxiety scores between the intervention and control groups (p=0.384, p=0.472).

After the application, the mean trait anxiety scores of the intervention and control groups were 41.33 ± 9.32 and 42.7 ± 7.21, respectively. No significant difference was found between the groups (p=0.456). In addition, no significant difference was found in the intra-group comparison of the trait anxiety scores between the intervention and control groups (p=0.216, p=0.367) (Table 4).

## DISCUSSION

This research was conducted to determine the effect of the imagery technique on the nursing students' self-effectiveness–efficacy and anxiety levels during skill teaching. The results showed that the students in the intervention and control groups had similar characteristics and that there was no significant difference between the groups (Table 1). Other studies using the imagery technique also reported descriptive characteristics similar to this results (25).

Self-effectiveness–efficacy is the perception of being able to complete an action successfully and being in control (26). The active participation of nursing students who are acquiring cognitive, psychomotor and affective skills in education and regular and systematic practice increase the level of success and self-efficacy (27,28).

High self-effectiveness–efficacy levels positively contribute to learning skills. In a previous study, it was determined that the clinical skill development of the students depended on their self-efficacy levels and that the students with high self-efficacy levels were very much successful in learning clinical skills (29). In this research, it was determined that the students in the intervention group had self-effectiveness–efficacy scores of 86.93 ± 13.18 before the application and 86.06 ± 12.18 after the application. Similarly, the students in the control group had self-effectiveness–efficacy scores of 88.93 ± 12.07 before the application and 88.15 ± 12.93 after the application (p>0.05). In parallel with

**Table 2.** Descriptive Characteristics of the Students (n: 85)

| Characteristics | | Intervention group (n: 40) | Control group (n: 45) | Test statistic | p |
|---|---|---|---|---|---|
| Sex | | | | | |
| Female | n (%) | 31 (68.2) | 29 (75.0) | : 0.202 | 0.653 |
| Male | n (%) | 14 (31.8) | 11 (25.0) | | |
| Age (years) | x ± SD | 19.66 ± 1.31 | 20.15 ± 1.49 | *U:* 1.555 | 0.538 |
| | Median (min–max) | 20 (18–27) | 20 (19–28) | | |

χ^2 : Chi square, U: Mann–Whitney U test, x ± SD: Arithmetic mean ± standard deviation

**Table 3.** Comparison of Self-Effectiveness–Efficacy Levels Between the Intervention and Control Groups (n: 85)

| Self-effectiveness–efficacy total score | | Intervention group | Control group | Test statistic [a] | p |
|---|---|---|---|---|---|
| Pre-test | x ± SD | 86.93 ± 13.18 | 88.93 ± 12.07 | 0.723 | 0.472 |
| | Median (min–max) | 90 (48–110) | 89 (56–114) | | |
| Post-test | x ± SD | 86.06 ± 12.18 | 88.15 ± 12.93 | 0.339 | 0.515 |
| | Median (min–max) | 92 (57–110) | 89.5 (60–110) | | |
| | Test statistic [b] | t: 0.270 | t: −1.112 | | |
| | p | 0.788 | 0.272 | | |

a Independent samples t-test b Paired-samples t-test, x ± SD: Arithmetic mean ± standard deviation

Bozok Tıp Derg 2023;13(3):81-89
Bozok Med J 2023;13(3):81-89

**Table 4.** Comparison of Anxiety Levels Between the Intervention and Control Groups (n: 85)

| Anxiety score | | | Intervention group | Control group | Test statistic | p |
|---|---|---|---|---|---|---|
| **State anxiety score** | | | | | | |
| Pre-test | x ± SD | 40.09 ± 11.72 | 40.2 ± 11.87 | | U: 890.500 | 0.933 |
| | Median (min–max) | 38 (23–74) | 37.5 (20–74) | | | |
| Post-test | x ± SD | 37.53 ± 9.28 | 41.75 ± 9.74 | | t: 2.043 | 0.044 |
| | Median (min–max) | 37 (20–61) | 40 (24–65) | | | |
| | Test statistic [b] | | z: 401.000 | −0.726 | | |
| | p | | 0.384 | 0.472 | | |
| **Trait anxiety score** | | | | | | |
| Pre-test | x ± SD | 45.16 ± 9.97 | 44.73 ± 12.57 | | U: 899.500 | 0.996 |
| | Median (min–max) | 44 (29–77) | 43.5 (23–80) | | | |
| Post-test | x ± SD | 41.33 ± 9.32 | 42.7 ± 7.21 | | t: 0.749 | 0.456 |
| | Median (min–max) | 42 (21–64) | 43 (24–62) | | | |
| | Test statistic [b] | | z: 370.500 | 0.912 | | |
| | p | | 0.216 | 0.367 | | |

U: Mann–Whitney U b Paired-samples t-test, z: Wilcoxon test, t: Independent samples t-test, x ± SD: Arithmetic mean ± standard deviation
*p < 0.05

our findings, Bramson et al. applied the imagery technique on medical students while practicing lumbar puncture and found no significant difference between the groups in terms of practice skills (25). It can therefore be argued that repeatedly practicing skills in the laboratory environment before clinical practice affects the students' self-efficacy perception positively. Nursing is a profession that heavily requires lifelong learning. Therefore, nurses can use the imagery technique to improve basic nursing practices.

In the present research, the mean state anxiety scores of the students in the intervention group before and after the application were 40.09 ± 11.72 and 37.53 ± 9.28, respectively, and the mean trait anxiety scores of the students in the control group before and after the application were 40.2 ± 11.87 and 41.75 ± 9.74, respectively. The state anxiety scores decreased significantly in the intervention group after the application of the imagery technique when compared with the control group ($p<0.05$). While a high level of anxiety negatively affects academic achievement, low level of anxiety also affects success negatively. In a previous study examining the relationship between academic achievement and anxiety, it was found that normal anxiety levels increased academic achievement (30). In another study, it was reported that as the knowledge level of individuals increased, anxiety levels decreased and they performed better (31). Studies examining the relationship between clinical practice and the anxiety level of nursing students reported that the anxiety levels were high before nurses performed a clinical practice for the first time and that it decreased gradually as they repeatedly performed the clinical practice (32-35). In this research, the level of anxiety decreased in intervention groups after skill practices in the laboratory. Consistent with the results of this research, three other studies also found that the anxiety levels of the students decreased after the mind-developing practices aimed at reducing anxiety (30, 31, 35). In a study examining the effect of the imagery technique on drawing blood, it was determined that the achievement level of the intervention group was significantly higher than that of the control group (27). Cognitive and psychomotor development of the mind in turn improve skill training practices.

The study includes university students in a particular region. Therefore, the results cannot be generalized to the whole population.These are the limitations of our study.

