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İÇİNDEKİLER

ORJİNAL ÇALIŞMA

1. Koroner Arter Bypass Greft Ameliyatı Geçiren Hastalarda Serum YKL-40, HMGB1, BDNF, NGF Düzeyleri ve Bilişsel Disfonksiyonlar Arasındaki İlişkinin İncelenmesi (İNGİLİZCE MAKALE) 374-381
Başak KOÇAK, Erkan IRIZ, Süreyya BARUN, Özlem GÜLBAHAR ZENGİN, Mustafa ARSLAN
2. COVID-19 Hastalarında Serum Nitrik Oksit Düzeylerindeki Değişiklikler (İNGİLİZCE MAKALE) 382-387
Özge Nur TÜRKERİ, Nezahat KURT, Fatma Betül ÖZGERİŞ, Ömer Faruk KOÇAK, Ebubekir BAKAN, Emine PARLAK
3. Üniversite Öğrencilerinin Cinsellik Hakkındaki Bilgi, Tutum ve Davranışlarının Değerlendirilmesi 388-395
Nahit Sabri ŞAHİN, Hande MEMİŞ, Mustafa BAKIRCI, Ethem Serdar YALVAÇ
4. Tıp Fakültesi 1. ve 5. Sınıf Öğrencilerinin Çocuk Hastaların Ağız ve Diş Sağlığı Konusunda Bilgi, Tutum ve Davranışlarının Karşılaştırmalı Değerlendirilmesi 396-401
Nevra KARAMÜFTÜOĞLU, Ceylin KARAGÖZ, Merve YÜKSEL, Emre BAKIR
5. Mastektomi Sonrası Sol Meme Kanserinde Tanjansiyel Temelli Hacimsel Modüleli Ark Terapisine Uyarlanan Derin İnhalasyonda Nefes Tutma Tekniğinin Dozimetrik Analizi (İNGİLİZCE MAKALE) 402-410
Dicle ASLAN, Mustafa Tarkan AKSOZEN
6. Sağlık Kurumlarında Çalışan Orta Yaş (45-65) Personelinin Sağlıklı Yeme Alışkanlıkları ve Diyet Kalitesinin Yaşam Kalitesi ve İş Performansı Üzerine Etkisi (İNGİLİZCE MAKALE) 411-419
Eda PARLAK, Emine Özlem KÖROĞLU, Betül GÜLŞEN, Abdullah ÇALISKAN
7. Dupuytren Hastalığında Kontraktür Gelişiminin Görüntüleme Yöntemleriyle Öngörülmesi: Multimodal Ultrasonografik Değerlendirme (İNGİLİZCE MAKALE) 420-429
Erdem ÖZKAN, Mehtap BALABAN, Elif Banu GÜLER, Atilla Hikmet ÇİLENGİR
8. Lateral Epikondilit mi, Yoksa Fibromiyalji Hassas Noktası mı? Tanısal Yanılgılar ve Gereksiz ESWT Uygulama Riski (İNGİLİZCE MAKALE) 430-437
Gülseren DEMİR KARAKILIÇ, Sefa Gümrük ASLAN, Ferda SUREL
9. Mezenşimal Kök Hücrelerin Uterus ve Plasenta Üzerine Etkisi (İNGİLİZCE MAKALE) 438-447
Selda KAHVECİ, Nezihe Tülün BOYLU, Mehtap KILIÇ EREN
10. Optik Nörit ve Non-Arteritik Anterior İskemik Optik Nöropatide Tam Kan Sayımından Elde Edilen İnflamatuar Biyobelirteçlerin Karşılaştırmalı Analizi (İNGİLİZCE MAKALE) 448-458
Meryem Tuba SÖNMEZ, Selda ÇELİK DÜLGER, Duygu ARSLAN MEHDİYEYEV, Hikmet SAÇMACI, Funda UYSAL TAN
11. Üçüncü Basamak Bir Sağlık Merkezinin Rehabilitasyon Kliniğinde Nöromusküler Hastalıklar Nedeniyle Takip Edilen Hastaların Demografik ve Klinik Özellikleri: 5 Yıllık Sonuçları (İNGİLİZCE MAKALE) 459-468
Ferda SUREL, Enes ACAR, Dilek DİZDAR, Müyesser ARAS, Halil UÇAN
12. Kronik Hastalığı Olanlarda Belirsizliğe Tahammülsüzlük Durumunun Değerlendirilmesi 469-476
Zeynep Tuğba OZAN, Hafize KIZILKAYA, Gurbet BOZKURT
13. Akromioklaviküler Eklem Çıkığı Tedavisinde Çift Dügme İmplant Fonksiyonel Sonuçlarda Kanca Plaktan Daha Fazla İyileşme Sağlar (İNGİLİZCE MAKALE) 477-483
Murat AÇCI, Mete GEDİKBAŞ
14. Epistaksis Vakalarının Retrospektif Analizi: Eşlik Eden Hastalık ve Rekürrensini Tedavi Yaklaşımları Üzerindeki Etkisi (İNGİLİZCE MAKALE) 484-490
Ahmet AKSOY, Barış ŞAPCI, Tuba DOĞAN KARATAŞ, Mansur DOĞAN

İÇİNDEKİLER

15. İnfertil Hastalarda Uygulanan Varikosektominin Spermogram Parametrelerine Etkisi
*Mehmet Şakir TAŞPINAR, Mostafa SULTANI AFGHAN, Mehmet CANİKLİOĞLU, Volkan SELMİ,
Ayşen CANİKLİOĞLU* 491-495
16. Adana'da 80 Yaş ve Üzeri Bireylerde Toplum Temelli Geriatrik Değerlendirme: Tanımlayıcı Kesitsel Bir Çalışma
Zeynep KAHYAOĞLU, Esmâ DAĞDELEN, Melih Gaffar GÖZÜKARA 496-501
17. İn Vitro İyotlu Kontrast Maddelerin Bağırsak Mikroorganizmaları Üzerindeki Etkilerinin Değerlendirilmesi
(İNGİLİZCE MAKALE)
Nisa BAŞPINAR, Damla Bağdu ÇİMEN, Zeynep SÜMER, İsmail SALK 502-506
18. Yozgat Bozok Üniversitesi Araştırma ve Uygulama Hastanesi Cerrahi Kliniklerinde Yatışı Yapılan Hastalarda
Obstrüktif Uyku Apne Sendromu Prevelansı ve Farkındalığının Değerlendirilmesi
Ümmühan Tuğba TÜRÜKLÜ, Vugar Ali TÜRKSOY, Zehra SEYFİKLİ 507-517
- OLGU SUNUMU**
19. Vestibüler Migren Tedavisinde Büyük Oksipital Sinir Blokajı: Yanlış Tanıdan Etkili Tedaviye (İNGİLİZCE MAKALE)
Sadettin ERSOY, Şule AYDIN TÜRKÖĞLU 518-521
20. Hemoglobin J (HbJ) Varyantının HbA1c Ölçümü Üzerindeki Etkisi: Bir Olgu Sunumu (İNGİLİZCE MAKALE)
Medine ALPDEMİR, Emine Feyza YURT, Hasan Alp TURGUT, Mehmet ŞENEŞ, Mehmet Fatih ALPDEMİR 522-525
- EDİTÖRE MEKTUP**
21. Editöre Mektup
Uğur KAHVECİ 526-526

CONTENTS

ORIGINAL ARTICLE

1. Evaluation of the Relationship Between Serum YKL-40, HMGB1, BDNF, NGF Levels and Cognitive Functions in Patients Undergoing Coronary Artery Bypass Grafting (ENGLISH ARTICLE) 374-381
Basak KOCAK, Erkan IRIZ, Sureyya BARUN, Ozlem GULBAHAR ZENGİN, Mustafa ARSLAN
2. Changes in Serum Nitric Oxide Levels in Covid-19 PATIENTS (ENGLISH ARTICLE) 382-387
Ozge Nur TURKERI, Nezahat KURT, Fatma Betül OZGERİS, Omer Faruk KOCAK, Ebubekir BAKAN, Emine PARLAK
3. Evaluation of University Students Knowledge, Attitudes and Behaviors About Sexuality 388-395
Nahit Sabri SAHİN, Hande MEMİS, Mustafa BAKIRCI, Ethem Serdar YALVAC
4. A Comparative Evaluation Of First- and Fifth-Year Medical Students' Knowledge, Attitudes and Behaviors Regarding Oral Health in Pediatric Patients 396-401
Nevra KARAMUFTUOĞLU, Ceylin KARAGOZ, Merve YUKSEL, Emre BAKIR
5. Dosimetric Analysis of Deep Inspiration Breath Hold Technique Adapted to Tangential-Based Volumetric Modulated Arc Therapy For Left Breast Cancer After Mastectomy (ENGLISH ARTICLE) 402-410
Dicle ASLAN, Mustafa Tarkan AKSOZEN
6. Effects of Healthy Eating Habits and Diet Quality on Quality of Life and Job Performance in Middle-Aged (45-65) Healthcare Workers (ENGLISH ARTICLE) 411-419
Eda PARLAK, Emine Ozlem KOROĞLU, Betül GULSEN, Abdullah CALISKAN
7. Imaging Predictors of Contracture in Dupuytren's Disease: Multimodal Ultrasonographic Perspective (ENGLISH ARTICLE) 420-429
Erdem OZKAN, Mehtap BALABAN, Elif Banu GULER, Atilla Hikmet CILENGİR
8. Lateral Epicondylitis or Fibromyalgia Tender Point? Diagnostic Pitfalls and The Risk of Unnecessary ESWT (ENGLISH ARTICLE) 430-437
Gulseren DEMİR KARAKILIC, Sefa Gumruk ASLAN, Ferda SUREL
9. Effect of Mesenchymal Stem Cells on Uterus and Placenta (ENGLISH ARTICLE) 438-447
Selda KAHVECI, Nezihe Tulun BOYLU, Mehtap KILIC EREN
10. Comparative Analysis of Cbc-Derived Inflammatory Biomarkers in Optic Neuritis and Non-Arteritic Anterior Ischemic Optic Neuropathy (ENGLISH ARTICLE) 448-458
Meryem Tuba SONMEZ, Selda CELİK DULGER, Duygu ARSLAN MEHDIYEV, Hikmet SACMACI, Funda UYSAL TAN
11. Demographic and Clinical Characteristics of Patients With Neuromuscular Diseases in A Rehabilitation Clinic of A Tertiary Health Center: 5-Year Results (ENGLISH ARTICLE) 459-468
Ferda SUREL, Enes ACAR, Dilek DIZDAR, Muyesser ARAS, Halil UCAN
12. Evaluation of Intolerance to Uncertainty in Patients with Chronic Disease 469-476
Zeynep Tuğba OZAN, Hafize KIZILKAYA, Gurbet BOZKURT
13. Suture-Button Fixation Outperforms Hook Plate in Functional Outcomes After Acromioclavicular Joint Dislocation (ENGLISH ARTICLE) 477-483
Murat ASCI, Mete GEDIKBAS
14. Retrospective Analysis of Epistaxis Cases: Impact of Comorbidity and Recurrence on Treatment Approaches (ENGLISH ARTICLE) 484-490
Ahmet AKSOY, Baris SAPCI, Tuba DOĞAN KARATAS, Mansur DOĞAN

CONTENTS

- 15. The Effect of Varicocele on Semen Parameters in Infertile Patients** 491-495
Mehmet Sakir TASPINAR, Mostafa SULTANI AFGHAN, Mehmet CANIKLIOGLU, Volkan SELMI, Aysen CANIKLIOGLU
- 16. Community-Based Geriatric Assessment in Individuals Aged 80 and Over in Adana: A Descriptive Cross-Sectional Study** 496-501
Zeynep KAHYAOGLU, Esmâ DAGDELEN, Melih Gaffar GOZUKARA
- 17. In Vitro Evaluation of The Effects of Iodinated Contrast Agents on Gut Microbiota (ENGLISH ARTICLE)** 502-506
Nisa BASPINAR, Damla Bagdu CIMEN, Zeynep SUMER, Ismail SALK
- 18. Evaluation of the Prevalence and Awareness of Obstructive Sleep Apnea Syndrome in Hospitalized Patients in the Surgical Clinics of Yozgat Bozok University Research and Training Hospital** 507-517
Ummuhan Tugba TUMUKLU, Vugar Ali TURKSOY, Zehra SEYFIKLI
- CASE REPORT**
- 19. Greater Occipital Nerve Block in The Management of Vestibular Migraine: A Case of Misdiagnosis and Recovery (ENGLISH ARTICLE)** 518-521
Sadettin ERSOY, Sule AYDIN TURKOGLU
- 20. The Impact of Hemoglobin J (HbJ) Variant on HbA1c Measurement: A Case Report (ENGLISH ARTICLE)** 522-525
Medine ALPDEMIR, Emine Feyza YURT, Hasan Alp TURGUT, Mehmet SENES, Mehmet Fatih ALPDEMIR
- LETTER TO THE EDITOR**
- 21. Letter to The Editor** 526-526
Ugur KAHVECI

EVALUATION OF THE RELATIONSHIP BETWEEN SERUM YKL-40, HMGB1, BDNF, NGF LEVELS, AND COGNITIVE FUNCTIONS IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

Koroner Arter Bypass Greft Ameliyatı Geçiren Hastalarda Serum YKL-40, HMGB1, BDNF, NGF Düzeyleri ve Bilişsel Disfonksiyonlar Arasındaki İlişkinin İncelenmesi

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ABSTRACT

Objective: Postoperative cognitive dysfunction (POCD) is characterised by symptoms that may inhibit planning, such as dementia, memory loss, attention deficiency and behavioural impairment. Although it frequently occurs after cardiac surgery, all manner of surgery can cause POCD. In this manuscript, we aimed to show the existence of a correlation between high-mobility group box 1 (HMGB1), YKL-40, brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and cognitive functions.

Material and Methods: Twenty-four patients who underwent coronary artery bypass graft (CABG) were analysed prospectively. Preoperative 2nd and postoperative 5–7th day blood samples were collected, and a cognitive test was performed synchronously. Correlations between YKL-40, BDNF, NGF and HMGB1 levels and cognitive test score (CTS) were examined.

Results: We found a significant postoperative decrease in NGF ($p = 0.010$). There was a positive correlation between postoperative NGF and postoperative CTS ($r = 0.542$, $p = 0.006$). Postoperative memory score increased ($p = 0.001$), but orientation and vigilance scores decreased ($p = 0.035$ and $p = 0.025$, respectively). There were also self-reliant positive correlations between preoperative and postoperative CTS ($r = 0.825$, $p < 0.0001$), preoperative and postoperative HMGB1 ($r = 0.529$, $p = 0.008$) and preoperative and postoperative NGF scores ($r = 0.454$, $p = 0.026$). Postoperative CTS had a negative correlation with age ($r = -0.447$, $p = 0.029$), duration of operation ($r = -0.506$, $p = 0.012$) and cardiopulmonary bypass (CPB) ($r = -0.403$, $p = 0.039$).

Conclusion: The data in this study suggest that NGF can be a notable parameter in POCD, and HMGB1 may be a crucial marker in heart disorders. To define appropriate diagnosis and treatment strategies, it is essential to detail the relationship between cognitive functions, neuroinflammation and neurotrophic factors.

Keywords: Coronary Artery Bypass Grafting; NGF; Postoperative Cognitive Dysfunction; Cognitive Impairment

ÖZET

Amaç: Postoperatif bilişsel disfonksiyon (POBD) demans, dikkat eksikliği, hafıza ve davranışsal bozulmalar, planlama yapamama gibi semptomlarla karakterize bir tablodur. Pek çok cerrahi işlem sonrası rastlanabilmekle beraber kardiyak cerrahi sonrası görülme sıklığı fazladır. Bu çalışmada, nöroinflamasyon ve nörotrofik faktör parametreleri ile kognitif test arasındaki korelasyon varlığını göstermeyi amaçladık.

Gereç ve Yöntemler: Elektif koroner arter bypass greft ameliyatı olan 24 hasta prospektif olarak incelendi. Preoperatif 2.gün ve postoperatif 5-7.gün serum örnekleri alındı ve eş zamanlı olarak kognitif test uygulandı. YKL-40, BDNF, NGF ve HMGB1 ile kognitif test skorları arasındaki korelasyon değerlendirildi.