## CONCLUSION

The results of this study show that the imagery technique resulted in a significant decrease in the state anxiety levels of the nursing students, while the trait

anxiety and self-effectiveness–efficacy levels were not affected. There are only limited studies in the literature evaluating the effectiveness of imagery technique in basic skill practice training of the nursing students. Therefore, the results of this study are expected to contribute to the nursing profession. We recommend that the academic nurses develop various imagery technique applications for skill training based on the results of this study. The imagery technique should not replace the skill practice in the laboratory but rather serve as a supporting method for areas involving psychomotor learning, such as professional skill teaching in nursing. Since the results obtained in this research are limited to students in a single university, more comprehensive randomised controlled studies should be conducted to support and validate the findings.

## ACKNOWLEDGEMENTS

We would like to thank the Student Nurses Association for supporting us during the research process and all the nursing students who participated in the research. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.The authors declare that they have no conflict of interest, and that the content has not been published or submitted for publication elsewhere.

## REFERENCES

**1.** Noble H, Shorten A. Nursing issues. Evidence-Based Nursing. 2018; 21(1): 4-6.

**2.** Almasi K, Mansour Bavani S, Mohammadpour Y. Examining the preferred learning styles (PLSs) of nursing and midwifery students of Urmia University of Medical Sciences. World Family Medicine. 2018; 16(1): 241-4.

**3.** Park EJ, Kang H. Nurse educators' experiences with student incivility: A meta-synthesis of qualitative studies. Journal of Educational Evaluation for Health Professions. 2020; 17.

**4.** Carvalho EC, Oliveira-Kumakura ARS, Morais SCRV. Raciocínio clínico em enfermagem: Estratégias de ensino e instrumentos de avaliação. Rev Bras Enferm. 2017; 70(3): 662-8.

**5.** Arkan B, Ordin Y, Yılmaz D. Undergraduate nursing students' experience related to their clinical learning environment and factors affecting to their clinical learning process. Nurse Education in Practice. 2018; 29: 127-32.

**6.** Suarez-Garcia JM, Maestro-Gonzalez A, Zuazua-Rico D, Sánchez-Zaballos M, Mosteiro-Diaz MP. Stressors for Spanish nursing students in clinical practice. Nurse Education Today. 2018; 64: 16-20.

**7.** Smith GD, Yang F. Stress, resilience and psychological well-being in Chinese undergraduate nursing students. Nurse Education Today. 2017; 49: 90-5.

**8.** Ye Y, Hu R, Ni Z, Jiang N, Jiang X. Effects of perceived stress and professional values on clinical performance in practice nursing students: A structural equation modeling approach. Nurse Education Today. 2018; 71: 157-62.

**9.** Ching SS, Cheung K, Hegney D, Rees CS. Stressors and coping of nursing students in clinical placement: A qualitative study contextualizing their resilience and burnout. Nurse Education in Practice. 2020; 42: 102690.

**10.** Aydoğan S. Ethical problems of nursing students related to acquisition of clinical skills. Turk Journal Bioeth. 2016; 3: 120-3.

**11.** Yılmaz Karabulutlu E, Gündüz Oruç F, Bahçecioğlu Turan G. Effect of stress experienced by students during nursing education on their development of professional self-concept. Gümüşhane University Journal of Health Sciences. 2019; 8(1): 10- 7.

**12.** Günerigök F, Yılmaz Kurt F, Küçükoğlu S. Determination of nursing student's self-confidence and anxiety levels in the process of clinical decision making: Example of two different programs. Journal of Anatolia Nursing and Health Sciences. 2020; 23(1): 77-94.

**13.** Uz D, Kitiş Y. Determination of healthy life style behaviors and self-efficacy of nurses working in a hospital. Gazi University Journal of Health Sciences. 2017; 2(3): 27-39.

**14.** Bilgiç Ş, Münire Temel M, Ülfiye Çelikkalp Ü. Assessment of learned resourcefulness, self-efficacy and hope levels of nursing students: A case study Tekirdağ. Journal of Health and Nursing Management. 2017; 3(4): 117-26.

**15.** Zhu B, Chen CR, Shi ZY, Liang HX, Liu B. Mediating effect of self-efficacy in relationship between emotional intelligence and clinical communication competency of nurses. International Journal of Nursing Sciences. 2016; 3: 162-8.

**16.** Chen JH, Björkman A, Zou JH, Engström M. Self–regulated learning ability, metacognitive ability, and general self-efficacy in a sample of nursing students: A cross-sectional and correlational study. Nurse Education in Practice. 2019; 37: 15-21.

**17.** George LE, Locasto LW, Pyo KA, Cline T. Effect of the dedicated education unit on nursing student self-efficacy: A quasi-experimental research study. Nurse Education in Practice. 2017; 23: 48-53.

**18.** Karabulut N, Daşdemir F. Formation of art work in the context of image, imaging and imaging concepts. EKEV Academy Journal. 2020; 24(82): 231-44.

**19.** Karademir T, Türkçapar Ü, Açak M, Eroğlu H. Investigation of imagination patterns in athletes with individual and team sports.

Journal of Physical Education and Sport Sciences. 2018; 20(3): 92-102.

**20.** Dinçer Ö. The Evaluation of imagination ability of students who study sports education at universities. Education Science Society Journal. 2016; 14(55): 138-49.

**21.** Sherer M, Maddux JE, Mercandante B, Prentice-dunn S, Jacobs B, Rogers RW. The self-efficacy scale: Construction and validation. Psychological Reports. 1982; 51(2): 663-71.

**22.** Gözüm S, Aksayan S. Reliability and validity of the Turkish form of the Self-Efficacy-Efficacy Scale. Journal of Atatürk University School of Nursing. 1999; 2(1): 21-34.

**23.** Spielberger CD, Gorsuch RC, Luschene RE. Manual for the State-Trait Anxiety Invenntory. Consulting Psychologists Press. California. 1970.

**24.** Oner, N. and Le Compte, A. Durumluluk Surekli Kaygi Envanteri El Kitabi. Bogazici Universitesi Yayinlari, Istanbul, 1983; 1-26.

**25.** Sanders CW, Sadoski M, Bramson R, Wiprud R, Van Walsum K. Comparing the effects of mental imagery rehearsal and physical practice on learning lumbar puncture by medical students. Annals of Behavioral Science and Medical Education. 2004; 17(2): 3-6.

**26.** Bandura, A. Self-efficacy mechanism in human agency. American Psychologist. 1982; 37(2): 122.

**27.** Sanders CW, Sadoski M, Wasserman R, Wiprud R, English M, Bramson R Comparing the effects of physical practice and mental imagery rehearsal on learning basic venipuncture by medical students. Imagination, Cognition, and Personality. 2008; 27: 117-27.

**28.** Dikmen Y, Denat Y, Başaran H, Filiz NY. Investigation of self-efficacy-efficacy levels of nursing students. Journal of Contemporary Medicine. 2016; 6(3): 206-13.

**29.** León SP, Augusto-Landa, JM, García-Martínez I. Moderating factors in university students' self-evaluation for sustainability. Sustainability. 2021; 13(8); 4199.

**30.** Polat E. Academic achievement and its relationship with anxiety level and academic self-efficacy. Journal of Management and Economics Research. 2017; 15 (1): 1-22.

**31.** Al-Ghareeb A, McKenna L, Cooper S. The influence of anxiety on student nurse performance in a simulated clinical setting: A mixed methods design. International Journal of Nursing Studies. 2019; 98; 57-66.

**32.** Salim Bahrami SH, Jahan F, Asadzadeh Dehraei H, Asl SN. Effectiveness of mindfulness training on anxiety reduction as well as ımprovement of life quality and perceived academic control of students. Avicenna Journal of Neuro Psycho Physiology. 2020; 7(2): 69-76.

**33.** Taş B, Yörük A. The effect of anxiety training programs on student anxiety levels. The Journal of Academic Social Science. 2018; 6 (68): 126-7.

**34.** Özdemir H, Khorshid L, Zaybak A. Determination of nursing students' stress level toward nursing education. Turkish Journal of Science and Health. 2020; 1(2): 20-8.

**35.** Cornine, A. Reducing nursing student anxiety in the clinical setting: An integrative review. Nursing education perspectives. 2020; 41(4): 229-34.

# AN UNUSUAL PRESENTATION OF HUGE GASTRIC CYSTIC GASTROINTESTINAL STROMAL TUMOR

## Büyük Mide Kistik Gastrointestinal Stromal Tümörünün Olağandışı Bir Sunumu

Nihan TURHAN[1], Didem ERTORUL[1], Elbrus ZARBALIYEV[2], Şafak COŞKUN[3], Dilek YILMAZ[4]

[1]Şehit Prof. Dr. İlhan Varank Sancaktepe Training and Research Hospital, Department Of General Surgery İstanbul, Türkiye
[2]Department of General Surgery, Gaziosmanpaşa Hospital, Yeni Yüzyil University, İstanbul, Türkiye
[3]Marmara University Hospital, Department Of General Surgery, İstanbul, Türkiye
[4]Şehit Prof. Dr. İlhan Varank Sancaktepe Training and Research Hospital, Department Of Pathology, İstanbul, Türkiye

Nihan TURHAN, Uzm. Dr. (0000-0002-8672-3853)
Didem ERTORUL, Op. Dr. (0000-0003-4595-5938)
Elbrus ZARBALIYEV, Op. Dr. (0000-0002-4595-8314)
Şafak COŞKUN, Uzm. Dr. (0000-0001-8443-1497)
Dilek YILMAZ, Dr. (0000-0003-4193-4558)

**İletişim:**
Dr. Elbrus ZARBALIYEV
Department of General Surgery, Gaziosmanpaşa Hospital, Yeni Yüzyil University, İstanbul, Türkiye

**Geliş tarihi/Received:** 09.08.2022
**Kabul tarihi/Accepted:** 30.07.2023
**DOI:** 10.16919/bozoktip.1159004

Bozok Tıp Derg 2023;13(3):90-93
Bozok Med J 2023;13(3):90-93

## ABSTRACT

Gastrointestinal stromal tumors (GISTs) are nonepithelial, mesenchymal tumors arising from the interstitial cells of Cajal. The diagnostic tool for the GISTs is tyrosine kinase growth factor receptor (c-KIT / CD117) expression. They most commonly occur in the stomach. Here we reported a rare case of GIST, presenting as a large cystic mass connected to the main tumor with a peduncle. A 44-year-old female patient presented to the emergency department with abdominal pain and intestinal obstruction. Emergency laparotomy revealed a cystic mass of approximately 25 cm in diameter. The pathological diagnosis was gastrointestinal stromal tumor with cystic degeneration. Tumor contained areas of necrosis, high mitotic index, c-KIT positive and was large in diameter. Imatinib mesylate treatment was given. Cystic GISTs have poor prognostic factors and patients should be followed closely in the postoperative period.

**Keywords:** *Gastrointestinal Stromal Tumor, Intraabdominal Mass, Gastric Tumors*

## ÖZET

Gastrointestinal stromal tümörler (GİST'ler), interstisyel Kajal hücrelerinden kaynaklanan epitelyal olmayan, mezenkimal tümörlerdir. GİST'ler için tanı aracı tirozin kinaz büyüme faktörü reseptörü (c-KIT/CD117) ekspresyonudur. En sık midede görülürler. Bu çalışmada tümöre pedikül ile bağlı büyük bir kistik kitle olarak ortaya çıkan nadir bir GİST olgusunu sunduk. 44 yaşında kadın hasta karın ağrısı ve barsak tıkanıklığı şikayetleri ile acil servise başvurdu. Acil laparotomide yaklaşık 25 cm çapında kistik kitle saptandı. Patolojik tanı kistik dejenerasyonlu GİST idi. Tümör nekroz alanları içeriyordu. Yüksek mitotik indeks, c-KIT pozitif ve çap olarak büyüktü. Imatinib Mesilat tedavisi verildi. Kistik GİST'ler kötü prognostik faktörlere sahiptir ve postoperatif dönemde hastalar yakın takip edilmelidir.

**Anahtar Kelimeler:** *Gastrointestinal Stromal Tümör, İntrabdominal Kitle, Mide Tümörleri*

## INTRODUCTION

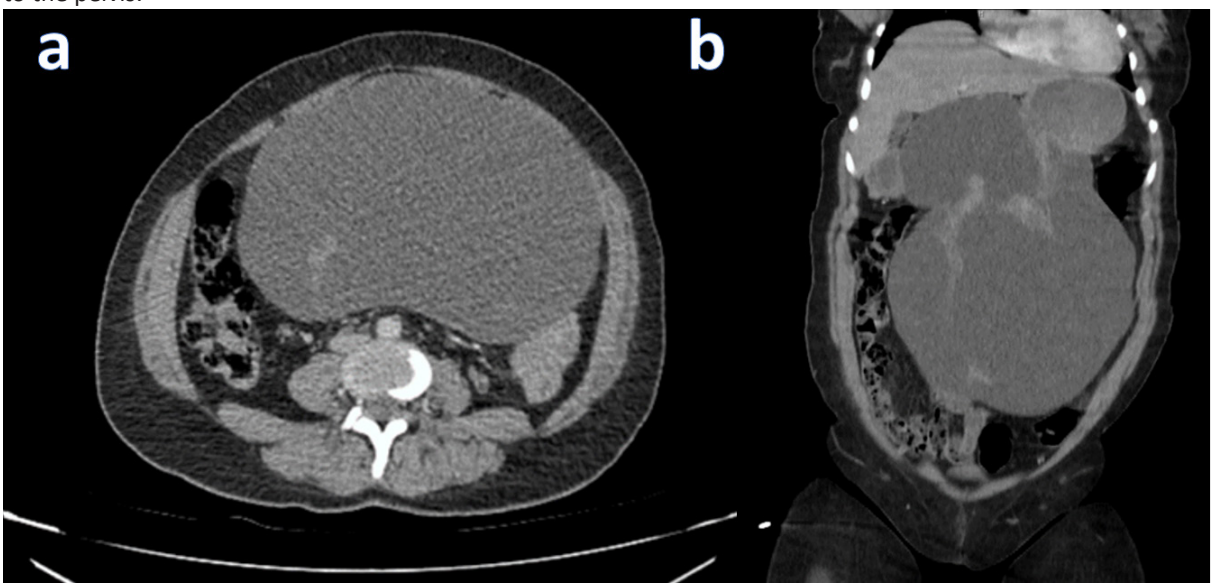
Gastrointestinal stromal tumors (GISTs) are nonepithelial, mesenchymal tumors arising from the interstitial cells of Cajal. These cells provide connection between myenteric and muscular layers in the gastrointestinal tract. Most of GISTs arise from muscularis propria and show extraluminal growth (1). GISTs are most commonly occur in the stomach (60-70%) (2). While stomach is the most common site for GISTs, pedunculated cystic GIST of stomach with extragastric growth presentation is very rare (3-5).We report a female patient with a giant gastric cystic GIST.