Bulgular: Çalışma sonucunda NGF değerinde postoperatif anlamlı düşüklük bulunmuştur. ($p=0,010$). Postoperatif NGF ile postoperatif kognitif test arasında pozitif korelasyon saptanmıştır. ($r=0,542$, $p=0,006$). Bellek puanı postoperatif artmış ($p=0,001$),oryantasyon ve uyukluk ise postoperatif azalmış olarak bulundu. ($p=0,035$ ve $p=0,025$, sırasıyla).Preoperatif ve postoperatif HMGB1 ($r=0,529$, $p=0,008$), NGF ($r=0,454$, $p=0,026$) ve kognitif test skorları ($r=0,825$, $p < 0,0001$) arasında ise pozitif korelasyon saptandı. Postoperatif kognitif test skorları ile yaş ($r=-0,447$, $p=0,029$), kardiyopulmoner bypass ($r=-0,403$, $p=0,039$) ve operasyon süresi ($r=-0,506$, $p=0,012$) arasında ise negatif korelasyon görüldü.

Sonuç: Çalışmamız sonucunda NGF 'nin POBD değerlendirmesinde önemli bir parametre olabileceğine dair veri elde edilmiştir. HMGB1'in kardiyak hastalıklarda bir marker olarak araştırılması gündeme gelmiştir. Kognitif fonksiyonlar ile nöroinflamasyon ve nörotrofik parametreler arasındaki ilişkinin detaylandırılmasının uygun tanı ve tedavi stratejilerinin belirlenmesi açısından önemli olduğunu düşünüyoruz.

Anahtar Kelimeler: Koroner Arter Bypass Greft; NGF; Postoperatif Komplikasyon; Kognisyon

INTRODUCTION

Cardiovascular diseases remain one of the major causes of mortality. Coronary artery bypass graft (CABG) is a frequently performed surgical procedure related to these diseases (1).

Studies indicate that approximately 15% of patients who underwent CABG return to the hospital after being discharged with diagnoses such as postoperative infections, cardiac failure, dysrhythmia and neurological conditions (2-4). Neurological complications of CABG are estimated to 1% – 5% (5). Postoperative cognitive dysfunction (POCD) is a central nervous system failure that results in impaired linguistic ability, memory and psychomotor speed. It also contributes to limited attention, memory loss and social impairment without specific signs of injury in the nervous system (6,7). One study examined the cerebral side effects experienced by older individuals who have undergone surgical procedures with anaesthesia and reported that individuals who underwent surgeries experienced postoperative symptoms such as dementia, the inability to recognise their relatives, a decline in physical activity in daily life, confusion and impaired interest in family members. Notably, these individuals did not exhibit any neurological complaints before the surgeries (8).

Neuroinflammation and its relationship with POCD by inhibiting neurogenesis, an essential component of cognitive functions, are commonly assumed, and neurotrophic factors (NF) play a vital role in sustaining neurogenesis (9). Nerve growth factor (NGF) affects the growth and survival of peripheral sensory and sympathetic neurons. Previous studies have shown that NGF reduces neuronal damage in rats before and after forebrain ischemia (10).

Brain-derived neurotrophic factor (BDNF) was first discovered in 1982 via purification from pig brains (11). Studies emphasise lower BDNF levels in cognitive functional failure-related disorders (12,13).

High-mobility group box 1 (HMGB1) is a tissue damage-related alarmin family member. HMGB1 is released in the blood in a delayed and has a periodic pattern of long-term continuous elevation (14). Research about HMGB1 underlines its relationship with microvascular thrombosis, acute coronary syndrome and cerebrovascular events (15). Studies

suggest that postoperative elevation of HMGB1 may cause cognitive dysfunction (16).

YKL-40, known as chitinase-3-like protein 1, a glial inflammatory marker, was higher in older individuals and patients with Alzheimer's (17-19). One study showed a negative correlation between YKL-40 and cortical thickness and tau protein-like effect of YKL-40 in the brain (20). YKL-40 is accepted as a biomarker in cardiovascular disease prognosis due to its role in inflammation (21).

We aimed to define the correlation between serum BDNF and NGF for neurotrophic factors and HMGB1 and YKL-40 for neuroinflammation. The Montreal Cognitive Test (MoCA) was used to evaluate cognitive function (22).

MATERIAL AND METHODS

Twenty-four volunteer patients who underwent CABG electively between December 2019 and December 2020 were evaluated following ethics committee approval. The study protocol was approved by Ankara City Hospital No:1 Medical Research Scientific Ethics Committee (date: 03.10.2019, no: E1/067/2019).

Informed consent was obtained from all patients. We planned to include patients aged 30 to 80 and established the following exclusion criteria: current neurological disease, transient ischemic attack, history of head trauma, diagnosis of a neuroinflammatory illness known to cause cognitive dysfunction, active infection and fever, illiteracy and failure to establish adequate cooperation with the patient.

We measured HMGB1, YKL-40, BDNF and NGF in the volunteer patients' serum taken on the preoperative 2nd day and postoperative 5–7th days. We also investigated the correlation between each marker and the MoCA test, which was administered to volunteers by the same tester (B.K.) after sampling. Additional parameters included duration of operation, hospitalisation, postoperative intensive care unit stay, CPB time, cross-clamp (CC) time, perioperative blood product transfusion, age, sex, ejection fraction, comorbidity, reoperation during hospitalisation and number of diseased vessels.

The serum samples were kept at room temperature for 2 hours in a standard yellow capped tube then centrifuged at 3000 rpm for 10 minutes and stored at

-80 °C until sample analysis (AFG Bioscience Human Nerve Growth Factor ELISA kit EK:711226, AFG Bioscience Human Brain-Derived Neurotrophic Factor ELISA kit EK:700371, AFG Bioscience Human High Mobility Group Box 1 Protein ELISA kit EK:716341 and AFG Bioscience Human Cartilage glycoprotein 39 ELISA kit EK:700392). The coefficients of variation of the kits were given as less than 8% and 10% (in-study and inter-study, respectively). The washing processes performed in the ELISA analysis were carried out using an ELx50 Bioelisa Washer, Bio-Tec. Instruments, Inc. An ELx800 UV Universal Microplate Reader, Bio-Tec. Instruments, Inc. was used for absorbance readings.

The Turkish version of MoCA was administered to volunteers and used as a rapid screening test for cognitive impairment and the parameters it evaluates with various subtests, including memory (short-term memory recall task and delayed recall (5 points all)), language (3-item confrontation naming task (3 points) and repetition of 2 syntactically complex sentences repetition (2 points)), visual structuring skills (three-dimensional cube copy (1 point) and a clock-drawing task (3 points)), executive functions (Trail-Making Test B (1 point), a phonemic fluency task (1 point) and a 2-item verbal abstraction task (2 points)), attention-concentration (digits forward and backward tasks (1 point each), letter detection by tapping (1 point), and a serial backward subtraction task (3 points)) and orientation (orientation in time and place (6 points)) (23). An individual can get a maximum of 30 points.

Scoring 21 points or higher indicates good cognitive function (24-25).

Statistical Analysis

Statistical analysis was performed using the specified tests in SPSS 20.0 (SPSS, Chicago, IL, USA). Data are given as median (25%–75%), (minimum–maximum), n (%). A p-value of less than 0.05 was considered statistically significant in all analyses. The Kolmogorov–Smirnov test was applied to the measurable parameters to determine whether the distribution was normal or abnormal. MoCA and other data were evaluated with a Wilcoxon signed-rank test in intragroup evaluations. The correlation between the parameters measured by MoCA was evaluated using Spearman correlation. A Spearman correlation coefficient (r) < 0.20 and values close to zero indicated no significant relationship or minimal correlation. We categorised the relationships between levels as mild (0.2–0.39), moderate (0.4–0.59), severe (0.6–0.79) and very severe (0.8–1).

RESULTS

The median age of the patients was 65.00 (56.25–69.75) (48–73), and there were 23 male patients and 1 female patient. The other demographic and perioperative characteristics of the patients are presented in Table 1. Preoperative and postoperative NGF, YKL-40, BDNF and HMGB1 levels are summarised in Table 2. There was a significant decrease in postoperative NGF levels from their preoperative values (p = 0.010). There were

Table 1. Patients’ demographic and perioperative data (mean±Standart Derivation (min-max. n (%))

	Median (25%-75%) (min-max) n =24
Age	65.00 (56.25-69.75) (48-73)
Sex (Male/Female)	23/1
Ejection fraction	60.00 (50.00-60.00)(40-65)
Diabetes mellitus (yes/no)	14 (58.3) /10 (41.7)
Other comorbidities (yes/no)	21(87.5) /3(12.5)
Duration of operation(minute)	375.00 (360.00-420.00) (300-480)
Duration of cardiopulmonary bypass(minute)	113.00 (99.75-137.25 (51-177)
Duration of cross-clamp(minute)	76.00 (60.50-96.25) (37-142)
Duration of intensive care unit stay (hour)	72.00 (48.88-96.00) (24-144)
Duration of hospitalization (day)	12.00 (11.00-13.75) (5-30)
Intraoperative transfusion	2.00 (1.00-3.00) (0-4)
Total transfusion	7.00 (6.00-7.75) (3-21)

min: minimum, max: maksimum

no significant differences between the preoperative and postoperative values of YKL-40, BDNF and HMGB1 ($p = 0.715$, $p = 0.543$, and $p = 0.465$, respectively). The patients' preoperative and postoperative MoCA scores and subgroup data are detailed in Table 3. There was no significant difference in the preoperative and postoperative MoCA scores. When examining subgroups of MoCA, the mean of the postoperative word repetition test for evaluating memory assessment was significantly higher than that of the preoperative

test ($p = 0.001$). For orientation assessment, volunteers were requested to respond with the name of the city they were in, as well as the date and current day. The median of the postoperative orientation assessment was considerably lower than the median of the preoperative evaluation ($p = 0.035$). Vigilance by letter tapping, which assesses attention-concentration, was remarkably less than the preoperative score. ($p = 0.025$). The other subgroups of the MoCA assessment showed no remarkable differences.

Table 2. Patients' YKL-40, BDNF, HMGB1 and NGF data (median (25%-75%) (min –max))

	Preoperative (n=24)	Postoperative (n=24)	P
YKL-40(ng/mL)	63.60 (55.63-85.60) (36.9-159.4)	62.65 (54.73-79.50) (36-140.9)	0.715
BDNF (pg/mL)	1434.50 (1279.50-1559.00) (664-2961)	1243 (1083.75-1814.00) (754-6381)	0.543
HMGB1 (pg/mL)	1186.00 (570.25-1911.75) (40-4589)	1305.00 (419.25-2613.25) (40-6066)	0.465
NGF (pg/mL)	1051.50 (674.25-1387.00) (418-1846)	743.00 (502.25-932.00)* (343-2412)	0.010

YKL-40: Chitinase-3 like-protein-1, BDNF: Brain-derived neurotrophic factor, HMGB1: High-mobility group box 1, NGF: Nerve growth factor, *: $p < 0.05$ (compared to preoperative), min: minimum, max: maksimum

Table 3. The data of preoperative and postoperative MoCA test scores ((median (25%-75%), min-max)) and subgroups (median (25%-75%))

	Preoperative (median (25%-75%) (min-max) (n=24))	Postoperative (median (25%-75%) (min-max) (n=24))	P
MoCA	20.00 (16.00-23.00) (12-26)	20.00 (18.00-22.00) (13-30)	0.135
Executive functions			
Trail-Making Test B	0.00 (0.00-0.75) (0-1)	0.00 (0.00-1.00) (0-1)	0.655
Phonemic fluency task	0.00 (0.00-1.00) (0-1)	0.00 (0.00-1.00) (0-1)	1.000
2-item verbal abstraction task	1.00 (0.00-1.00) (0-2)	0.00 (0.00-1.75) (0-2)	0.655
Visual structuring skills			
Three-dimension cube copy	1.00 (1.00-1.00) (0-1)	1.00 (1.00-1.00) (0-1)	1.000
Clock drawing task	3.00 (2.25-3.00) (0-3)	3.00 (2.25-3.00) (0-3)	0.380
Language			
3-item confrontation naming task	3.00 (2.00-3.00) (1-3)	3.00 (2.00-3.00) (1-3)	0.527
Repetition of 2 syntactically complex sentences	1.00 (1.00-2.00) (0-2)	1.00 (0.00-2.00) (0-2)	0.564
Memory			
Short-term memory recall task and delayed recall test	0.00 (0.00-1.75) (0-3)	1.00 (0.00-3.75)* (0-5)	0.001
Attention-concentration			
Digits forward	0.50 (0.00-1.00) (0-1)	1.00 (0.00-1.00) (0-1)	0.180
Digits backward	1.00 (0.00-100) (0-1)	1.00 (1.00-1.00) (0-1)	0.157
Letter detection by tapping	1.00 (1.00-1.00) (1-1)	1.00 (1.00-1.00)* (0-1)	0.025
Serial backward subtraction task	2.00 (2.00-3.00) (0-3)	2.00 (2.00-3.00) (0-3)	1.000
Orientation			
Time, place, date	6.00 (6.00-6.00) (5-6)	6.00 (5.00-6.00)* (4-6)	0.035

* $p < 0.05$ (compared to preoperative), min: minimum, max: maksimum, MoCA: Montreal Cognitive Test

Preoperative MoCA scores and correlations with other parameters—YKL-40, BDNF, HMGB1, NGF, age, ejection fraction, diabetes mellitus and other comorbidities—showed no notable difference. However, there was a positive moderate correlation between postoperative NGF and postoperative MoCA ($r = 0.542, p = 0.006$). In contrast, there were negative correlations between postoperative MoCA and age, duration of operation and CPB, as seen in Table 4. ($r = -0.447, p = 0.029, r = -0.5506, p = 0.012, r = -0.403, p = 0.039$, respectively). It was found that there were self-reliant moderate relationships between volunteers' preoperative HMGB1 levels and postoperative HMGB1 levels, and volunteers' preoperative and postoperative NGF levels ($r = 0.529, p = 0.008; r = 0.454, p = 0.026$, respectively). There was also a very severe relationship between preoperative MoCA and postoperative MoCA scores ($r = 0.825, p < 0.0001$).

DISCUSSION

We hypothesised that neuroinflammation parameters would increase after the operation and that neurotrophic factors and MoCA scores would decrease. We found a significant decrease in postoperative NGF values caused by neuronal damage based on

the neuroinflammatory process. The literature shows a relationship between decreases in systemic and cerebral NGF levels after stress exposure and exogenous NGF administration in neurodegenerative diseases (9). Although there are currently no definitive data to explain the decline in NGF levels after cardiac surgery that we noted, one possible explanation is neuroinflammation after CABG. In light of our results, we believe that NGF can be used as a marker to evaluate cognitive functions in the postoperative period, but further research is necessary.

The symptoms of POCD may appear without any evidence of injury and can be observed throughout an extensive spectrum (6,7). For this purpose, although there was no notable decrease in postoperative MoCA scores compared to preoperative MoCA scores, we wanted to comment on the other results we gained from our research.

The significant decrease in postoperative tests of vigilance and orientation is consonant with our hypothesis, as well as the literature data showing a relationship between NGF and REM sleep and wakefulness (26). More research investigating why this decline does not occur in other cognitive function tasks is needed.