## CASE REPORT

A 44-year-old female patient presented to the emergency department with complaints of abdominal pain, swelling, nausea, and multiple bilious vomiting for the past few days. The patient was evaluated in the emergency room with the signs of intestinal obstruction. She was dehydrated, conscious, cooperative and oriented. Vital signs were blood pressure: 110/70 mmHg, pulse: 98/min, fever: 36.8 °C, respiratory rate: 20/min. On physical examination of the abdomen, there were distention, tenderness and defense. There were fullness filling the entire abdomen on palpation and dullness on percussion. There was intestinal content coming from the nasogastric tube inserted in the patient. In the rectal examination, there were no palpable mass and blood.

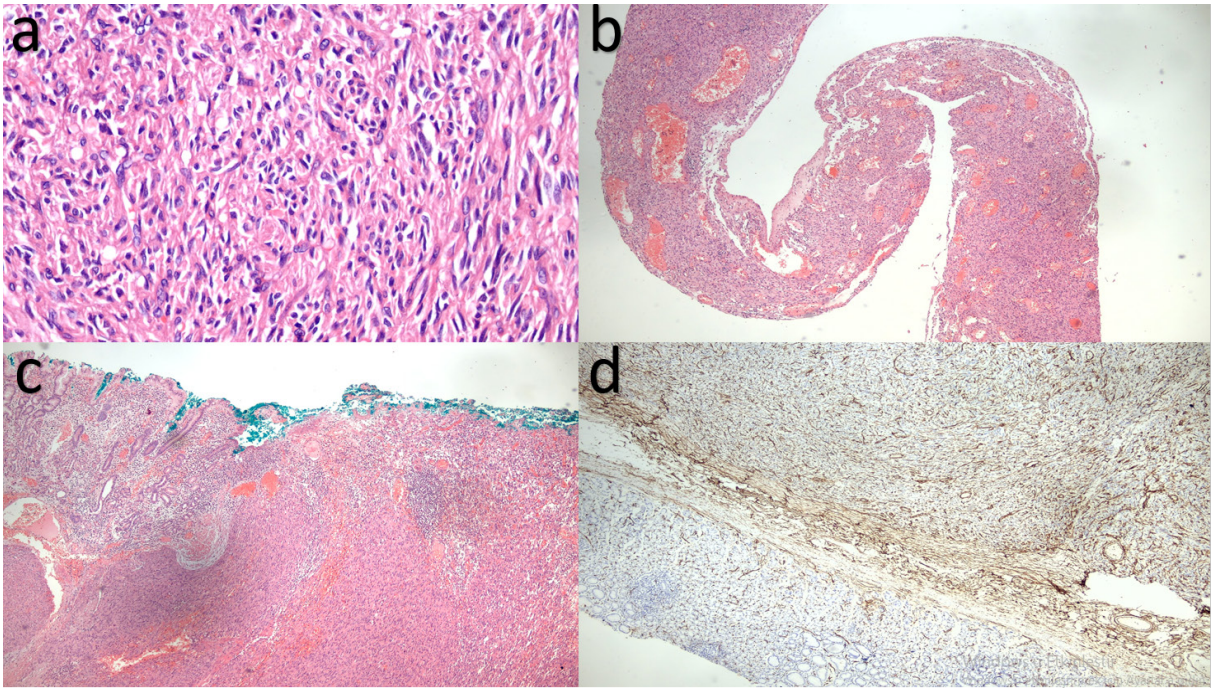
Hb was 9.7 g/dL (11.00-15.00), CRP: 93.9 mg/l (0-5). Leukocyte, thrombocyte, liver function tests, blood electrolytes, blood urea nitrogen and creatinine values were within normal limits. Abdominal computed tomography (CT) showed a septated cystic mass in the midline of the abdomen with a diameter of 25x16 cm, thought to be of mesenteric origin (Figure 1a, b). The patient was operated on urgently with those findings. The abdomen was entered by laparotomy with a midline incision. During the exploration, it was observed that there was a cystic mass of approximately 25 cm in diameter, located in the midline, extending from the stomach to the pelvis. This mass was associated with a mass of approximately 2 cm in diameter arising from the posterior corpus wall at the greater curvature of the stomach. Although the cystic mass had some adhesions with the surrounding omentum, there was no invasion to other surrounding organs. When the exploration was continued, it was observed that there was another mass of 2-3 cm in size, which was thought to originate from the stomach wall in the pre-pyloric part of the stomach. The cystic mass was removed en bloc by distal gastrectomy, including two palpable solid masses. Histopathological sections showed two tumoral masses, one of which showed cystic degeneration in the gastric wall. No infiltration into the surrounding tissue was observed. The cystic tumor was connected with a pedicle consisted of tumor cells. The resected tumors were 24.5x19x8 cm and 3x2x1.5 cm in size. The tumor cells had eosinophilic cytoplasm and round nuclei with spindle and epithelioid cell morphology. There was significant superficial ulceration in submucosa and mucosa layers of cystic mass. Mitosis of 20 / 50 HPF was noted (Figure 2 a, b, c). Immunohistochemistry showed CD 117, CD 34, DOG 1, SMA positive, Desmin & Myogenin negative (Figure 2d). Ki 67 proliferation index was 1%. Lateral, proximal and distal clean surgical margins were more than 1 cm. The diagnosis was gastrointestinal stromal tumor with cystic degeneration. The patient, who had no problems in the postoperative follow-up, was discharged on the 7th postoperative day with good recovery. No tumor was detected in any other area in the upper and lower gastrointestinal system endoscopy and positron emission tomography (PET-CT) performed in the postoperative period. As the patient's tumor was c-KIT positive, big in size and high mitotic index, the patient was started on Imatinib treatment.

**Figure 1.**
**a-** CT scan of 25x16 cm diameter cystic mass in the midline of abdomen
**b-** CT scan of 25x16 cm diameter septated cystic mass in the midline of abdomen extending from the stomach to the pelvis.



Bozok Tıp Derg 2023;13(3):90-93
Bozok Med J 2023;13(3):90-93

**Figure 2.**
**a-** GIST with spindle and epithelioid cell morphology H&E x200,
**b-** GIST with wall appearance in areas of cystic degeneration H&E x40,
**c-** GIST showing superficial ulceration in submucosa and mucosa H&E x40,
**d-** GIST cells stained positive with




The patient is followed in the 10th postoperative month without any additional problems. A written statement was obtained from the patient for this report.