Table 4. The correlation of postoperative MoCA scores and other parameters

	r	P
YKL-40(ng/mL)	-0.238	0.262
BDNF (pg/mL)	0.347	0.096
HMGB1 (pg/mL)	0.223	0.294
NGF (pg/mL)	0.542	0.006*
Age	-0.447	0.029*
Ejection fraction	0.071	0.741
Diabetes mellitus	-0.092	0.668
Other comorbidities	-0.307	0.144
Duration of operation (minute)	-0.506	0.012*
Duration of cardiopulmonary bypass (minute)	-0.403	0.039*
Duration of cross-clamp(minute)	-0.262	0.216
Number-vessel bypass	-0.361	0.083
Duration of intensive care unit stay (hour)	0.328	0.118
Duration of hospitalization (day)	-0.316	0.132
Intraoperative transfusion	-0.322	0.125
Total transfusion	-0.084	0.697

YKL-40: Chitinase-3 like-protein-1/BDNF: Brain-derived neurotrophic factor/HMGB1: High-mobility group box 1/ NGF: Nerve growth factor, min: minimum, max: maksimum

MoCA was administered two days before surgery and 5–7 days after surgery. The intervening time's relative proximity may explain the scores of the preoperative and postoperative controls. Word repetition question evaluates memory functions in the MoCA and its score significantly increased in the postoperative control. Similar to our research, in the literature, the word repetition score assessing memory function, which has been the main subject of varied studies in cardiac surgery, significantly increased in the postoperative period in contrast to the score for other questions (27,28). A study highlighted the difference in word repetition during short-term follow-up between patients who underwent CABG and those with atherosclerotic heart disease (AHD) who did not have CABG (29). The study implied that the test application field, AHD severity, and time could be related to different results. Longer follow-up, such as 2 or 3 months after surgery, should be designed to obtain more specific outcomes related to this factor (30). Volunteers' preoperative stress levels might also be related to increased postoperative word repetition scores. The literature supports stress-induced alterations in gene expression and action variations, although the precise mechanisms have not been definitively elucidated (31).

There is research on MoCA's capability to define cognitive reserve. 'Cognitive reserve' is described as 'adaptability that helps to explain differential susceptibility of cognitive abilities or day-to-day function to brain aging, pathology, or insult (32). It may be related to the very severe relationship between preoperative and postoperative MoCA scores in our paper. Considering the negative correlation between age and postoperative MoCA, age, education and lifestyle might help this relationship.

The operation type, hypoperfusion, cerebral microembolisms, duration of hospitalization, operation, CC and CPB are thought to affect POCD (33). We found a negative correlation between the duration of operation and CPB with postoperative MoCA, as hypothesised.

YKL-40 did not significantly change, contrary to our hypothesis. An exciting paper about cardiac surgery and revascularisation markers, including YKL-40 has been published (34). The sampling time was similar to our study, but they found a significant elevation of

YKL-40 levels on the 7th day and an average level in 3 months. Additionally, there was an inspirational but not very detailed comment by various researchers on Malmeström's paper that highlighted that YKL-40 could have differed in different stages of neuroinflammatory disease due to immunosuppressive therapy (35). On-pump cardiac surgery might have affected our levels through immunosuppression.

Unexpectedly, there was neither a notable elevation of the postoperative HMGB1 level nor any correlation between other parameters. In light of these findings, we comment on the moderate relationship between the preoperative and postoperative HMGB1 values related to HMGB1's potential as a cardiac marker. Our HMGB1 values were measured by ELISA, and four participants had rheumatological comorbidities. Having a rheumatological condition before surgery affects HMGB1's release pattern after surgery.

Explaining the relationship between cardiac surgery and POCD, especially considering factors other than CPB, is needed. We believe POCD studies should be detailed, such as associating the type of prosthesis used in patients undergoing valve replacement or the existing difference between arterial and venous grafts in individuals who have undergone CABG surgery. Urgency of the operation, the number of lesions, and differences in the graft material used should be examined in future examinations.

One limitation of the current study is that we performed the procedure in a single centre with limited patients. We originally planned for our study to have 45 patients and four time-point controls: preoperative 2nd day, postoperative 5–7th days, postoperative 3rd week and postoperative 2nd month. Unfortunately, 3 months into the study, the COVID-19 pandemic hit our country. Travel restrictions affected the postoperative 3rd week and 2nd month controls. Under these circumstances, we had to limit the number of volunteers and the follow-up period to collect data from the beginning. We had to change the study protocol and the number of volunteers. The relative proximity of the intervening time mentioned before may explain the scores of the preoperative and postoperative controls.

For these reasons, the test application time can be considered another limitation of our study.

CONCLUSION

Our study showed a significant decrease in postoperative NGF and a positive correlation between postoperative MoCA and NGF. A moderate relationship between preoperative and postoperative NGF levels was also observed; given this, NGF might be an essential parameter for POCD assessment. A very severe relationship between preoperative and postoperative MoCA scores was noted, and a correlation of postoperative NGF with postoperative MoCA score was also found. We also noted a moderate relationship between preoperative and postoperative HMGB1, which may be a sign of HMGB1's possible relationship with cardiac diseases. Postoperative memory scores increased, but orientation and vigilance scores decreased. Future studies are necessary for the appropriate diagnosis and treatment of POCD.

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The authors declare that they have no competing interests.

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CHANGES IN SERUM NITRIC OXIDE LEVELS IN COVID-19 PATIENTS

COVID-19 Hastalarında Serum Nitrik Oksit Düzeylerindeki Değişiklikler

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ABSTRACT

Objective: Coronavirus 2 (SARS-CoV-2), the etiological agent of the COVID-19 pandemic that is rapidly affecting the entire world both in terms of health and economy, belongs to the beta coronavirus family. Although oxidative stress imbalance occurs in COVID-19 patients, how changing nitric oxide (NO) levels affect COVID-19 pathogenesis is not fully understood. For this purpose, NO levels were evaluated in the serum of COVID-19 patients.

Material and Methods: A total of 50 adult COVID-19 patients and 32 healthy control individuals were included in the study. COVID-19 patients were classified as Mild-COVID-19, Moderate-COVID-19, and Intensive Care-COVID-19 according to national guidelines. NO concentrations were measured spectrophotometrically from serum samples of all patients. Biochemical data were also collected.

Results: NO levels were lower in the patient group compared to the control group, but this difference was not statistically significant ($p>0.05$).

Conclusion: The variability in NO levels suggests that it may be a result of immune inflammation and vascular dysfunction in COVID-19 patients.

Keywords: COVID-19; Free Radical; Nitric Oxide

ÖZET

Amaç: Tüm dünyayı hem sağlık hem de ekonomik açıdan hızla etkileyen COVID-19 pandemisinin etiyolojik ajanı olan Koronavirüs 2 (SARS-CoV-2), beta koronavirüs ailesine aittir. COVID-19 hastalarında oksidatif stres dengesizliği meydana gelmesine rağmen, değişen nitrik oksit (NO) seviyelerinin COVID-19 patogenezinin nasıl etkilediği tam olarak anlaşılmamıştır. Bu amaçla COVID-19 hasta serumlarında NO düzeyleri değerlendirildi.

Gereç ve Yöntemler: Çalışmaya toplam 50 yetişkin COVID-19 hastası ve 32 sağlıklı kontrol birey dahil edildi. COVID-19 hastaları ulusal kılavuzlara göre Hafif-COVID-19, Orta-COVID-19 ve Yoğun Bakım-COVID-19 olmak üzere sınıflandırıldı. NO konsantrasyonları tüm hastaların serum örneklerinden spektrofotometrik olarak ölçüldü. Ek olarak biyokimyasal verileri toplandı.

Bulgular: NO düzeyleri hasta grupta kontrol grubuna göre düşüktü fakat bu fark istatistiksel olarak anlamlı değildi ($p>0,05$).

Sonuç: NO seviyelerindeki değişiklik COVID-19 hastalarında immün inflamasyon ve vasküler disfonksiyonun bir sonucu olabileceğini düşündürmektedir.

Anahtar Kelimeler: COVID-19; Serbest Radikal; Nitrik Oksit

INTRODUCTION

Coronavirus (SARS-CoV-2) first emerged in December 2019 in Wuhan Province, China. SARS-CoV-2 is a severe pathogenic human coronavirus (1). SARS-CoV-2 has been reported as the seventh human coronavirus to infect humans after HCoV-NL63, HCoV-229E, HCoV-OC43, HCoV-HKU1, SARS-CoV and MERS-CoV. The disease caused by SARS-CoV-2 has been defined as COVID-19 by the World Health Organization (WHO) (2). As the disease spread rapidly and affected the whole world, WHO declared this disease a pandemic in March 2020 (3). While some cases are reported as symptomatic, some cases have symptoms such as fever, dry cough, shortness of breath and myalgia. In severe cases, cerebrovascular diseases, impaired consciousness, encephalopathy, encephalitis, peripheral nervous system damage, lung damage or multiple organ failure are observed (4). In severe COVID-19 cases, uncontrolled cytokine response triggers excessive endothelial inflammatory reactions and vascular thrombosis (5). The disruption of the balance between antioxidants and free radicals in biological systems is defined as oxidative stress (6). Recent studies show that oxidative stress plays an important role in viral infections such as SARS-CoV and SARS-CoV-2 infections (7-9). Nitric oxide (NO) was first identified as endothelium-derived relaxation factor (EDRF) (10). NO carries an unpaired electron in its last orbit and is therefore called a free radical. The role of NO depends on the place of production and its concentration. While all concentrations of other free radicals are quite dangerous for cells, low concentrations of NO have very important physiological functions. However, situations where NO synthesis is excessive and uncontrolled are harmful to the cell (11). Studies conducted to date have determined that NO is a very important regulatory molecule, second messenger and transmitter found in the cardiovascular, nervous, urogenital, digestive and immune systems. In addition to its physiological functions, it also plays a role in the pathophysiology of diseases such as neurodegenerative diseases, stroke, septic shock, and hypertension (12). Although oxidative stress imbalance is emphasized in COVID-19 patients, the contributions of NO formation to the pathogenesis of COVID-19 have not been sufficiently defined. It is known

that NO, known as a free radical, has an important pathophysiological role in many systems, especially the nervous system, immune system, and cardiovascular system. In recent studies, the variability in NO levels in COVID-19 patient groups is particularly striking. For this reason, we aimed to understand the levels of NO in COVID-19 (+) patients and the effects of NO on COVID-19 disease pathophysiology and to investigate the development mechanisms of this disease.

MATERIALS AND METHODS

Ethical approval for this study was obtained from the Clinical Research Ethics Committee of Atatürk University School of Medicine (Approval number: 24.06.2021). The study was approved with the reference number B.30.2.ATA.0.01.00/36.

This study included 50 patients and 32 healthy volunteers diagnosed with nasopharyngeal and oropharyngeal swab samples and real-time polymerase chain reaction (RT-PCR) tests at Atatürk University Research Hospital between July and August 2021. The study population was divided into a healthy control group (HG) and a patient group (PG). All COVID-19 cases were managed in accordance with national guidelines.

RT-PCR positive patients (n=50) were further categorized based on disease severity into:

Mild COVID-19 (n=12): Symptomatic (fever, joint and muscle pain, cough, sore throat) without respiratory distress, respiratory rate <24/min, SpO₂ >93% on room air, and normal chest X-ray or CT.

Moderate COVID-19 (n=25): Symptoms similar to mild cases with respiratory rate <30/min, SpO₂ >90%, and mild to moderate pneumonia on chest imaging.

ICU-COVID-19 (n=13): Symptoms as above, with respiratory rate ≥30/min, SpO₂ ≤90%, and bilateral diffuse pneumonia on imaging.

Some of the blood samples were sent to the Atatürk University hospital laboratory for routine analysis and recorded with Neutrophil (NE), Lymphocyte (LY), pH, Carbon Dioxide (CO₂), Bicarbonate (HCO₃⁻), Lactate (Lac), Methemoglobin (MetHb) and patient age information. The other part was sent to the Research Laboratory of the Department of Medical Biochemistry, Atatürk University Faculty of Medicine for NO analysis. Samples were stored at -80°C until the analysis day.

On the analysis day, samples were allowed to thaw gradually at +4°C. All samples were analyzed under the same conditions on the same day. NO levels in serum samples were measured by spectrophotometric method using a commercial colorimetric analysis kit (Cayman, Nitrate/Nitrite Colorimetric Assay kit (780001)). The intraassay coefficient of variation (CV) of the kit used was 2.7% and the interassay coefficient of variation (CV) was 3.4%.

Statistical Analysis

SPSS 21.0 (Statistical Package for the Social Sciences v21.0 Armonk, NY: IBM Corp. 2012) package program was used for statistical analysis. Data were presented as mean±standard deviation, 95% Confidence Interval for Mean (Lower Bound-Upper Bound) and Interquartile Range. Kolmogorov-Smirnov test was used to determine the homogeneity of the data. Since data do not show normal distribution, Mann Whitney U test was used for paired group comparisons; and Kruskal Wallis test was used for three-group comparisons. Statistical significance level was taken as p<0.05 for all data.

RESULTS

The mean age was 50.80 (±18.8) in the patient group and 52.68 (± 14.86) in the healthy group. There was no statistically significant difference between the mean ages of the patient and control groups (p=0.637). Serum NO levels were lower in the patient group compared to the control group, but this decrease was not statistically significant (p= 0.052). However, both NE and LY counts were significantly decreased in COVID-19 patients compared to controls (p <0.001). These data are presented in Table 1. A graphical comparison of serum NO levels between

the control and patient groups is provided in Figure 1. Although NO levels tended to decrease in COVID-19 patients, the variation was high, particularly in the patient group, which may have contributed to the lack of statistical significance. This trend could reflect potential disruptions in NO metabolism due to viral pathogenesis and inflammatory responses, even in the absence of severe hypoxia.

In the analysis where COVID-19 patients were subdivided according to severity, NO levels tended to increase in parallel with the worsening of the clinical picture. The mean NO levels in the mild, moderate, and intensive care unit (ICU) groups were 3.83 ± 2.56 µM/L, 4.79 ± 2.64 µM/L, and 5.43 ± 2.92 µM/L, respectively (p = 0.339). The median values were 3.02, 4.60, and 5.14 µM/L, respectively.

The box plot presented in Figure 2 visually supports this trend. The plot shows an increase in median NO levels as disease severity increases. In the ICU group, both the median and upper quartile values were found to be higher than in the other groups. This suggests that nitric oxide levels, a marker of oxidative stress, increase with advanced disease severity. However, statistical analysis revealed no significant difference between the groups (p> 0.05). Therefore, although the observed trend toward an increase in NO levels was clinically significant, it could not be statistically confirmed.

Among the biochemical parameters evaluated, pH levels were found to be significantly higher in the ICU-COVID-19 group compared to the other subgroups (p = 0.027), possibly indicating a compensatory respiratory alkalosis in critically ill patients. Other parameters, including NE, LY, CO₂, HCO₃, lactate, and MetHb, did not differ significantly across COVID-19 subgroups (p> 0.05).

Table 1. Age and Biochemical Values of The Healthy Control Group and Patients with COVID-19 (+)

Groups	PG (n:50)			HG (n:32)			P value
	Mean±SD	Med (IQR)	%95(CI)	Mean±SD	Med (IQR)	%95(CI)	
LY (×10 ³)	1477.8±834.88	1250(855)	1240.5-1715	2539.6±1150.7	2295 (2202.5)	2124.7-2954.5	0.001*
NE(×10 ³)	3829.4±1746.2	3555(2152.5)	3333.1-4325.6	5396.9±2193.2	4588.5 (3832)	4606.1-6187.6	0.001*
NO(µM/L)	4.73±2.7	4.44 (4.19)	3.96 - 5.5	6.02±2.9	5.1(3.45)	4.97-7.07	0.052
Age (year)	50.82±18.8	48.5(27.25)	45.45- 56.18	52.68±14.86	51 (22.25)	47.3 -58.04	0.637

*: Statistically significant. PG: COVID-19 (+) patient group; HG: Healthy control group. NO: Nitric Oxide, NE: Neutrophil, LY: Lymphocyte SD: Standard deviation; Med:Median (IQR: InterquartileRange), CI: Confidence Interval for Mean

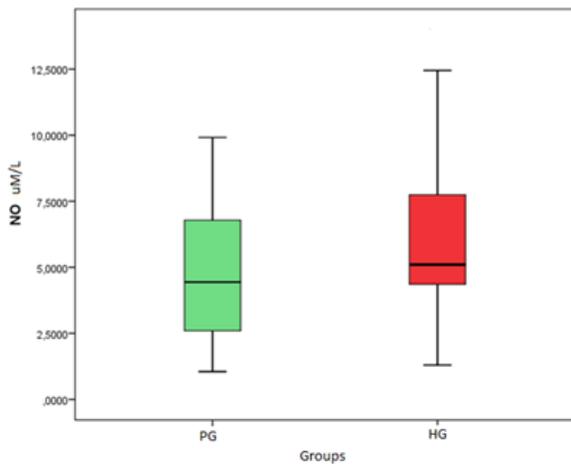


Figure 1. Serum NO Levels in Control and COVID-19(+) Patient

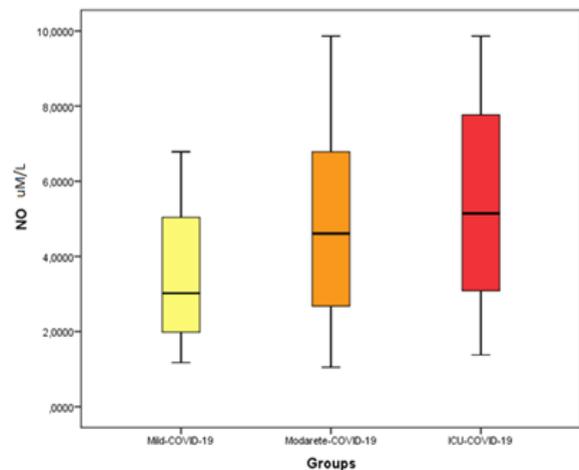


Figure 2. Comparison of Serum NO Levels Among COVID-19 Subgroups Based on Disease Severity

DISCUSSION

Following the declaration of COVID-19 as a pandemic by the WHO, numerous studies have been conducted on the pathogenesis, course, and treatment approaches of the disease. A significant portion of these studies have focused on NO, which plays a critical role in processes such as the immune response, endothelial dysfunction, and hypoxia. NO stands out as a potential marker and therapeutic target in the clinical picture of COVID-19 due to its both immune response-modulating and vasodilatory effects.

The effects of NO vary depending on the stage of infection, the degree of tissue hypoxia, intracellular antioxidant capacity, and the isoforms in which it is synthesized (13).

Studies have shown notable differences in NO levels in COVID-19 patients. Some studies have reported decreased NO levels in COVID-19 patients due to increased oxidative stress and endothelial dysfunction. This decrease in NO levels has been attributed to the formation of peroxynitrite (ONOO^-) as a result of interactions with reactive oxygen species (ROS) and subsequent NO depletion. Therefore, monitoring nitrite/nitrate (NO_x) levels and even supplementing them with exogenous nitrate or nitrite have been recommended in COVID-19 patients (14,15). Some studies have shown that NO levels in the patient group are significantly higher than in healthy individuals. This increase has been attributed to macrophage activation, which is common during inflammatory immune

responses. Following inflammation, the amount of inducible nitric oxide synthase (iNOS) in macrophages can increase 2-3-fold, causing the release of large amounts of NO, leading to local and systemic increases in nitrate or nitrite (16-18).

In our study, serum NO levels were found to be lower in COVID-19 patients compared to healthy controls. However, this difference was not statistically significant. Our findings are consistent with those of Özdemir & Yazıcı and Fang et al., while consistent with the studies conducted by both studies, our results are supported by demonstrating that decreased endothelium-derived nitric oxide (NO) production and NO bioavailability may play a critical role in COVID-19-related deaths (19,20). Interestingly, some studies, particularly in severe cases and intensive care patients, have found increased NO production due to increased iNOS expression due to macrophage activation. Mandal made a noteworthy point in this regard: in some cases, NO levels were found to be higher in COVID-19 patients than in non-COVID hypoxemic cases, and this was associated with a silent hypoxemia condition called "happy hypoxia." He emphasized that increased NO levels, particularly in erythrocytes, can facilitate oxygen release to the tissue, while excessive NO accumulation can cause mitochondrial dysfunction, triggering apoptosis and cellular damage (13).

In our study, when examining COVID-19 subgroups, the highest NO levels were observed in intensive care patients and the lowest in mild cases, but these

Table 2. Biochemical values of patient subgroups with COVID-19 (+)

GROUPS		Subgroups of PG			P value
		MildCOVID-19 (n=12)	ModareteCOVID-19(n=25)	ICUCOVID-19 (n=13)	
Age (year)	Mean±SD	37.42 ± 17.69	53 ± 18.93	59 ± 13.80	0.151
	Med (IQR)	35 (27)	50 (28)	59 (23)	
	%95(CI)	26.17 - 48.66	45.18 - 60.82	50.66 - 67.34	
NO(µM/L)	Mean±SD	3.83 ± 2.56	4.79 ± 2.64	5.43 ± 2.92	0.339
	Med (IQR)	3.02 (3.84)	4.6 (4.2)	5.14 (5.52)	
	%95(CI)	3.69 - 5.88	3.69 - 5.88	3.67 - 7.2	
NE(×10 ³)	Mean±SD	3908.3 ±2306.1	3499.6 ±1609.9	4390.77 ± 1347.3	0.48
	Med (IQR)	3285 (1783)	3460 (2154)	4390 (1905)	
	%95(CI)	2443.09-5373.57	2835.04 -4164.16	3576.6 - 5204.94	
LY (×10 ³)	Mean±SD	1815 ± 971.42	1478.8 ± 887.54	1164.6 ± 431.01	0.330
	Med (IQR)	1660 (972.5)	1170 (980)	1000 (570)	
	%95(CI)	1197.7 - 2432	1112.44 -1845.15	904.15 -1425.07	
pH	Mean±SD	7.38 ± 0.17	7.41 ± 0.02	7.43 ± 0.04	0.027*
	Med (IQR)	7.38 (0.02)	7.41 (0.04)	7.42 (0.08)	
	%95(CI)	7.39 - 7.4	7.39 - 7.43	7.4 - 7.46	
CO ₂ (mmHg)	Mean±SD	42.06 ± 1.82	43.16 ± 8.72	41.87 ± 10.65	0.933
	Med (IQR)	41.75 (2.6)	42.8 (12.22)	36.9 (21.6)	
	%95(CI)	40.15 - 43.97	37.62 - 48.7	34.71 - 49.02	
HCO ₃ (mEq/Lt)	Mean±SD	24.01 ± 1.39	24.8 ± 2.24	23.72 ± 1.55	0.373
	Med (IQR)	23.6 (2.1)	24.35 (3)	23.8 (2.7)	
	%95(CI)	22.55 -25.48	23.38 - 26.23	22.68 - 24.77	
Lactate	Mean±SD	1.23 ± 0.24	1.34 ± 0.43	1.5 ± 0.59	0.523
	Med (IQR)	1.2 (0.25)	1.35 (0.47)	1.4 (0.9)	
	%95(CI)	0.97 - 1.48	1.06 - 1.62	1.1 - 1.89	
MetHb	Mean±SD	1.56 ± 0.17	1.55 ± 0.21	1.5 ± 0.26	0.781
	Med (IQR)	1.55 (0.3)	1.55 (0.5)	1.55 (0.3)	
	%95(CI)	1.38 - 1.75	1.42 - 1.69	1.32 - 1.67	

PG: COVID-19(+) patient group NO :Nitric Oxide, NE :Neutrophil, LY: Lymphocyte, pH:Potential hydrogen, CO₂: Carbondioxide, HCO₃: Bicarbonate, MetHb: methemoglobin, SD: Standard deviation; med: Median (IQR: Interquartile Range), CI: Confidence Interval for Mean.

differences were not statistically significant. This finding suggests that increased NO production may occur as a compensatory mechanism against hypoxia in later disease stages. Furthermore, as highlighted in Mandal's study, increased mitochondrial NO levels during periods of low partial oxygen pressure and their resulting inhibition of the respiratory chain can lead to impaired cellular energy production. Another notable observation in our study was the significantly decreased neutrophil and lymphocyte counts in COVID-19 patients, supporting the hypothesis of immune suppression or redistribution during active

infection. The markedly elevated pH levels in intensive care patients may reflect respiratory alkalosis due to increased ventilatory drive, a known compensatory response in intensive care patients. Taken together, our findings suggest that although serum NO levels tend to decrease in COVID-19, especially in the early stages, dynamic changes occur throughout the disease. Further longitudinal studies are needed to clarify the clinical significance of NO fluctuations and their potential role in guiding treatment or prognosis.

CONCLUSION

When examining clinical subgroups based on COVID-19 disease severity, NO levels differ. This reflects various factors related to disease mechanisms, individual responses, and differences in analytical methods. Therefore, prospective and standardized studies are still necessary to better understand NO's role not only in COVID-19 progression but also in its long-term effects and potential as a biomarker for similar respiratory infections.

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ÜNİVERSİTE ÖĞRENCİLERİNİN CİNSELLİK HAKKINDAKİ BİLGİ, TUTUM VE DAVRANIŞLARININ DEĞERLENDİRİLMESİ

Evaluation of University Students Knowledge, Attitudes and Behaviors About Sexuality

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ÖZET

Amaç: Bu çalışmanın amacı, üniversite öğrencilerinin cinsellik konusundaki bilgi düzeylerini, tutumlarını ve davranışlarını kapsamlı bir şekilde değerlendirmektir.

Gereç ve Yöntemler: Bu araştırma, Yozgat Bozok Üniversitesi Tıp Fakültesi'nde Jinekoloji ve Obstetrik eğitimi almamış toplam 166 öğrenci ile gerçekleştirilmiş bir kesitsel çalışmadır. Araştırma verileri, cinsel sağlıkla ilgili bilgi ve tutumları ölçmek amacıyla oluşturulmuş 20 sorudan oluşan bir anket aracılığıyla toplanmıştır.

Bulgular: Katılımcıların %22,9'u cinsel deneyim yaşadığını belirtirken, bu oran kadınlarda %10,6, erkeklerde ise %43,5 olarak bulunmuştur. Erkeklerin cinsel deneyime sahip olma oranı, kadınlara göre istatistiksel olarak anlamlı bir ilişki vardır ($p<0,001$). Öğrencilerin %83,7'si okullarda cinsel eğitimin verilmesini desteklerken, %4,8'i bunun gereksiz olduğunu ifade etmiştir. Cinsellik konusundaki bilgilerin en yaygın kaynağı sosyal medya ve internet (%42,2) olarak belirtilmiştir. Katılımcıların en fazla bildiği doğum kontrol yöntemleri prezervatif (%42,2) ve oral kontraseptifler (%35,5) olmuştur. Öğrencilerin %41,6'sı oral kontraseptif kullanırken, %33,1'i prezervatif kullanmaktadır.

Sonuç: Çalışma bulguları, üniversite öğrencilerinin büyük bir kısmının cinsel sağlık bilgilerini sosyal medya ve internetten edindiğini ortaya koymaktadır. Öğrenciler cinsel deneyimler yaşamış olsalar da cinsel sağlıkla ilgili yanlış anlamalar ve riskli korunma yöntemlerinin kullanımına dair ciddi bir eğitim eksikliği bulunmaktadır. Bu durum, ülkemizde cinsel sağlık eğitime dair politikaların güçlendirilmesi gerektiğini göstermektedir.

Anahtar Kelimeler: Cinsel Sağlık; Cinsellik; Doğum Kontrol Yöntemleri; Üniversite Öğrencileri

ABSTRACT

Objective: The aim of this study is to comprehensively assess the knowledge, attitudes, and behaviors of university students regarding sexuality.

Material and Methods: This research is a cross-sectional study conducted with a total of 166 students from the Faculty of Medicine at Yozgat Bozok University, who had not received training in Gynecology and Obstetrics. Data for the study were collected through a 20-item questionnaire designed to measure knowledge and attitudes related to sexual health.

Results: 22.9% of the participants reported having sexual experience, with 10.6% of females and 43.5% of males indicating such experience. The proportion of males with sexual experience is significantly higher than that of females ($p=0.001$). 83.7% of the students support the provision of sexual education in schools, while 4.8% consider it unnecessary. The most common source of information on sexuality is social media and the internet (42.2%). The most widely known methods of contraception are condoms (42.2%) and oral contraceptives (35.5%). 41.6% of participants use oral contraceptives, while 33.1% use condoms.

Conclusion: The findings of this study show that the majority of university students obtain their sexual health information primarily from social media and the internet. Although the students have sexual experiences, there is a significant lack of education regarding sexual health, which leads to misunderstandings and the use of risky protection methods. This highlights the need for strengthening sexual health education policies in the country.

Keywords: Sexual Health; Sexuality; Contraceptive Methods; University Students

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Giriş

Üniversite çağındaki gençlerin bilgi düzeyi, yalnızca toplumsal ve kültürel yapının bir yansıması değil, aynı zamanda bir toplumun eğitim seviyesinin belirleyicisi olarak da önemli bir gösterge kabul edilmektedir. Üniversite öğrencilerinin en belirgin özelliği, eğitim düzeylerinin yanı sıra, geldikleri toplumların koşullarının şekillendirdiği kişilik gelişimi ve çatışmalardır (1). Bu dönemde cinsellik gibi özel ve önemli bir konudaki bilgi ve tutumlar, sosyokültürel farklılıklar, büyüme süreçlerinde yetersiz cinsel eğitim almaları, bireylerin genel sağlıkları ve toplum içindeki ilişkileri üzerinde doğrudan etkiler yaratmaktadır (2). Çeşitli sosyoekonomik ve kültürel faktörlerin bu yaş grubunun cinsel sağlık hakkındaki bilgi düzeyini şekillendirdiği ve bireylerin cinsel sağlıklarını koruma yönündeki tutumlarını belirlediği görülmektedir (3). Bu bağlamda, cinsel sağlık eğitiminin eksikliği, cinsel sağlıkla ilgili risklerin artmasına yol açabilmektedir (4). Cinsel sağlık eğitimi, gençler ve toplum arasında cinsellik hakkında var olan bilgi eksikliklerini gidermeyi amaçlamaktadır (5). Cinsellik konusunda doğru ve yeterli bilgi edinmek, yalnızca bireylerin kişisel gelişimlerine katkı sağlamakla kalmaz, aynı zamanda toplumsal düzeyde farklı yaşam tarzlarına karşı duyulan saygıyı artırır (6). Cinsel eğitim, ideal olarak ailede başlanması gereken bir süreçtir; ancak toplumsal ve kültürel engeller, bu konudaki açık ve sağlıklı tartışmaların yapılmasını zorlaştırmakta, sonuç olarak genç bireylerin sosyal yaşantılarına başlamadan önce sınırlı bilgiyle karşı karşıya kalmalarına yol açmaktadır (7). Çoğu aile, çocuklarının ergenlik dönemine girmesiyle birlikte cinsel eğitim vermekten kaçınmakta ve bu eksiklik, gençlerin cinsellik hakkındaki tutumlarını, sınırlı kişisel deneyimlere dayalı olarak şekillendirmelerine neden olmaktadır (8). Cinsellik konusunda eğitim almış bireylerin bulunduğu toplumlarda, cinsel yolla bulaşan hastalıklar ve istenmeyen gebelikler gibi sağlık sorunlarının prevalansında belirgin bir azalma gözlemlenmektedir (9). Üniversite çağındaki gençler, cinsellik ve üreme sağlığı konusunda çeşitli bilgiler edinmekte, ancak bu bilgilerin doğruluğu ve kapsamı önemli ölçüde değişkenlik göstermektedir (10). Özellikle kontrasepsiyon kullanımı, istenmeyen gebeliklerin önlenmesi açısından kritik bir yer tutmaktadır. Ayrıca, öğrencilerin kontraseptif yöntem

kullanma oranları, genellikle cinsel sağlık eğitiminin ne kadar kapsamlı ve erişilebilir olduğuna bağlı olarak değişmektedir (11). İstenmeyen gebelikler ve cinsel yolla bulaşan hastalıkların önlenmesi açısından, bu yaş grubunun doğru bilgiye sahip olması, toplumsal sağlık düzeyini yükseltmede önemli bir rol oynamaktadır (12). Üniversite öğrencilerinin kontraseptif yöntemler konusundaki farkındalık düzeyleri ve kullanma oranları, toplumsal cinsiyet rolleri, kültürel normlar ve aileden alınan eğitim gibi faktörlerle şekillenmektedir (13). Bu nedenle, cinsel sağlık eğitiminin güçlendirilmesi, gençlerin bu konuda daha bilinçli ve sorumlu davranmalarını sağlamaktadır (14). Bu bulgular, cinsel sağlık eğitiminin güçlendirilmesinin halk sağlığını iyileştirmek açısından önemli bir strateji olduğunu ortaya koymaktadır (15). Bu çalışmanın temel amacı, üniversite öğrencilerinin cinsellik konusundaki bilgi düzeylerini, tutumlarını ve davranışlarını değerlendirmektir. Ayrıca, öğrencilerin cinsel deneyimlerini inceleyerek, cinselliğe bakış açılarını analiz etmek ve kontraseptif yöntemlere dair farkındalıklarını ve bu yöntemleri kullanma oranlarını ortaya koymaktır.