## DISCUSSION

GISTs are cellular spindle cell, epithelioid or pleomorphic mesenchymal tumors of gastrointestinal tract, first defined in 1983. Before that time, they were classified as smooth muscle tumors like leiomyoma, cellular leiomyoma, leiomyoblastoma and leiomyosarcoma (6). GISTs arises from Cajal cells of the gastrointestinal system. The diagnostic tool for the GISTs is tyrosine kinase growth factor receptor (c-KIT / CD117) expression. Only a small subgroup of GISTs which lack KIT expression are presented in literature. Other diagnostic criteria include positivity for CD34 (70%), smooth muscle actin expression (20-30%), S100 protein expression (10%) and negativity for Desmin (only 2-4% are positive). DOG1 positivity is considered clinically significant in diagnosing GIST (1, 5, 7). GISTs incidence is 1.5/1.000.000/ year. GISTs are more common in elderly ages and in males (8). GISTs are usually small masses located in the submucosal area and are diagnosed incidentally during examinations or surgeries performed for reasons other than symptomatic presentations. The most common complaints in symptomatic GISTs are compression symptoms due to mass compression effect. Although the need for emergency surgery is rare (<15%) for GISTs, intestinal obstruction, gastrointestinal system bleeding, tumor rupture, intussusception are surgical emergencies (1, 9). Intestinal obstruction is in the form of extraluminal compression or intussusception due to the extraluminal exophytic growth of the submucosal tumor (9). The Armed Forces Institute of Pathology (AFIP) classification system. discovered that in addition to tumor size and mitotic rate, anatomical location and the total area for mitotic counting (5 $mm^2$) is important for prognosis (10). High mitotic activity (mitosis of > 5 / 50 HPF), big tumor diameter (greater than 5 cm),

and c-KIT (CD 117) expression are associated with malignant behavior of GISTs. Apart from these, positive surgical margins, tumor rupture, tumor necrosis, peripheral organ invasion and distant metastasis are considered among the poor prognostic factors (10).

It has been reported that esophageal and gastric GISTs have a better prognosis than colorectal and small bowel GISTs. Gastric GISTs presenting as a pedunculated cystic mass, on the other hand, have a poor prognosis due to their large size, high number of mitoses, and areas of tumor necrosis (4, 5, 11). Although stomach (60-70%) is the most common site for GISTs, they can occur from esophagus to anus in every organs in the gastrointestinal tract (1, 7). In the literature, there are few case reports of GIST presenting as a large cystic mass connected to the main tumor with a peduncle (5). It has been suggested that aggressive tumor growth, congestion, intratumoral hemorrhage and necrosis are effective in the formation of large cystic spaces in the tumor and formation of cystic GIST (11, 12).

The most effective treatment for GISTs is surgery. These tumors generally do not invade the surrounding tissue. The tumor should be removed en bloc. For pedunculated GISTs complete surgical resection (R0) should be provided by wedge resection of the organ which is in continuity with the mass. The recommended approach is R0 resection with wide margins of about 1–2 cm (1, 4, 13).

The efficacy of chemotherapy and radiotherapy in the treatment of GISTs is controversial. The recognition of c-KIT positive patients has an impact on the treatment protocol. Imatinib mesylate is approved for use in GISTs, as it inhibits the tyrosine kinase activity of the c-KIT receptor (1). The cystic GIST of our patient contained areas of necrosis, high mitotic index, c-KIT positive and was large in diameter. Imatinib mesylate treatment was started because of the poor prognostic factors.

Cystic GISTs should be kept in mind in differential diagnosis of intra-abdominal cystic tumors. The frequency of endoscopic and radiological follow-up of GIST patients after treatment should be done individually, taking into account prognostic parameters. Poor prognosis of gastric cystic GISTs should not be forgotten, and patients should be followed closely in the postoperative period.

## REFERENCES

**1.** Miettinen M, Lasota J. Gastrointestinal stromal tumors--definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. Virchows Arch. 2001;438(1):1-12.

**2.** Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. Hum Pathol. 1999;30(10):1213-20.

**3.** Naitoh I, Okayama Y, Hirai M, Kitajima Y, Hayashi K, Okamoto T, et al. Exophytic pedunculated gastrointestinal stromal tumor with remarkable cystic change. J Gastroenterol. 2003;38(12):1181-4.

**4.** Cavallaro G, Sadighi A, Polistena A, Rossi V, Cristaldi M, Paparelli C, et al. Pedunculated giant GISTs of the stomach with exophytic growth: report of two cases. Int J Surg. 2008;6(6):e80-2.

**5.** Wang L, Liu L, Liu Z, Tian Y, Lin Z. Giant gastrointestinal stromal tumor with predominantly cystic changes: a case report and literature review. World J Surg Oncol. 2017;15(1):220.

**6.** Sripathi S, Rajagopal K, Srivastava RK, Ayachit A. CT features, mimics and atypical presentations of gastrointestinal stromal tumor (GIST). Indian J Radiol Imaging. 2011;21(3):176-81.

**7.** Bülbül Doğusoy G. Gastrointestinal stromal tumors: A multicenter study of 1160 Turkish cases. Turk J Gastroenterol. 2012, 23(3):203-11.

**8.** Mehta D. Commentary to: Atypical Presentation of Gastrointestinal Stromal Tumours-A Case Report by Kalpana Raja et al. Indian J Surg. 2014;76(5):425.

**9.** Akyüz C, Torun M. Mide Gastrointestinal Stromal Tümörünün Neden Olduğu Rekürren Gastroduodenal İntussepsiyon. Clin Exp Health Sci 2017;7:178-80.

**10.** Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. Arch Pathol Lab Med. 2006;130(10):1466-78.

**11.** Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M. Gastrointestinal stromal tumors: radiologic features with pathologic correlation. Radiographics. 2003;23(2):283-304, 456; quiz 532. doi: 10.1148/rg.232025146.

**12.** Gurram RP, Gnanasekaran S, Midha K, Biju P, Kalayarasan R. Atypical Presentation of Gastrointestinal Stromal Tumor as Multiple Intra-Abdominal Cysts: A Case Report. Cureus. 2020;12(5):e7999.

**13.** Hatipoğlu E, Ergüney MS, Ertem M. Evaluating the laparoscopic approach to proximally located benign gastric tumors. Laparosc Endosc Surg Sci. 2020;27(1):9-15.