GEREÇ VE YÖNTEMLER

Çalışmamız için etik onay, Yozgat Bozok Üniversitesi etik kurulundan 13/09/2023 tarihinde alınmış olup, onay numarası 2017-KAEK-189_2023.09.13_3 olarak kaydedilmiştir. Çalışma etik prensiplere uygun olarak yapılmıştır. Tüm yazarlar araştırma ve yayın etiğine uygun çalıştığını beyan eder.

Bu çalışmada bir üniversite hastanesinde kadın hastalıkları ve doğum eğitimi almamış olan 1, 2 ve 3. sınıf üniversite öğrencilerinin cinsellik konusundaki bilgi, tutum ve davranışlarını değerlendirmeyi amaçladık. Kadın hastalıkları ve doğum eğitimi almamış öğrencilerin seçilme gerekçesi, bu gruptaki öğrencilerin benzer yaş aralıklarına sahip ve aynı eğitim düzeyini paylaşan bireyler olmaları varsayımına dayanmaktadır. Çalışma, tanımlayıcı ve kesitsel bir araştırma tasarımıyla yapılmış olup, veriler belirli bir zaman diliminde toplanmıştır.

Araştırmanın evrenini, 2022 yılı aralık ayında ile 2023 yılı ocak ayında Yozgat Bozok Üniversitesi'nde öğrenim gören öğrenciler oluşturmuştur. Örneklem, çalışmaya gönüllü olarak katılmayı kabul eden 166 öğrenciyi

dayanmakta olup, katılımcılardan “bilgilendirilmiş olur” alındıktan sonra anket uygulanmıştır.

Araştırmanın örneklem büyüklüğü, ortalama karşılaştırmaları için etki büyüklüğü orta düzeyde ($d=0,3$) varsayılmış, hata oranı ($\alpha=0,05$), çalışmanın gücü ($1-\beta=0,95$) olarak hedeflenmiştir. Güç analizi sonucunda, anlamlı farklılıkları tespit etmek için en az 111 katılımcının gerekli olduğu hesaplanmıştır. Çalışmaya toplam 166 katılımcının dâhil edilmesiyle, güç analizi gerekliliklerinin karşılandığı görülmüştür.

Veriler, araştırmacılar tarafından literatür taraması yapılarak geliştirilen, 20 sorudan oluşan bir anketle toplanmıştır. Anketin içeriği, literatürden edinilen bilgilerle desteklenmiştir. Anket, cinsellik ile ilgili bilgi, tutum ve davranışları ölçmeyi amaçlayan kapalı uçlu ve açık uçlu sorular içermektedir. Anketin başlıkları, cinsellik hakkındaki bilgi düzeyini, bilgi kaynaklarını ve cinsel deneyimlere dair tutumları yansıtan sorularla uyumlu olacak şekilde tasarlanmıştır.

Anketin dağıtımı, öğrencilere bireysel olarak yapılmış ve katılımcılar, gerekli bilgilendirmeler yapıldıktan sonra anonim olarak ankete katılım sağlamışlardır. Katılımcılar, anketi doldurup mühürlü zarfta geri teslim etmişlerdir. Bu yöntem, yanıtların doğruluğunu ve güvenilirliğini artırmayı amaçlamaktadır.

Elde edilen verilerin hesaplanması ve istatistiksel analizleri IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, ABD) kullanılarak yapıldı. Veri analizi sırasında, tanımlayıcı istatistikler (frekans, yüzdelik dilimler, ortalama) hesaplanmış, cinsiyet, yaş ve yerleşim yeri gibi demografik özelliklere göre gruplar arası farklar incelenmiştir. Ayrıca, cinsellik bilgisi, tutum ve davranışları ile demografik faktörler arasındaki ilişkiler normallik testi, Mann Whitney U testi ve Ki Kare testi ile değerlendirilmiştir. İstatistiksel anlamlılık düzeyi $p<0,05$ olarak kabul edilmiştir.

BULGULAR

Katılımcıların çoğunluğu (%57,2) cinselliği doğal ve normal bir olgu olarak tanımlamıştır. Cinsel deneyime sahip olduklarını belirten katılımcıların oranı ise %22,9’dur. Cinsel deneyime sahip bireyler arasında %28,94’ü kadın, %71,05’i erkek olarak tanımlanmıştır. Yapılan istatistiksel analizlerde, erkek öğrencilerin cinsel deneyim açısından kadın öğrencilerden anlamlı ve orta derecede daha fazla deneyime sahip

olduğu görülmüştür ($p<0,001$). İlk cinsel deneyimin ortalama yaşı 18,61 olarak belirlenmiş olup, cinsiyetler arasında ilk cinsel deneyim yaşına ilişkin anlamlı bir fark bulunmamıştır ($p=0,659$). Katılımcıların cinsel deneyimlerine dair bildirdikleri davranışlar arasında %28,3’ü öpüşme, %22,9’u cinsel ilişkiye girme ve %16,9’u el tutma olarak sıralanmıştır. Erkek öğrenciler en sık cinsel ilişkiye girme (%43,5) davranışını bildirirken, kadın öğrenciler ise en çok öpüşmeyi (%28,8) tercih ettiklerini ifade etmişlerdir. İstatistiksel olarak bulgular cinsiyet ile yaşanan cinsel deneyim davranışları arasında anlamlı bir ilişki olduğunu göstermiştir ($p<0,001$). Evlilik dışı cinsellik konusunda kadın katılımcıların %62,5’i bunu kabul edilemez olarak değerlendirirken, erkek katılımcıların %53,2’si evlilik dışı cinselliği normal olarak kabul etmektedir. Cinsiyet ile evlilik dışı cinsellik tutumları arasında istatistiksel olarak anlamlı bir ilişki gözlemlenmiştir ($p<0,001$). Katılımcıların %59’u, gelecekteki eşlerinin cinsel deneyiminin önemli bir faktör olduğunu belirtirken, %41’i bunun belirleyici bir unsur olmaması gerektiğini ifade etmiştir. Katılımcıların cinsel tutumlarını şekillendiren en önemli faktör, kişisel dünya görüşleri (%58,4) olarak belirlenirken, toplumsal yapı ise en az önemli faktör (%11,4) olarak değerlendirilmiştir. Cinsel bilgi kaynağı olarak en sık sosyal medya ve internet (%42,2) tercih edilmekte, bunu sırasıyla arkadaşlar (%24,1), ebeveynler (%12,7), kardeşler (%8,4), öğretmenler (%6), aile hekimleri (%4,2) ve basılı medya (%2,4) izlemektedir. Sosyal medya ve internetin bilgi kaynağı olarak kullanım oranı kadın öğrencilerde %41,3, erkek öğrencilerde ise %43,5 olarak tespit edilmiştir. Ayrıntılar Tablo 1’de sunulmaktadır.

Katılımcılara bilinen doğum kontrol yöntemleri sorulduğunda, %42,2’si kondomu en yaygın bilinen yöntem olarak ifade etmiştir. Diğer doğum kontrol yöntemleri ise sırasıyla oral kontraseptifler (OKP) %35,5, rahim içi araç (RİA) %9,6, takvim yöntemi %7,2 ve geri çekilme yöntemi %4,8 oranlarında bildirilmiştir. Tercih edilen doğum kontrol yöntemi sorusuna ise katılımcıların %41,6’sı oral kontraseptifleri (OKP) tercih ettiğini belirtmiştir. Bunu takiben, %33,1’lik bir oran kondomları, %13,3’lük bir oran takvim yöntemini, %9’u RİA ve %3’ü geri çekilme yöntemini tercih etmiştir. Kadın öğrenciler arasında en fazla tercih edilen yöntem kondom (%43,3), erkek öğrencilerde ise oral

Tablo 1. Cinsiyet ve Cinsellik, Cinsel Deneyim ve Cinsel Tutumlar Açısından Öğrencilerin Demografik Özellikleri

	Kadın		Erkek		Toplam	
Ortalama Yaş					21,06	
	n	(%)	n	(%)	n	(%)
Tüm Öğrenciler	104	(62,7)	62	(37,3)	166	(100)
Yaşadığı Yer						
İl	68	(65,4)	36	(58,1)	104	(62,7)
İlçe	26	(25)	14	(22,6)	40	(24,1)
Köy - Kasaba	10	(9,6)	12	(19,4)	22	(13,3)
Cinsellik Tanımı						
Konuşulmamalı	6	(5,8)	4	(6,5)	10	(6)
Sıradan ve olağan	60	(57,7)	35	(56,5)	95	(57,2)
Sadece eş ile	38	(36,5)	23	(37,1)	61	(36,7)
Cinsel Deneyim Tecrübesi						
El ele tutuşmuş	20	(19,2)	8	(12,9)	28	(16,9)
Öpüşmüş	30	(28,8)	17	(27,4)	47	(28,3)
Cinsel ilişki yaşamış	15	(11,5)	27	(43,5)	39	(22,9)
Hiçbir tecrübe yaşamamış	42	(40,4)	10	(16,1)	52	(31,3)
Evlilik Öncesi Cinsel İlişki						
Kabul edilemez	65	(62,5)	13	(21)	78	(47)
Olabilir	31	(29,8)	33	(53,2)	64	38,6)
Evlilik kesin ise yaşanabilir	8	(7,7)	16	(25,8)	24	(14,5)
Seksüel Davranışı Etkileyen Faktör						
Dini görüş	37	(35,6)	13	(21)	50	(30,1)
Sosyal yapı	13	(12,5)	6	(9,7)	19	(11,4)
Kendi görüşü	54	(51,9)	43	(69,4)	97	(58,4)
Cinsel Deneyim						
Evet	11	(10,6)	27	(43,5)	38	(22,9)
Hayır	93	(89,4)	35	(56,5)	128	(77,1)
Evlendiği Kişinin Cinsel Tecrübesinin Önemi						
Evet	65	(62,5)	33	(53,2)	98	(59)
Hayır	39	(37,5)	29	(46,8)	68	(41)
Cinsel Bilginin Kaynağı						
Ebeveynler	16	(15,4)	5	(8,1)	21	(12,7)
Kardeşler	8	(7,7)	6	(9,7)	14	(8,4)
Doktor	6	(5,8)	1	(1,6)	7	(4,2)
Öğretmen	6	(5,8)	4	(6,5)	10	(6,0)
Sosyal Medya/İnternet	43	(41,3)	27	(43,5)	70	(42,2)
Arkadaşlar	22	(21,2)	18	(29)	40	(24,1)
Yazılı Basın	3	(2,9)	1	(1,6)	4	(2,4)

kontraseptifler (%53,2) olmuştur. Bilinen ve tercih edilen doğum kontrol yöntemleri arasında anlamlı bir ilişki saptanmıştır (p<0,001). Ayrıntılı veriler Tablo 1 ve Tablo 2’de sunulmaktadır.

Katılımcılar arasında uyuşturucu kullanımı %7,8 olarak saptanmıştır. Alkol kullanımı %40,4, sigara içme oranı ise %27,7 olarak belirlenmiştir. Kadın katılımcıların %1,9’u uyuşturucu kullandığını bildirirken, erkek katılımcılar arasında bu oran %17,7’ye çıkmaktadır.

TARTIŞMA

Cinsellik, tarih boyunca insan yaşamının ayrılmaz bir parçası olmuştur. Dünya Sağlık Örgütü’ne (DSÖ) göre cinsellik, fiziksel, duygusal, entelektüel ve sosyal unsurların birleşiminden oluşur ve kişiliği, iletişimi ve sevgiyi zenginleştirir. Cinsellik, bireylerin yalnızca fiziksel değil, duygusal, entelektüel ve sosyal bütünlüğünü de deneyimlemelerini sağlayarak kişilik gelişimini, iletişimi ve sevgi paylaşımını destekler. Psikolojik, sosyal, ekonomik, politik, kültürel, yasal, dini, biyolojik ve manevi faktörlerin etkileşimi, cinsellik üzerinde belirleyici bir rol oynar.

DSÖ, cinsel sağlığı “hastalık, işlev bozukluğu ya da engellilik olmamasının ötesinde, cinsellikle ilişkili duygusal, zihinsel ve sosyal iyilik halinin pozitif bir durumu” olarak tanımlar. Cinsel sağlık, bireylerin güvenli ve tatmin edici cinsel deneyimler yaşamasını, cinsel hakların korunmasını ve yerine getirilmesini gerektirir. Cinsel sağlıkla ilgili bilgi edinimi çocukluk ve ergenlik döneminde başlar. Çalışmamızda öğrencilerin öncelikli bilgi kaynaklarının ilk sırada sosyal medya/ internet, ikinci sırada arkadaşlar olduğu belirlenmiştir. Literatürde 288 lisans öğrencisinin katıldığı bir çalışmada öğrencilerin cinsel sağlık ile ilgili bilgilerini en çok arkadaşlarından öğrendiği vurgulanmıştır (16). Galler’deki üniversite öğrencileri üzerinde yapılan bir çalışmada ise, cinsel sağlıkla ilgili bilgi kaynakları arasında birinci sırada %49,1 gibi yüksek bir oranla internet yer alırken, ikinci sırada ise aile hekimleri bulunmuştur (17). Cinsellik ve cinsel sağlık hakkında doğru bilgi edinimi ve doğru kaynak kullanımı, bireylerin genel sağlığında kritik bir rol oynamaktadır. Bu önemi vurgulayan gelişmelerden birisi de gelişmiş ülkelerin cinsel sağlık hakkında yaptıkları yatırımlardır. Amerika Birleşik Devletleri’nde 2018 yılında okul çağındaki gençlere yönelik cinsel risklerden kaçınma

eğitimi sağlamak amacıyla yaklaşık 80 milyon dolar bütçe ayrılmıştır. Bu eğitim programı, evlilik öncesi cinsel ilişkilerden kaçınmayı ve toplumda evlilik dışı cinsel davranışların normalleşmesini engellemeyi amaçlamıştır. Cinsel sağlık eğitimi üzerine yapılan çalışmalarda, bu tür programların bireylerin cinsel yolla bulaşan hastalıklar ve temel sağlık konuları hakkında daha doğru bilgi edinmesini sağladığı bildirilmiştir.

Çalışmamızda, öğrencilerin %57,2’si cinselliği doğal bir olgu olarak tanımlarken, %47’si evlilik öncesi cinselliği kabul edilemez bulmuştur. Kadın öğrencilerin %62,5’i evlilik öncesi cinselliği kabul edilemez olarak tanımlarken, erkek öğrencilerin %53,2’si bu durumu normal olarak değerlendirmiştir. Cinsiyetler arasında evlilik öncesi cinselliğe yönelik tutumlarda istatistiksel olarak anlamlı bir fark saptanmıştır. Bulgular, üniversite öğrencileri arasında cinsel deneyimlerin cinsiyetler arasında farklılık gösterdiğini ve erkek öğrencilerin cinsel deneyim yaşama oranlarının genellikle daha yüksek olduğunu ortaya koymaktadır. Türkiye’de 2007-2023 yılları arasında üniversite öğrencileri ile evlilik öncesi cinsel ilişki konusunda yapılan çalışmaların derlemesinde kadınların evlilik öncesi ilişki yaşamada hala toplumsal bir baskının olduğu sonucuna varılmıştır (18). İnönü Üniversitesi’nde Gülsen ve arkadaşlarının yaptığı bir çalışmada, kadınların %74,5’i evlilik öncesi cinsel ilişkiyi kabul edilemez bulurken, erkeklerin %49,6’sı benzer bir görüş bildirmiştir (19). Bu bulgular, çalışmamızdaki sonuçlarla paralellik göstermektedir ve üniversite öğrencilerinin cinselliğe yönelik tutumlarının, cinsiyet ve kültürel faktörlerle şekillendiğini göstermektedir.

Katılımcıların %77,1’i cinsel ilişki deneyimi yaşamadıklarını belirtmiştir (%89,4 kadın, %56,5 erkek). Cinsel deneyim yaşadığını belirtenlerin oranı ise %22,9 olup, bu grupta öpüşme (%28,3), cinsel ilişki (%23,5) ve el ele tutuşma (%16,9) olarak cevaplanmıştır. Çin’deki orta büyüklükteki bir şehir olan Hefei’de 1.500 üniversite öğrencisi arasında gençlerin cinsel davranışları hakkında yapılan bir çalışmada katılanların %12,6’sının (erkeklerin %15,4’ü, kadınların %8,6’sı) evlilik öncesi cinsel deneyimi olduğu görülmüştür (20). Farklı çalışmalarda evlilik öncesi cinsel deneyim oranlarının değişkenlik göstermesi, kültürel normlar, katılımcı profili ve zamanla değişen toplumsaldinamiklerden kaynaklanabilir.

Çalışmamızda en çok bilinen kontrasepsiyon yönteminin cinsiyet ayrımı olmaksızın %42,2 oranında kondom kullanımı olduğu ancak en çok tercih edilen yöntemin ise oral kontraseptifler olduğu bulunmuştur. 2012 yılında Ege Üniversitesi'nde 331 üniversite öğrencisi ile yapılan bir anket çalışmasında cinsel aktif gençlerin %25,4'ü herhangi bir doğum kontrol yöntemi kullanırken, %71,4 oranında kondomu tercih ettikleri saptanmıştır. Bunu %14,3 ile geri çekme ve %9,5 ile oral kontraseptif kullanımı izlemiştir (21). Çalışmamızda %41,6 ile en sık oral kontraseptifler, azalan sırasıyla kondom, takvim yöntemi, RİA tercih edildiği bulunmuş, yalnızca %3 oranında katılımcı ise geri çekme yöntemini kullandığını belirtmiştir. Bu farklılıklar, toplumlar arası ve zaman içindeki değişen tutumları, bilgi düzeyini ve sosyal normları yansıtabilir. Kondomun, cinsel yolla bulaşan hastalıkların korunmasında etkili bir yöntem

olarak algılanması ve yaygın kullanımı, kadınlar ve erkekler arasında korunma konusunda farklı anlayışlar ve tercihler olabileceğini gösteriyor. Oral kontraseptiflerin tercih edilmesinin, bu yöntemle ilgili bilgiye sahip olmanın yanı sıra, gebelikten korunma ile ilgili daha yüksek güvenlik algısıyla da ilişkili olabileceği düşünülmektedir. Bu nedenle, doğum kontrol yöntemlerine ilişkin toplumsal farkındalık ve eğitim, tercih edilen yöntemleri etkileyen önemli faktörlerdir. Çalışmamızda, katılımcıların %7,8'inin madde kullandığı ve madde kullanan ile kullanmayan bireyler arasında cinsel deneyim oranları açısından anlamlı bir fark bulunmadığı saptanmıştır. Literatürde, madde kullanan bireylerde riskli cinsel davranışların daha yaygın olduğu belirtilmektedir. Demet ve ark. yaptığı çalışmada madde kullanan bireylerin erken yaşta cinselliği deneyimine sahip oldukları bulunmuştur (22).

Tablo 2. Bilinen Doğum Kontrol Yöntemleri ile Tercih Edilen Doğum Kontrol Yöntemleri

Bilinen Doğum Kontrol Yöntemleri	Tercih Edilen Doğum Kontrol Yöntemleri					Total	p
	Takvim Yöntemi	Geri Çekme	Kondom	Oral Kontraseptif	Intrauterin Araç		
Takvim Yöntemi	11	0	0	1	0	12	
Geri Çekme	1	5	2	0	0	8	
Oral Kontraseptif	5	0	53	1	0	59	
Kondom	4	0	66	0	0	70	
Intrauterin Araç	1	0	5	6	15	16	
Total	22	5	55	68	15	165	<0,001

Tablo 3. Cinsiyet ile Yaşanılan Cinsel Deneyim Tecrübeleri

	El ele tutuşmuş	Öpüşmüş	Cinsel İlişki Yaşamış	Hiçbir tecrübe yaşamamış	Toplam	p
Kadın	20	30	12	42	104	
Erkek	8	17	27	10	62	
Total	28	47	39	52	166	<0,001

Tablo 4. Cinsiyet ile Evlilik Öncesi Cinsel İlişkiye Karşı Tutum

	Kabul Edilemez	Olabilir	Evlilik Kesin ise Yaşanabilir	Total	p
Kadın	65	31	8	104	
Erkek	13	33	16	62	
Total	78	64	24	166	<0,001

Tablo 5. Cinsiyet ile Cinsel Deneyim Yaşama Yaşı

	n	Ortanca Sıra	Sıra Toplamı	p
Kadın	11	18,77	206,50	
Erkek	28	20,48	573,50	
Total	39	-	-	0,659

Çalışmamızda benzer bir sonuç beklenirken, anlamlı bir farkın gözlenmemesi, katılımcıların yüksek eğitim düzeyi ve madde kullananların azlığı ile açıklanabilir. Eğitim düzeyi yüksek bireylerin riskli cinsel davranışlara ve madde kullanımına karşı daha temkinli oldukları bulunmuştur (23). Ayrıca, çalışmamızdaki madde kullanım oranı literatürle kıyaslandığında daha düşük bulunmuştur.

Çalışmamızın temel sınırlılığı, katılımcıların yalnızca tek bir kurumdan seçilmiş olmasıdır. Bu durum, sonuçların genellenebilirliğini sınırlamaktadır.

SONUÇ

Sonuç olarak, çalışmamız üniversite öğrencilerinin cinselliğe yönelik tutumlarının, cinsiyet, kültürel normlar ve toplumsal yapı gibi çeşitli faktörlerden etkilendiğini göstermektedir. Cinsel sağlık konusunda doğru bilgi kaynaklarının kullanımının artırılması ve bu alanda eğitim programlarının geliştirilmesi, bireylerin sağlıklı tutumlar geliştirmesi ve riskli davranışlardan kaçınması için önemlidir. Çalışmada elde edilen bulgular, gençlerin cinsellik, doğum kontrol yöntemleri ve bağımlılık yapıcı madde kullanımı konusundaki farkındalıklarını artırmaya yönelik kapsamlı politikaların ve müdahalelerin gerekliliğini vurgulamaktadır. Bu doğrultuda, farklı demografik gruplar ve kültürel bağlamlar dikkate alınarak daha geniş çaplı araştırmalar yapılması önerilmektedir.

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TIP FAKÜLTESİ 1. VE 5. SINIF ÖĞRENCİLERİNİN ÇOCUK HASTALARIN AĞIZ VE DIŞ SAĞLIĞI KONUSUNDA BİLGİ, TUTUM VE DAVRANIŞLARININ KARŞILAŞTIRMALI DEĞERLENDİRİLMESİ

A Comparative Evaluation Of First- and Fifth-Year Medical Students' Knowledge, Attitudes and Behaviors Regarding Oral Health in Pediatric Patients

Nevra KARAMUFTUOĞLU¹, Ceylin KARAGOZ², Merve YUKSEL², Emre BAKIR²

ÖZET

Amaç: Bu çalışmada, tıp fakültesi öğrencilerinin çocuk ağız ve diş sağlığına yönelik bilgi, tutum ve davranış düzeylerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu kesitsel ve tanımlayıcı araştırma, yaşları 18–29 arasında değişen Yozgat Bozok Üniversitesi Tıp Fakültesi'nde öğrenim gören 230 gönüllü (1. ve 5. sınıflar) öğrenciyle yürütülmüştür. Katılımcılara genel ağız-diş sağlığı bilgisi, danışmanlık ve koruyucu/edici uygulamalara yönelik bilgi düzeylerini ölçen 25 maddelik yapılandırılmış anket uygulanmıştır. Her doğru yanıt 4 puan olarak değerlendirilmiş, toplam puan 100 üzerinden hesaplanmıştır. Bilgi düzeyi <52 puan “yetersiz”, 52–72 “orta”, >72 puan “yeterli” olarak sınıflandırılmıştır. Veriler SPSS 27.0 ile analiz edilmiştir. Normal dağılım Kolmogorov-Smirnov ve Shapiro-Wilk testleriyle değerlendirilmiş; grup karşılaştırmaları için bağımsız örneklem t-testi, Mann-Whitney U ve Ki-kare testi kullanılmıştır. İstatistiksel anlamlılık düzeyi $p < 0,05$ 'tir.

Bulgular: 5. sınıf öğrencilerinin bilgi puan ortalaması 1. sınıflardan anlamlı düzeyde yüksektir ($56,7 \pm 12,3$ vs. $48,2 \pm 10,1$; $p < 0,05$). Ancak yalnızca %4,3'ü yeterli bilgi düzeyine ulaşmıştır. 1. sınıf öğrencilerinin %78,5'i yetersiz bilgiye sahipken, bu oran 5. sınıfta %58,3'e düşmüştür. Tutum ve davranış açısından da 5. sınıflar anlamlı şekilde daha olumlu skorlar göstermiştir.

Sonuç: Bu çalışmada, tıp öğrencilerinin çocuk ağız ve diş sağlığına yönelik bilgi, tutum ve davranış düzeyleri değerlendirilmiş; 1. sınıfların çoğunlukla yetersiz, 5. sınıfların ise orta düzeyde bilgi ve davranış sergilediği belirlenmiştir. Tıp eğitimi süreci olumlu katkı sağlasa da, yeterli düzeye ulaşamamıştır. Bu nedenle, çocuk hastalara yönelik ağız-diş sağlığı eğitiminin tıp müfredatına daha yapılandırılmış, uygulamalı ve disiplinler arası şekilde entegre edilmesi önerilmektedir.

Anahtar Kelimeler: Ağız-Diş Sağlığı; Tıp Öğrencileri; Çocuk Sağlığı; Bilgi, Tutum ve Davranış

ABSTRACT

Objective: This study aimed to evaluate the knowledge, attitudes, and behaviors of medical students regarding pediatric oral health.

Material and Methods: This cross-sectional and descriptive study was conducted with 230 volunteer students (1st and 5th year) aged 18–29 at Yozgat Bozok University Faculty of Medicine. A structured 25-item questionnaire was administered to assess participants' knowledge on general oral health, counseling, and preventive/therapeutic practices. Each correct answer was scored as 4 points, and total scores were calculated out of 100. Knowledge levels were classified as <52 “insufficient,” 52–72 “moderate,” and >72 “adequate.” Data were analyzed using SPSS 27.0. Normality was assessed via Kolmogorov-Smirnov and Shapiro-Wilk tests; group comparisons were made using independent sample t-test, Mann-Whitney U test, and Chi-square test. A p-value <0.05 was considered statistically significant.

Results: The mean knowledge score of 5th-year students was significantly higher than that of 1st-year students (56.7 ± 12.3 vs. 48.2 ± 10.1 ; $p < 0.05$). However, only 4.3% reached an adequate level of knowledge. While 78.5% of 1st-year students had insufficient knowledge, this rate decreased to 58.3% among 5th-year students. In terms of attitudes and behaviors, 5th-year students showed significantly more positive scores.

Conclusion: The study revealed that while 1st-year students mostly had insufficient knowledge, 5th-year students demonstrated moderately sufficient knowledge and behavior levels regarding pediatric oral health. Although medical education positively influenced knowledge and behavior, adequacy was not fully achieved. Therefore, it is recommended to integrate pediatric oral health education into the medical curriculum through more structured, practical, and interdisciplinary approaches.

Keywords: Oral Health; Medical Students; Pediatric Health; Knowledge, Attitudes and Behaviors

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Giriş

Ağız ve diş sağlığı, genel sağlığın önemli bir parçasıdır ve bireyin sağlıklı bir yaşam sürmesinde etkili rol oynar. Dünyada en sık karşılaşılan halk sağlığı sorunlarından biri ağız ve diş sağlığı hastalıklarından biri olan diş çürüğüdür (1). Diş çürüğü tedavisi ilerleyen aşamalarda zaman, emek ve yüksek maliyet gerektirdiği için çocuklarda ağız ve diş sağlığının erken yaşlardan itibaren korunmasına yönelik çalışmalar halk sağlığının iyileştirilmesi açısından büyük önem taşımaktadır (2-5). Çocukluk döneminde ağız ve diş sağlığı; beslenme, büyüme ve gelişim, konuşma ve estetik açıdan önemlidir (6). Süt dişleri yaklaşık 6 yaşına kadar bu fonksiyonları yerine getirir ve daimi dişlere yer tutucu olarak rehberlik ederler. Süt dişlerinin erken ve gereksiz çekimi çocuğun çene yapısını, diş dizilimini, fiziksel ve mental gelişimini ve özgüvenini olumsuz etkiler. Ayrıca 6 yaşından sonra çıkan daimi dişlerin ömür boyu ağızda kalacağı göz önünde bulundurulduğunda, korunmaları ve gerektiğinde tedavi edilmeleri gerekmektedir (7). Tüm bu faktörler göz önüne alındığında çocukların ağız ve diş sağlığının yalnızca diş hekimlerine bırakılması yerine tıp doktorlarının da bu konuda yeterli bilgiye sahip olmaları önemlidir. Tıp doktorlarının yeterli bilgi seviyesine ulaşmalarındaki en önemli adım, tıp fakültelerinde aldıkları eğitimdir. Bu çalışmanın amacı, bir tıp fakültesi 1. ve 5. sınıf öğrencilerinin çocuk hastaların ağız ve diş sağlığı konusunda bilgi düzeylerini belirlemek, aldıkları eğitime bağlı olarak bu durumun değişip değişmediğini saptamak ve verilen eğitimin kalitesini değerlendirmektir.

GEREÇ VE YÖNTEMLER

Çalışmanın yürütüldüğü Yozgat Bozok Üniversitesi Tıp Fakültesi Dekanlığı ve Yozgat Bozok Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu 2024-GOKAEK-246_2024.07.10_85 karar numaralı izin alındıktan sonra, 1. ve 5. sınıf öğrencileri ile tanımlayıcı bir anket çalışması yapılmıştır. Çalışmaya tıp fakültesinde öğrenim gören 18–29 yaş aralığındaki toplam 230 gönüllü öğrenci dâhil edilmiştir. Anket formu, öğrencilerin çocuk ağız ve diş sağlığına ilişkin bilgi düzeyini ölçmeye yönelik 25 sorudan oluşmaktadır. Anketler, gözlemci eşliğinde yüz yüze uygulanmıştır. Her doğru cevap 4 puan, her yanlış cevap 0 puan olarak değerlendirilmiş; maksimum toplam puan 100

olacak şekilde bilgi düzeyi hesaplanmıştır. Bilgi düzeyi; <52 puan “yetersiz”, 52–72 puan “orta”, >72 puan ise “yeterli” olarak sınıflandırılmıştır. Sorular, üç ana başlık altında gruplanmıştır: çocuk ağız ve diş sağlığına dair temel bilgiler, hastaları yönlendirme bilgisi ve süt/daimi dişlerin korunması ve tedavi yöntemleri. Araştırmanın verileri SPSS 27.0 (IBM Corp., Armonk, NY, USA) istatistik programı kullanılarak analiz edilmiştir. Tanımlayıcı istatistikler kapsamında; öğrencilerin yaş, cinsiyet ve sınıf düzeylerine ilişkin frekans ve yüzde dağılımları, toplam bilgi puanlarına ilişkin ortalama, medyan, standart sapma, minimum ve maksimum değerler hesaplanmıştır. Veri setinin normal dağılıma uygunluğu Shapiro-Wilk testi ile değerlendirilmiştir. İki grup karşılaştırmalarında (1. ve 5. sınıf öğrencileri arasında) toplam bilgi puanları ve alt ölçek puanları için dağılıma bağlı olarak bağımsız örneklem t-testi veya Mann-Whitney U testi kullanılmıştır. Bilgi düzeyi kategorileri (yetersiz, orta, yeterli) ile sınıf düzeyi arasında anlamlılık düzeyini belirlemek üzere Ki-kare testi uygulanmıştır. İstatistiksel anlamlılık düzeyi $p < 0,05$ olarak kabul edilmiştir.

BULGULAR

Çalışmaya yaşları 18-29 arasında değişen toplam 230 gönüllü öğrenci katılmıştır. Tablo 1’de öğrencilerin sosyodemografik özellikleri sunulmuştur. Öğrencilerin büyük çoğunluğunu kadınlar oluşturmakta olup, yaş ortalaması $21,3 \pm 2,1$ olarak hesaplanmıştır. Çalışmaya 1. sınıf ($n=103$) ve 5. sınıf ($n=89$) öğrencileri dahil edilmiştir.