# BOZOK TIP DERGİSİ

Yayın hakkı devir ve çıkar çatışması beyan formu

**Makale Adı:**
**Makale Numarası:**
Bu form ile yazar(lar) bildirir ki:
**1.** Yayın hakları yazının sınırsız olarak basılmasını, çoğaltılmasını ve dağıtılmasını ve mikrofilm, elektronik form (offline, online) veya başka benzer reprodüksiyonlarını kapsamaktadır.
**2.** Ben (biz) makale ile ilgili herhangi bir konuda ortaya çıkabilecek herhangi bir çıkar çatışması veya ilişkisi olduğu durumlarda, makale yayınlanmadan önce Bozok Tıp Dergisi editörünü bilgilendirmeyi taahhüt ediyorum(z). Bu ilişki ilaç firmaları, biyomedikal alet üreticileri veya ürün veya hizmetleri makalede geçen konular ile ilgili olabilecek veya çalışmayı destekleyen diğer kuruluşları kapsamaktadır.
**3.** Yazar(lar) makaleyi herhangi bir dağıtım amacı ile herhangi bir şekilde çoğaltmak istediğinde Bozok Tıp Dergisi'nden izin almak zorundadır.
**4.** Biz aşağıda isim ve imzaları bulunan yazarlar, Bozok Tıp Dergisi'nde yayınlanmak üzere gönderdiğimiz yazımızın original olduğunu; eşzamanlı olarak herhangi bir başka dergiye değerlendirilmek üzere sunulmadığını; daha önce yayınlanmadığını; gerekli görülen düzeltmelerle birlikte her türlü yayın hakkımızı, yazı yayına kabul edildiği taktirde "Bozok Tıp Dergisi"ne devrettiğimizi kabul ederiz.

**Katkıda bulunanlar:**

| | |
|---|---|
| Çalışmanın düşünülmesi ve planlanması: | |
| Verilerin elde edilmesi: | |
| Verilerin analizi ve yorumlanması: | |
| Yazının kaleme alınması: | |
| Eleştirel gözden geçirme: | |
| İstatistiksel değerlendirme: | |

**Makaledeki Sırasıyla Yazarın Adı Soyadı İmza Tarih**
**1.**
**2.**
**3.**
**4.**
**5.**
**6.**

# BOZOK MEDICAL JOURNAL

Copyright transfer and conflict of interest statement

**Article Title:**
**Manuscript Number:**
With this form all author(s) certify and accept that:
**1.** The copyright covers unlimited rights to publish, reproduce and distribute the article in any form of reproduction including microfilm electronic form (online, offline) and any other forms.
**2.** We grant to inform the editor of the Bozok Medical Journal about real or apparent conflict(s) of interest that may have a direct bearing on the subject matter of the article before the article is published. This pertains to relationships with pharmaceutical companies, biomedical device manufacturers or other corporation whose products or services may be related to the subject matter of the article or who have sponsored the study.
**3.** Author(s) must obtain permission from the Bozok Medical Journal to reproduce the article in any medium for distribution purposes.
**4.** The author(s) undersigned hereby declare that the manuscript submitted for publication in the Bozok Medical Journal is original; has not previously been published elsewhere nor is it under consideration by any other journal; and agree to transfer all copyright ownership to the "Bozok Medical Journal" effective upon acceptance of the manuscript for publication with all necessary revisions In the order that they appear in the manuscript

**Author Contributions:**

| | |
|---|---|
| Study conception and design: | |
| Acquisition of data: | |
| Analysis and interpretation of data: | |
| Drafting of manuscript: | |
| Critical revision: | |
| Statistical Analysis: | |

**Author Name Surname Sign Date**
**1.**
**2.**
**3.**
**4.**
**5.**
**6.**

# Yazarlara Bilgi

**Kapsam**

Bozok Tıp Dergisi, Yozgat-Bozok Üniversitesi Tıp Fakültesi'nin bilimsel içerikli, resmi yayınıdır.

Mart, Haziran, Eylül, Aralık aylarında olmak üzere yılda 4 sayı olacak şekilde yayımlanır.

Bozok Tıp Dergisi, tıbbın tüm alanlarında, cerrahi, klinik ve temel tıp bilimleri orijinal araştırma makaleleri, derlemeler, editör görüşleri, editöre mektup ve olgu sunumları yazılarının yayımlandığı "çift-kör" danışmanlık (peer-review) ilkelerine dayanan uluslararası bir dergidir.

Bozok Tıp Dergisi'nde makale başvuru veya işlem ücreti uygulanmamaktadır. Yayınlanan yazılar için herhangi bir ücret ya da karşılık ödenmez.

**Amaç**

Bozok Tıp Dergisi; tıbbın tüm alanlarında, cerrahi, klinik ve temel tıp bilimleri alanlarına ulusal ve uluslararası düzeyde katkı yapan özgün araştırma makaleleri, derlemeler, olgu sunumları, editör görüşleri ve editöre mektupları yayımlamayı amaçlamaktadır.

**Genel Bilgiler**

Yayımlanmak için gönderilen makalelerin daha önce başka bir yerde yayımlanmamış veya yayımlanmak üzere gönderilmemiş olması gerekir. Eğer makalede daha önce yayımlanmış; alıntı yazı, tablo, resim vs. mevcut ise makale yazarı, yayın hakkı sahibi ve yazarlarından yazılı izin almak ve bunu makalede belirtmek zorundadır.

Dergi, yayımlanan makalelerin bilimsel ve etik kurallar çerçevesinde hazırlanmış olması ve ticari kaygılarda olmaması şartını gözetmektedir. Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğundadır. Makalenin değerlendirilmesi aşamasında, yayın kurulunun gerek görmesi halinde, makale ile ilgili araştırma verilerinin ve/veya etik kurul onayı belgesinin sunulması yazarlardan talep edilebilir.

Dergiye gönderilen makale biçimsel esaslara uygun ise, editör ve en az iki danışmanın incelemesinden geçip, gerek görüldüğü takdirde, istenen değişiklikler yazarlarca yapıldıktan sonra yayımlanır. Yazarlar taslağın son halini tek bir word dosyası olarak sisteme yüklemelidir. Gönderilmiş olan makalelerdeki yazım ve dilbilgisi hataları, makalenin içeriğine dokunmadan, editorial komitemiz tarafından düzeltilmektedir.

Makalelerin değerlendirilmeye alınabilmesi için, 'Telif Hakkı', 'Potansiyel Çıkar Çatışması Beyanı' ve klinik araştırmalarda 'Etik Kurul Onayı' nın bir kopyası sisteme yüklenmelidir. Bu formları içermeyen yazılar değerlendirilmeye alınmayacaktır. Potansiyel çıkar çatışması beyanı için IJME'nin formu dikkate alınmaktadır. Aşağıdaki bağlantıdan indirilebilir:
https://www.jmcp.org/pb-assets/pdf/ICMJE%20coi_disclosure-1554411604567.pdf

Yayınlanmak üzere kabul edilen yazıların her türlü yayın hakkı dergiyi yayımlayan kuruma aittir. Yazılardaki düşünce ve öneriler tamamen yazarların sorumluğundadır ve yazarlara gönderdikleri yazıları karşılığında herhangi bir ücret ödenmez.

**Yazım Kuralları**

• Yazılar çift aralıklı, yazı boyutu 12 punto olmalı, kenarlardan 2,5 cm boşluk bırakılarak, standart A4 sayfasına, Microsoft Office Word belgesi veya rich text format olarak hazırlanmalıdır.

• Her bölüm yeni bir sayfadan başlamalıdır.