Genel bilgi puanları incelendiğinde, her iki sınıf grubunda da “yetersiz” bilgi düzeyinin baskın olduğu; ancak 5. sınıf öğrencilerinin ortalama puanının 1. sınıflara göre daha yüksek olduğu tespit edilmiştir. 1. sınıf öğrencilerinin ortalama bilgi puanı 48,2 ($SS=10,1$), 5. sınıf öğrencilerinin ise 56,7 ($SS=12,3$) olarak hesaplanmıştır. Gruplar arası fark istatistiksel olarak anlamlı bulunmuştur ($p < 0,05$).

Anketin üç alt başlığına (1. Temel bilgiler, 2. Yönlendirme bilgisi, 3. Koruma ve tedavi bilgisi) ilişkin puanlar karşılaştırıldığında; her üç başlıkta da 5. sınıf öğrencileri daha yüksek ortalamalara sahip olmakla birlikte, bu farkların istatistiksel olarak anlamlı olmadığı gözlemlenmiştir ($p > 0,05$).

Bilgi düzeyleri kategorik olarak değerlendirildiğinde; 1.

sınıf öğrencilerinin %78,5'inin yetersiz düzeyde bilgiye sahip olduğu, bu oranın 5. sınıf öğrencilerinde %58,3'e gerilediği; orta düzeyde bilgiye sahip olanların oranı sırasıyla %19,5 ve %37,4; yeterli bilgiye sahip olanların oranı ise %2,0 ve %4,3 olarak hesaplanmıştır. Sınıf düzeyi ile bilgi düzeyi kategorileri arasındaki ilişki Ki-kare testi ile anlamlı bulunmuştur ($p<0,05$).

Tablo 2'te anketin her bir sorusuna verilen doğru cevap yüzdeleri gösterilmektedir. Genel olarak, temel bilgi sorularında doğru cevap oranları daha yüksek bulunurken, yönlendirme ve koruma/tarama alt başlıklarında daha düşük doğru cevap oranları gözlenmiştir. Bu durum, öğrencilerin teorik bilgiye daha hâkim olduklarını, ancak pratik uygulama ve

yönlendirme konusunda eksiklik yaşadıklarını ortaya koymaktadır.

Şekil 1, 1. ve 5. sınıf öğrencilerinin çocuk ağız ve diş sağlığına ilişkin bilgi puanlarının ortalamalarını göstermektedir. 5. sınıf öğrencilerinin bilgi düzeyi ortalaması ($56,7 \pm 12,3$), 1. sınıf öğrencilerine kıyasla ($48,2 \pm 10,1$) istatistiksel olarak anlamlı düzeyde daha yüksek bulunmuştur ($p<0,05$).

Şekil 2, 1. ve 5. sınıf öğrencilerinin bilgi düzeylerinin (yetersiz, orta ve yeterli) yüzdesel dağılımını göstermektedir. 1. sınıf öğrencilerinin %78,5'inin bilgi düzeyi yetersiz iken, bu oran 5. sınıflarda %58,3'e düşmüştür. Orta düzeyde bilgiye sahip öğrencilerin oranı 1. sınıflarda %19,5 iken, 5. sınıflarda %37,4'e

Tablo 1. Soruların doğru cevap yüzdesi

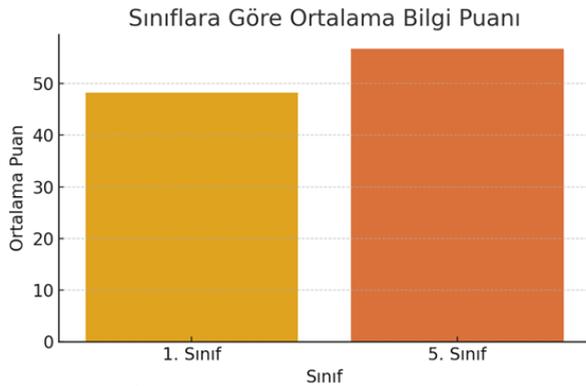
Soru	Doğru %*
Soru 1	75,52
Soru 2	50,0
Soru 3	71,35
Soru 4	8,33
Soru 5	60,94
Soru 6	40,62
Soru 7	40,1
Soru 8	56,77
Soru 9	53,65
Soru 10	46,35
Soru 11	28,12
Soru 12	3,65
Soru 13	28,12
Soru 14	29,17
Soru 15	73,44
Soru 16	44,27
Soru 17	14,58
Soru 18	8,33
Soru 19	18,75
Soru 20	16,15
Soru 21	48,96
Soru 22	31,25
Soru 23	34,9
Soru 24	56,77
Soru 25	36,46
Soru 26	6,25
Soru 27	41,15

*%: Kolon yüzdesi

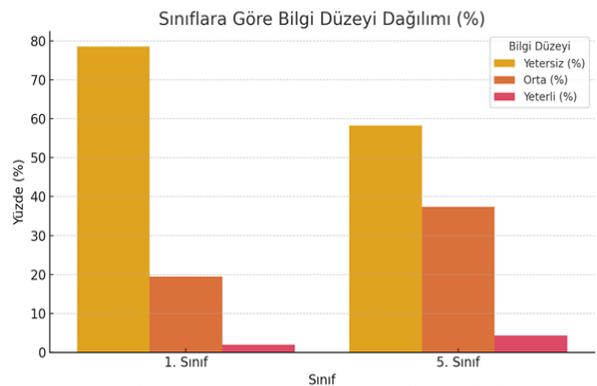
Tablo 2. Öğrencilerin sosyodemografik özellikleri

		n	%
Sınıf	1.	103,0	53,65
	5.	89,0	46,35
Cinsiyet	Kız	126,0	65,62
	Erkek	66,0	34,38

n: Sayı, *%: Kolon yüzdesi



Şekil 1. Sınıflara Göre Ortalama Bilgi Puanı.



Şekil 2. Sınıflara Göre Bilgi Düzeyi Dağılımı (%).

yükselmıştır. Yeterli düzeyde bilgiye sahip öğrenci oranı ise her iki grupta da oldukça düşüktür (sırasıyla %2,0 ve %4,3). Bu dağılım, sınıf düzeyi ile bilgi seviyesi arasındaki farkın anlamlı olduğunu göstermektedir ($p<0,05$).

Tablo 3, 1. ve 5. sınıf öğrencilerinin çocuk ağız ve diş sağlığına yönelik bilgi puanlarının ortalamasını, standart sapmasını ve bilgi düzeyi kategorilerine göre (yetersiz, orta, yeterli) dağılımlarını göstermektedir. Elde edilen bulgulara göre, 5. sınıf öğrencileri 1. sınıflara göre daha yüksek bilgi puanı ortalamasına sahip olsa da, her iki grupta da yeterli bilgi düzeyine ulaşan öğrenci oranı oldukça düşüktür. Bu durum, bilgi artışına rağmen eğitimin hedeflenen bilgi düzeyini sağlamada yetersiz kaldığını göstermektedir.

Bu bulgular, tıp eğitimi süresince çocuk ağız ve diş sağlığına yönelik bilgi düzeyinde bazı gelişmeler olduğunu ancak yeterli düzeye ulaşmada eksikliklerin devam ettiğini ortaya koymaktadır. Özellikle 5. sınıf öğrencilerinde gözlenen görece artış, eğitimin olumlu etkisini gösterse de, her iki grubun da genel olarak hedeflenen yeterlilik seviyesinin altında kaldığı görülmektedir. Bu durum, çocuklara yönelik ağız ve

diş sağlığı konularının tıp müfredatında daha güçlü ve yapılandırılmış biçimde ele alınması gerektiğine işaret etmektedir. Öğrencilerin çocuk hastaların ağız ve diş sağlığı konusundaki bilgi seviyeleri değerlendirildiğinde, 5. sınıf öğrencilerinin bilgi düzeylerinin 1. sınıf öğrencilerine göre anlamlı olarak daha yüksek olduğu görülmüştür. Ancak bilgi seviyesi kategorik olarak değerlendirildiğinde, 5. sınıf öğrencilerinin de henüz yeterli düzeyde olmadığı bulunmuştur. Bilgi soruları gruplar arasında karşılaştırıldığında; çocuk ağız ve diş sağlığı temel bilgileri, hastaları yönlendirme bilgileri ve süt ile daimi dişlerin korunma ve tedavi yöntemlerine dair bilgiler açısından anlamlı bir farklılık saptanmamıştır.

TARTIŞMA

Çocuklarda ağız ve diş sağlığı, genel sağlığın korunmasında temel bir bileşen olarak kabul edilmekte; bu kapsamda hekimlerin erken müdahalesi, yaşam boyu sürecek sağlık davranışlarının oluşmasında belirleyici rol oynamaktadır. Tıp fakültesi öğrencilerinin bu alandaki bilgi düzeylerinin değerlendirilmesi, geleceğin hekimlerinin koruyucu sağlık hizmetlerine

Tablo 3. Sınıf düzeylerine göre bilgi puanı ve dağılımı

Sınıf	Ortalama Puan	Standart Sapma	Yetersiz (%)	Orta (%)	Yeterli (%)
1. Sınıf	48,2	10,1	78,5%	19,5%	2,0%
5. Sınıf	56,7	12,3	58,3%*	37,4%	4,3%

*p<0,05

katkısını anlamak açısından önem arz etmektedir. Bu çalışma, bir tıp fakültesi 1. ve 5. sınıf öğrencilerinin çocuk ağız ve diş sağlığına yönelik bilgi düzeylerini karşılaştırmalı olarak analiz etmeyi amaçlamıştır.

Çalışma bulgularına göre, 5. sınıf öğrencileri, 1. sınıflara kıyasla istatistiksel olarak anlamlı şekilde daha yüksek bilgi puanlarına sahiptir (p<0,05). Bununla birlikte, yalnızca %4,3'lük bir kesimin "yeterli" bilgi düzeyine ulaştığı, büyük çoğunluğun "yetersiz" ya da "orta düzeyde yeterli" kategorisinde kaldığı görülmüştür. Bu durum, bilgi düzeyinde bir artışın varlığına rağmen eğitim sürecinin öğrencileri beklenen yeterlilik seviyesine ulaştırmada yetersiz kaldığını göstermektedir. Bu bulgu, öğrencilerin teorik olarak bazı kazanımlar elde ettiğini ancak bu kazanımların klinik uygulamalara ve pratik karar verme süreçlerine taşınmasında eksiklik olduğunu düşündürmektedir. Başka bir ifadeyle, tıp eğitiminin ağız ve diş sağlığı açısından temel bilgiyi aktarmakta başarılı olmakla birlikte, bunu davranışa dönüştürecek yeterli fırsatlar sunmadığı söylenebilir.

Bu sonuçlar, literatürdeki benzer bulgularla örtüşmektedir. Ayan ve ark., tıp fakültesi öğrencilerinin ağız ve diş sağlığına yönelik farkındalıklarının sınırlı olduğunu ve özellikle erken çocukluk dönemiyle ilgili yönlendirici bilgi eksikliklerinin devam ettiğini raporlamıştır (8). Karakaş ve ark. ise, intern doktorların florür kullanımı ve hastaların ilgili sağlık birimlerine yönlendirilmesi konusunda yeterli bilgiye sahip olmadığını belirtmiştir (9). Çalışmamızın sonuçları bu literatür ile uyumlu olup, farklı üniversite örneklemelerinde benzer eğilimlerin gözlenmesi sorunun sistemik olduğunu göstermektedir. Bu açıdan bakıldığında, müfredat düzeyinde yapısal bir revizyon ihtiyacı bulunmaktadır.

Bu çalışmada anketin üç temel alt başlığı olan "temel bilgiler", "yönlendirme bilgisi" ve "koruma/tarama bilgisi" açısından 5. sınıf öğrencilerinin ortalama puanları daha yüksek olmasına rağmen, farkların

istatistiksel olarak anlamlı düzeyde olmaması (p>0,05), bilgi ediniminin davranışsal düzeye yansımada önemli sınırlılıkların bulunduğunu ortaya koymaktadır. Kılınc ve ark. tarafından yapılan çalışmada da benzer şekilde, öğrencilerin ağız ve diş sağlığı konularında teorik olarak bilgili oldukları, ancak bu bilgiyi uygulamaya aktarmakta yetersiz kaldıkları ifade edilmiştir (10). Bu paralellik, tıp eğitiminin bilişsel öğrenmeye ağırlık verdiğini ancak davranışsal çıktıları yeterince desteklemediğini göstermektedir. Özellikle yönlendirme ve koruma/tarama başlıklarındaki eksiklikler, öğrencilerin koruyucu sağlık hizmetleri içinde ağız ve diş sağlığını ikincil planda gördüğünü düşündürmektedir.

Kurt tarafından yapılan bir başka çalışmada, öğrencilerin infant oral sağlığı konusundaki bilgi düzeylerinin düşük olduğu, ancak eğitime duydukları ihtiyacın yüksek olduğu saptanmıştır. Bu sonuçlar, müfredatlara çocuk ağız-diş sağlığına özel içeriklerin entegre edilmesi gerektiğini güçlendirmektedir (11). Benzer şekilde, Civan ve ark. yaptıkları çalışmalarında eğitimsel eksikliklerin yalnızca bilgi değil, aynı zamanda davranışsal çıktılar üzerinde de doğrudan etkili olduğunu bildirmiştir (12). Çalışmamızın bulguları da bu görüşü desteklemektedir. Özellikle erken dönemde çocuk hastalarla karşılaşma deneyimi sınırlı olan tıp fakültesi öğrencilerinde, bu alanın teorik düzeyde işlenmesi yeterli olmamakta; uygulamalı eğitim, disiplinler arası iş birlikleri ve klinik rotasyonlarla desteklenmesi gerekmektedir. Böylece öğrencilerin hem bilgi hem de davranış düzeyinde güçlenmeleri sağlanabilir.

Ağız-diş sağlığına yönelik eğitimin yalnızca bilgi aktarımına değil, aynı zamanda klinik entegrasyona, iletişim becerilerine, multidisipliner işbirliğine ve hasta merkezli yaklaşımlara odaklanacak biçimde yapılandırılması önemlidir. Ağız ve diş sağlığı eğitimine yönelik yapılandırılmış programların artırılması, öğretim üyeleri tarafından uygulamalı modüllerle

desteklenmesi ve pediatri, halk sağlığı ve diş hekimliği alanlarıyla entegrasyonun sağlanması, bu alandaki eksiklikleri gidermede etkili olacaktır.

SONUÇ

Bu çalışmanın bulguları, tıp fakültesi öğrencilerinde çocuk ağız ve diş sağlığına ilişkin bilgi düzeylerinde eğitimle birlikte artış olduğunu ancak yeterli seviyeye ulaşamadığını ortaya koymaktadır. Bu nedenle, müfredatların daha kapsamlı, disiplinler arası ve uygulamalı içeriklerle zenginleştirilmesi, çocuk hastalara yönelik koruyucu sağlık hizmetlerinin etkinliğini artırmak açısından stratejik bir gereklilik olarak karşımıza çıkmaktadır.

Tasdik ve Teşekkür

Çalışmaya gönüllü olarak katılan 1. ve 5. sınıf tıp fakültesi öğrencilerine, zaman ayırarak anketi samimiyetle doldurdukları için teşekkür ederiz.

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DOSIMETRIC ANALYSIS OF DEEP INSPIRATION BREATH HOLD TECHNIQUE ADAPTED TO TANGENTIAL-BASED VOLUMETRIC MODULATED ARC THERAPY FOR LEFT BREAST CANCER AFTER MASTECTOMY

Mastektomi Sonrası Sol Meme Kanserinde Tanjansiyel Temelli Hacimsel Modüleli Ark Terapisine Uyarlanan Derin İnhalasyonda Nefes Tutma Tekniğinin Dozimetrik Analizi

Dicle ASLAN¹, Mustafa Tarkan AKSOZEN¹

ABSTRACT

Objective: To evaluate the dosimetric properties of the deep inspiration breath hold (DIBH) technique adapted to tangential-based volumetric modulated arc therapy (TVMAT) in left breast cancer patients with mastectomy.