• Yazılar başlık sayfasından başlanarak numaralanmalı, sayfa numaraları sağ alt köşeye yazılmalıdır.

• Kapak sayfasında; yazının başlığı (Türkçe ve İngilizce), sayfa başlarında kullanılacak 40 karakteri aşmayan kısa başlık, en az 3 ve en çok 6 anahtar sözcük, tüm yazarların ad-soyadları, akademik ünvanları, kurumları, iş telefonu-GSM, e-posta ve yazışma adresleri bulunmalıdır. Ayrıca yazının hazırlanması için alınmış herhangi bir destek ya da bağış varsa belirtilmelidir.

• Özetler; Türkçe ve İngilizce olarak yazının çeşidine uygun olarak hazırlanmalıdır.

• Anahtar kelimeler; en az 3 en çok 6 olmak üzere Türkçe ve İngilizce yazılmalıdır. Kelimeler birbirlerinden noktalı virgül (;) ile ayrılmalıdır. İngilizce kelimeler Index Medicus taki Medical Subjects Headings listesine uygun olmalıdır (Bkz: www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler Türkiye Bilim Terimleri (TBT)'ne uygun olarak verilmelidir (Bkz: www.bilimterimleri.com).

• Şekil, resim, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli; sırayla numaralanmalı ve yazıdan ayrı olarak sunulmalıdır. Şekil, resim, tablo ve grafiklerin açıklamaları makale sonuna eklenmelidir. Kullanılan kısaltmalar şekil, resim, tablo ve grafiklerin altındaki açıklamada belirtilmelidir. Görseller EPS, TIFF, JPG ve PDF formatında gönderilmeli ve fotograflar 300 dpi ve vektörel çizimler ise 600 dpi çözünürlükte olmalıdır.

• Teşekkür kısmında; çıkar çatışması, finansal destek, bağış ve diğer bütün editöryal (istatistiksel analiz, İngilizce/Türkçe değerlendirme) ve/veya teknik yardım varsa, metnin sonunda sunulmalıdır.

• Yazının sonundaki kaynak listesi kaynakların yazıdaki geliş sıralarına göre hazırlanmalıdır. Kaynak yazımı için kullanılan format Index Medicus'a uygun olmalıdır. (Bkz: www.icmje.org). Kaynaklar yazıda, ilgili cümle sonunda parantez içine alınarak belirtilmelidir. Kaynak numaraları birbirini takip ediyorsa başlangıç ve bitiş sayıları arasına kısa çizgi konur. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli; 6'dan fazla ise, sadece ilk 6 isim yazılmalı ve diğerleri et al şeklinde gösterilmelidir. Kongre bildirileri, kişisel deneyimler, basılmamış yayınlar, tezler ve internet adresleri kaynak olarak gösterilemez. On-line yayınlar için; DOI tek kabul edilebilir on-line referanstır.

• Kaynak seçiminin ulusal yayınlardan yapılması tavsiye edilmektedir.

Kaynakların yazımı için örnekler (Lütfen noktalama işaretlerine dikkat ediniz):

• Makale için; Yazar(lar)ın soyad(lar)ı ve isim(ler)inin başharf(ler)i, makale ismi, dergi ismi, yıl, cilt, sayı, sayfa no'su belirtilmelidir.

*Rempel D, Dahin L, Lundborg G. Pathophysiology of nevre compression syndromes: response of peripheral nerves to loading. J Bone Joint Surg. 1999;81(11):1600-10.

•Kitap için; Yazar(lar)ın soyad(lar)ı ve isim(ler)inin başharf(ler)i, bölüm başlığı, editörün(lerin) ismi, kitap ismi, kaçıncı baskı olduğu, şehir, yayınevi, yıl ve sayfalar belirtilmelidir.

*Kozin SH, Bishop AT, Cooney WP. Tendinitis of the wrist. In Cooney WP, Linscheid RL, Dobins JH, eds. The wrist: diagnosis and operative

treatment. Vol. 2. St. Louis: Mosby, 1998. p. 1181-96.

• Digital Object Identifier (DOI):

*Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752.

• Diğer kaynak türleri için, Bkz. "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References".

**Yazı çeşitleri**

**Orijinal araştırmalar:**

Prospektif veya retrospektif, tıbbın tüm alanları ile ilgili her türlü deneysel ve klinik çalışmalardır.

İçerik:

- Özet; Türkçe ve İngilizce olarak, ortalama 200-250 kelime olacak şekilde; amaç, gereç ve yöntemler, bulgular ve sonuç bölümlerinden oluşmalıdır.
- Giriş
- Gereç ve yöntemler
- Bulgular
- Tartışma / sonuç
- Teşekkür
- Kaynaklar

*Makalenin tamamı, yaklaşık 5000 sözcükten uzun olmamalı, şekil ve tablo sayısı altıyı geçmemeli, kaynaklar 40'ı aşmamalıdır.

**Klinik Derlemeler:**

Doğrudan veya davet edilen yazarlar tarafından hazırlanır. Tıbbi özellik gösteren her türlü konu için son tıp literatürünü de içine alacak şekilde hazırlanmalıdır. Yazarın o konu ile ilgili basılmış yayınlarının olması özellikle tercih nedenidir.İçeriği;

- Özet (Ortalama 200-250 kelime, bölümsüz, Türkçe ve İngilizce)
- Konu ile ilgili başlıklar
- Kaynaklar

*Derleme 5000 sözcüğü aşmamalı, şekil ve tablo en fazla 4, kaynak sayısı en fazla 100 olmalıdır.

**Kısa bildiriler:**

-2000 sözcüğü aşmamalı, şekil ve tablo en fazla 2, kaynak sayısı en fazla 20 olmalıdır.

**Olgu Sunumu:**

Nadir görülen, tanı ve tedavide farklılık gösteren makalelerdir. Yeterli sayıda fotoğraflarla ve şemalarla desteklenmiş olmalıdır.

İçerik:

- Özet (ortalama 100-150 kelime; bölümsüz; Türkçe ve İngilizce)
- Giriş
- Olgu Sunumu
- Tartışma
- Kaynaklar

**Editöre mektup**

Son bir yıl içinde dergide yayınlanmış makalelere yanıt olarak gönderilir. Yazı hakkında okuyucuların farklı görüş, deneyim ve sorularını içerir.

İçerik:

- Başlık ve özet bölümleri yoktur
- Mektuplar en fazla 500 kelimelik yazılardır, kaynak sayısı 5 ile sınırlıdır, şekil ve tablo içermez.
- Hangi makaleye (sayı, tarih verilerek) ithaf olunduğu belirtilmeli ve sonunda yazarın ismi, kurumu, adresi bulunmalıdır.
- Mektuba cevap, editör veya makalenin yazar(lar)ı tarafından, yine dergide yayımlanarak verilir.

**Kontrol Listesi**

Makale aşağıda gösterildiği gibi ayrı dosyalar halinde hazırlanmalıdır:

1.Başvuru Mektubu
2.Başlık sayfası
3.Özet
4.Ana metin (makale metni, teşekkür, kaynaklar, tablolar ve şekil başlıkları)
5.Şekiller
6.Yayın Hakları Devir Formu

# Instructions For Authors

**Scope**

Bozok Medical Journal is the official publication of Yozgat-Bozok University, Faculty of Medicine that offers scientific content. It is printed 4 times in a year in the months of March, June, September and December.

Bozok Medical Journal is a national journal, based on peer-review consultation principles publishing clinic and basic science, original research articles, reviews, editor views and case reports in every field of medicine.

Bozok Medical does not request application or process fees. Also, it does not pay any kind of compensation or fee for the published articles

**Aim**

The journal aims to publish research, original work, review and case reports that contribute in its field on national and international levels in basic medical sciences and clinical branches.

**General Information**

Articles are accepted for publication on the condition that they are original, are not under consideration by another journal, or have not been previously published. Direct quotations, tables, or illustrations that have appeared in copyrighted material must be accompanied by written permission for their use from the copyright owner and authors.

The Journal commit to rigorous peer review, and stipulates freedom from commercial influence, and promotion of the highest ethical and scientific standards in published articles. It is the authors' responsibility to prepare a manuscript that meets scientific criterias and ethical criterias. During the evaluation of the manuscript, the research data and/or ethics committee approval form can be requested from the authors if it's required by the editorial board.

All articles are subject to review by the editors and at least two referees. Acceptance is based on significance, and originality of the material submitted. Authors should upload the final version of the draft to the system as a single word file If the article is accepted for publication, it may be subject to editorial revisions to aid clarity and understanding without changing the data presented.

A copyright release form signed by all authors, a copy of conflict of interest and a copy of the approval of ethics committee must be uploaded to the system simultaneously with the manuscript. Submissions received without these forms (copyright, conflict of interest and approval of ethics committee) cannot be sent out for review. The form of IJME should be used for copyright release statement. This form can be dowloaded from the link below: https://www.jmcp.org/pb-assets/pdf/ICMJE%20coi_disclosure-1554411604567.pdf

The publisher owns the copyright of all published articles. Statements and opinions expressed in the published material herein are those of the author(s). Manuscript writers are not paid by any means for their manuscripts

**Editorial Policies**

• Text should be double spaced with 2,5 cm margins on both sides of a standard A4 page, using 12-point font. Manuscripts should be written with Microsoft Office Word document or rich text format.

• Each section should start on a separate page.

• The pages should be numbered consecutively, beginning with the title page and the page numbers should be placed in the lower right corner of each page.

• The title page should be organized as follows: Full title of the article, both in Turkish and English, all author's full names with academic degrees, and names of departments and institutions, short title of not more than 40 characters for page headings, at least 3 and maximum 6 key words, corresponding author's e-mail, postal address, telephone and fax numbers, any grants or fellowships supporting the writing of the manuscript.

• Abstracts should written Turkish and English according to categories of articles.

• Key words should be minimally 3 and maximum 6, and should written Turkish and English. The words should be separated by semicolon (;), from each other. English key words should be appropriate to "Medical Subject Headings (MESH)" (Look: www.nlm.nih.gov/mesh/MBrowser.html). Turkish key words should be appropriate to "Türkiye Bilim Terimleri (TBT)" (Look: www.bilimterimleri.com).

• All figures, pictures, tables and graphics should be cited at the end of the relevant sentence and numbered consecutively and kept separately from the main text. Explanations about figures, pictures, tables and graphics must be placed at the end of the article. All abbrevations used, must be listed in explanation which will be placed at the bottom of each figure, picture, table and graphic. Submit your figures as EPS, TIFF, JPG or PDF files, use 300 dpi resolution for pictures and 600 dpi resolution for line art.

• In acknowldgements section; conflict of interest, financial support, grants, and all other editorial (statistical analysis, language editing) and/or technical asistance if present, must be presented at the end of the text.

• The list of the references at the end of the paper should be given according to their first appearance in the text. Journal abbreviations should conform to the style used in the Cumulated Index Medicus (please look at: www.icmje.org). Citations in the text should be identified by numbers in brackets at the end of the relevant sentence. If reference numbers follow each other, the hyphen is placed between the starting and ending numbers. All authors should be listed if six or fewer, otherwise list the first six and add the et al. Declarations, personal experiments, unpublished papers, thesis can not be given as reference. Format for on-line-only publications; DOI is the only acceptable on-line reference.

• Choosing references from national magazines is recommend.

Examples for writing references (please give attention to punctuation):

• Format for journal articles; iinitials of author's names and surnames, titles of article, journal name, date, volume, number, and inclusive pages, must be indicated.

* Rempel D, Dahin L, Lundborg G. Pathophysiology of nevre compression syndromes: response of peripheral nerves to loading. J Bone Joint Surg. 1999;81(11):1600-10.

• Format for books; initials of author's names and surnames, chapter title, editor's name, book title, edition, city, publisher, date and pages.

* Kozin SH, Bishop AT, Cooney WP. Tendinitis of the wrist. In Cooney WP, Linscheid RL, Dobins JH, eds. The wrist: diagnosis and operative

treatment. Vol. 2. St. Louis: Mosby, 1998: 1181-96.

• Article with a Digital Object Identifier (DOI):

*Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752.

• For other reference style, please refer to "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References".

**CATEGORIES OF ARTICLES**

**Original Research Articles:**

Original prospective or retrospective studies of basic or clinical investigations in areas relevant to medicine.

Content: - Abstract (200-250 words; the structured abstract contain the following sections: Objective, material and methods, results, conclusion; both in Turkish and English)
- Introduction
- Material and Methods
- Results
- Discussion/ Conclusion
- Acknowledgements
- References

*Original articles should be no longer than 5000 words and should include no more than 6 figures / tables and 40 references.

**Review Articles**

The authors may be invited to write or may submit a review article. Reviews including the latest medical literature may be prepared on all medical topics. Authors who have published materials on the topic are preferred.

Content: - Abstract (200-250 words; without structural divisions; both in Turkish and English)
- Titles on related topics
- References

* These manuscripts should be no longer than 5000 words and include no more than 4 figures and tables and 100 references.

**Short Communications**

It should be no longer than 2000 words and include no more than 2 figures and tables and 20 references.

**Case Reports**

Brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens. They should include an adequate number of photos and figures.

Content: - Abstract (average 100-150 words; without structural divisions; both in Turkish and English)
- Introduction
- Case report
- Discussion
- References

**Letter to the Editor**

These are the letters that include different views, experiments and questions of the readers about the manuscripts that were published in this journal in the recent year.

Content: - There's no title, abstract, any figures or tables
- It should be no more that 500 words, the number of references should not exceed 5.
- Submitted letters should include a note indicating the attribution to an article (with the number and date) and the name, affiliation and address of the author(s) at the end.
- The answer to the letter is given by the editor or the author(s) of the manuscript and is published in the journal.

**Checklist**

The manuscript should be prepared as separate files in the following order:

1. Cover Letter
2. Title Page
3. Abstract
4. Main Text (text, acknowledgments, references, tables, and figure legends)
5. Figures
6. Copyright Form