Material and Methods: Forty-three patients who underwent mastectomy and received chest wall and regional lymph node irradiation were included in the study. Simulation computed tomography (CT) was performed in DIBH and free-breathing (FB). Two plans were created for each patient; DIBH-TVMAT and FB-TVMAT. Both plans were realized using a mono-isocentric technique with two partial arc rotations, and the same gantry angles were used. The standard fractionation schedule for each patient was set to 50 Gy in 25 fractions. Paired-sample T-test was used to evaluate the dosimetric parameters.

Results: The comparison between FB-TVMAT and DIBH-TVMAT plans revealed mean heart doses of 8.9 Gy and 5.4 Gy, respectively ($p < 0.001$). A 6.2% reduction was encountered in left lung volume receiving 5 Gy (V5) in the DIBH-TVMAT plan ($p = 0.01$). A reduction of 1.3 Gy at a percentage of 28% was monitored in the mean dose of the right lung in DIBH-TVMAT ($p < 0.001$). The mean right breast dose was 0.7 Gy lower in DIBH-TVMAT ($p < 0.001$).

Conclusion: The results support that the adaptation of DIBH to TVMAT allows an optimal target volume dose coverage as well as leads to significant dose reductions in the left lung, right lung, heart, LADCA, and right breast for the left breast cancer patients with mastectomy.

Keywords: Breast Cancer; Tangential Volumetric Modulated Arc Therapy; Deep Inspiration Breath Hold; Radiotherapy; Mastectomy

ÖZET

Amaç: Bu çalışmada, mastektomi uygulanmış sol meme kanseri hastalarında, tanjansiyel temelli hacimsel modüleli ark terapisine (TVMAT) entegre edilen derin inhalasyonda nefes tutma (DIBH) tekniğinin dozimetrik özelliklerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya mastektomi geçirmiş ve torakal duvar ile bölgesel lenf nodlarına radyoterapi uygulanan 43 hasta dâhil edilmiştir. Simülasyon bilgisayarlı tomografileri (BT), hem DIBH hem de serbest solunum (FB) modlarında alınmıştır. Her hasta için DIBH-TVMAT ve FB-TVMAT olmak üzere iki ayrı tedavi planı oluşturulmuştur. Her iki plan da mono-izosentrik tekniğe ve iki parsiyel ark rotasyonu kullanılarak, aynı gantri açılarıyla planlanmıştır. Tüm hastalar için fraksiyonasyon şeması 25 fraksiyonda toplam 50 Gy olacak şekilde standartlaştırılmıştır. Dozimetrik parametrelerin karşılaştırılmasında eşleştirilmiş örneklem t-testi kullanılmıştır.

Bulgular: FB-TVMAT ve DIBH-TVMAT planları karşılaştırıldığında, sırasıyla ortalama kalp dozları 8,9 Gy ve 5,4 Gy olarak bulunmuştur ($p < 0,001$). DIBH-TVMAT planında sol akciğerin 5 Gy aldığı hacimde (V5) %6,2'lik bir azalma gözlenmiştir ($p = 0,01$). Sağ akciğerin ortalama dozunda 1,3 Gy, yani %28 oranında anlamlı bir düşüş kaydedilmiştir ($p < 0,001$). Ayrıca, sağ memeye alınan ortalama doz DIBH-TVMAT planında 0,7 Gy daha düşük bulunmuştur ($p < 0,001$).

Sonuç: Bulgular, DIBH tekniğinin TVMAT planlamasına entegre edilmesinin hedef hacim üzerinde yeterli doz kapsamı sağladığını ve sol meme kanseri nedeniyle mastektomi uygulanmış hastalarda kalp, LADCA, sol ve sağ akciğer ile karşı meme dozlarında anlamlı azalmalar sağladığını göstermektedir.

Anahtar Kelimeler: Meme Kanseri; Tanjansiyel Hacimsel Modüleli Ark Terapisi; Derin İnspiryumda Nefes Tutma; Radyoterapi; Mastektomi

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INTRODUCTION

Radiotherapy (RT) is an essential treatment modality to prevent locoregional recurrence and prolong overall survival in breast cancer (1-3). However, it has been reported to increase the risk of early cardiac mortality, ischemic heart disease, and radiation pneumonia, especially after left breast cancer (LBC)(4,5). This risk increases even more in post-mastectomy patients with lymph node positivity. In these patients, the RT field should mostly cover the chest wall and the regional lymph nodes (RLN). Complications may develop in the heart, coronary arteries, and lungs due to the anatomical changes after mastectomy and the proximity of the treatment area to organ-at-risk (OAR) (6,7). The distance between the treatment area and OAR can be adjusted by monitoring respiratory movements. As the distance between the target volume and the organs increases, lung and heart volumes entering the irradiation area decrease (8,9). Because of that, during RT application, the patient's position in deep inspiration breath holding (DIBH) is used, where this distance is the safest(10,11). Tangential-based three-dimensional (3D) RT and intensity-modulated RT (IMRT) techniques are frequently used in the postmastectomy treatment of LBC (12). Two opposing fields are used in the tangential-based 3D conformal therapies, whereas multiple fields are used in the (IMRT). Donovan et al. have reported that IMRT increases target dose coverage and reduces doses to OAR (13). Volumetric modulated arc therapy (VMAT) is a relatively newer treatment modality. It increases target volume coverage and homogeneity with multileaf collimator and gantry rotations. However, it requires fewer monitoring unit and shortens treatment duration compared with IMRT and 3D conformal therapies. Besides, it protects normal tissue and OAR better in atypical target volumes. Because of this reason, it is frequently used in prostate and head-neck cancers (14,15). Despite all these advantages, it increases low-dose fields in the irradiated volume and normal tissue during treatment compared with tangential field techniques or IMRT since it is performed by full or continuous arc. Consequently, the dose applied to the contralateral breast and lung may increase. It may increase the development risk for secondary cancer (16). Tangential VMAT (TVMAT)

utilizes partial arcs compatible with tangential fields like other tangential field techniques and multileaf collimator and gantry rotations such as VMAT. It does not elevate low-dose volume compared to VMAT and shortens treatment duration using tangential arc. It is quite a novel treatment technique (17).

Despite the presence of studies that have compared DIBH and free-breath (FB) techniques following left breast-conserving surgery, there is no adequate information in the literature on determining the appropriate treatment technique and positioning in the patients requiring chest wall (CW)+ RLN irradiation after mastectomy. The present study aimed to discuss the dosimetric effects of integration of DIBH to TVMAT technique and compare dosimetric characteristics of DIBH-TVMAT and free breathing (FB)-TVMAT in LBC patients who underwent mastectomy and needed to receive RLN irradiation.

MATERIALS AND METHODS

We included 43 patients who were (a) diagnosed with LBC, (b) with mastectomy, (c) required adjuvant RT to the CW and RLN, and (d) able to perform computed tomography (CT) scanning in both DIBH and FB with an identical position between January 2016 and January 2022. The exclusion criteria were a history of post-mastectomy implant reconstruction, breast-conserving surgery, inability to hold breath on deep inspiration, and poor performance status. The study was conducted following the Helsinki Declaration of 1975, revised in 2000. Our study was approved by the independent ethics committee/institutional review board. The first ethics committee approval was obtained prior to the initiation of the study, with the approval number 2020/32 and the date 15.01.2020. The second ethics committee approval was granted under the approval number 2024/175 on 13.03.2024.

Training nurse taught breath management to patients before simulation CT. The patients were in the supine position as placed with both arms bent on the breast board before CT imaging. Opaque substances were placed on the midsternal, midaxillary, medial, and lateral lines of the operation scar to determine the scar and chest wall fields. Before CT imaging, an infrared reflecting block was placed approximately 2 cm below the xiphoid for breath monitoring. With infrared

tracking cameras, breath monitoring was performed using an infrared reflecting block and a real-time position management system (RPM, Varian Medical System, Palo Alto, USA). We obtained 1.5 mm thick images using a CT scanner (Siemens Somatom Emotion Duo). The upper and lower margins were assigned to the 1st cervical and 2nd lumbar vertebra. CT procedures were performed consecutively in DIBH and FB with the same position. The images in DIBH and FB, respiratory curve, and gating window were transferred to the Eclipse Version 13.6.23 Treatment planning system (TPS) (Varian Medical System, Palo Alto, USA). The target volume and OAR contouring process were performed in DIBH and FB imagings. An identical observer performed contouring to avoid interobserver variability. Chest wall, axillary lymph nodes (ALN), supraclavicular lymph nodes (SCLN), internal mammary lymph nodes (IMLN), ipsilateral lung, heart, left anterior descending coronary artery (LADCA), contralateral lung, contralateral breast, esophagus, thyroid, and spinal canal were contoured for each slice. The Radiation Therapy Oncology Group (RTOG) Guideline was accepted as the reference for contouring. In contouring the chest wall, cranial and caudal margins were the clavicular head's caudal aspect and the contralateral breast's caudal aspect, respectively. The midaxillary line was accepted as the reference when determining the lateral margin. The medial margin was the sternal rib junction. The opaque substance inside the scar tissue was included in the treatment area. Supraclavicular lymph nodes were contoured between the cricoid cartilage and the caudal aspect of the clavicular head, respectively. ALN contouring was performed by referencing the pectoralis major and minor muscles. Internal mammary lymph nodes were contoured between the cranial aspect of the 1st rib and the superior aspect of the 4th rib. The combination of CW and RLN was defined as CTV. The planning target volume (PTV) was created by a 5-mm margin to the CTV. The PTV was cropped from the skin by a 3-mm margin. The whole pericardium, myocardium, and endocardium were included in the treatment field in contouring the heart.

Treatment planning was created separately for DIBH and FB using the TVMAT technique. A mono-isocentric technique was used to design these plans with two

partial arc rotations. In our plans, the first arc angle started at 271-311.2 and stopped at 130.3-163.7. The second arc was completely inverse of the first arc. Equal degree arcs were used in both plans. These arc angles were determined based on the patient's anatomy. A photon energy of 6 MV was used. The prescribed dose was 50 Gy with 2 Gy per fraction daily for PTV. The treatment aimed to deliver 95% of the targeted dose to 95% of the PTV and to keep the dose to OAR as low as possible. Dose concentrations for the OAR and PTV were summarized in Table 1. The plans were approved with appropriate doses (Fig. 1, Fig. 2). Conformity, homogeneity, and quality assurance (QA) were similar for the plans. The grid size that was used for dose calculation was 2.5 mm. We used the progressive resolution optimizer (Version 13.6.23) and analytical anisotropic algorithm (Version 13.6.23) for optimizations.

Dosimetric parameters of DIBH-TVMAT and FB-TVMAT plans were determined from the dose-volume histogram (DVH) (Fig. 3). The heart and LADCA volumes receiving 5-30 Gy doses (V5, V10, V25, V30), mean and maximum doses (Dmean, Dmax), the V5, V10, V20 values of the left lung (V5, V10, V20), Dmean, D2% values of the right lung and, Dmean value of the right breast were taken.

IBM SPSS Version 24.0 (SPSS Inc., IL, USA) was used for statistical analyses. The distribution of the continuous variables was tested with the Kolmogorov-Smirnov and Shapiro-Wilk test. Mean and standard deviation were used for normally distributed data. Paired-sample T-test was used to determine the dose differences between DIBH-TVMAT and FB-TVMAT plans. $p < 0.05$ was accepted as the statistical significance.

RESULTS

Table 2 summarizes patient characteristics. The median age was 44 (range 29-78). The dosimetric parameters for OAR were evaluated in DIBH-TVMAT and FB-TVMAT plans. There is no statistically significant difference between the plans regarding PTV. The values obtained for OAR are listed in Table 3.

The Dmean value of the heart was 5.4 Gy for the DIBH-TVMAT plan and 8.9 Gy for the FB-TVMAT plan ($p < 0.001$). That result indicated an average dose reduction of 3.4 Gy at a percentage of 38.2% after the DIBH plan.

Table 1. Dose targets for the critical organs

Structure	Parameter	Objective
PTV	V98 Gy (%)	≥ 98%
	D98 Gy (%)	≥ 98%
	D5 Gy (%)	≤110%
Heart	V25 Gy (%)	≤25%
	Dmean (Gy)	≤10 Gy
	Dmax (Gy)	≤50 Gy
LADCA	Dmax (Gy)	≤50 Gy
Left Lung	V10 Gy (%)	≤50%
	V20 Gy (%)	≤20%
Right Lung	Dmean (Gy)	≤5 Gy
Right Breast	Dmean (Gy)	≤6 Gy
Esophagus	Dmean (Gy)	≤34 Gy

PTV: planning target volume, LADCA: left anterior descending coronary artery

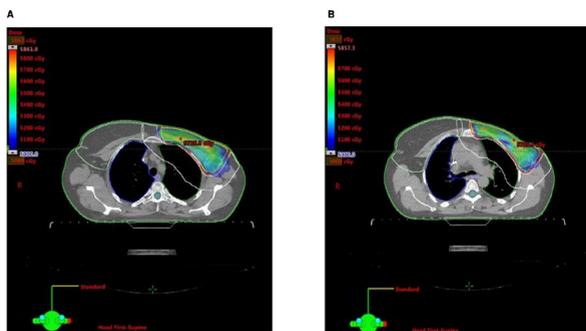


Figure 1. Dose distribution in axial views.
A. Tangential-based volumetric modulated arc therapy (TVMAT) plan with deep inspiration breath-hold technique,
B. TVMAT plan with free breath technique

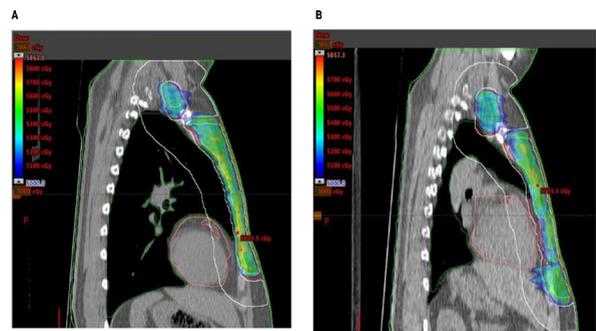


Figure 2. Dose distribution in sagittal views.
A. Tangential-based volumetric modulated arc therapy (TVMAT) plan with deep inspiration breath-hold technique,
B. TVMAT plan with free breath technique

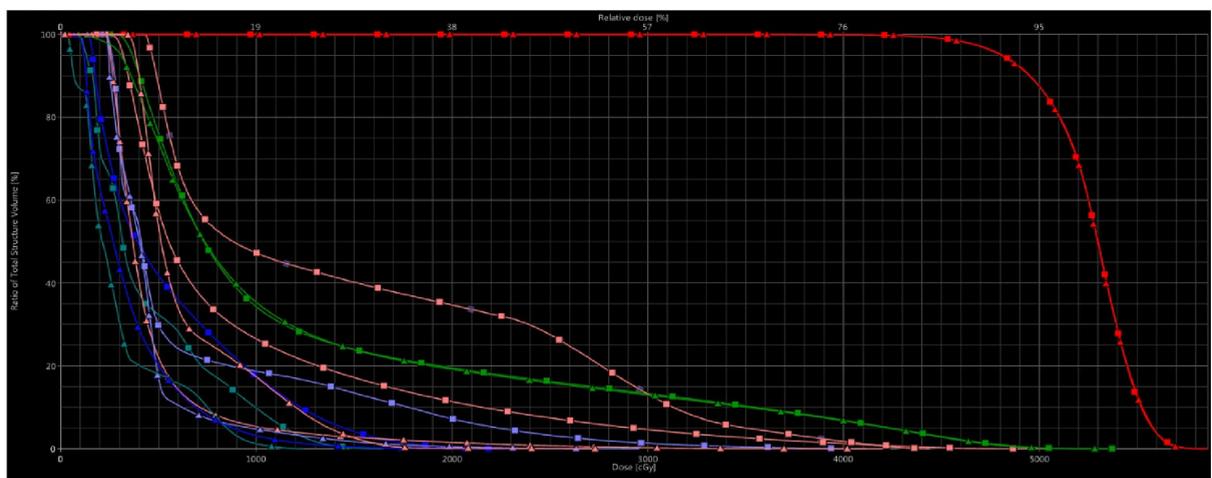


Figure 3. Dose-volume histograms for organs-at-risk and target volumes in deep inspiration breath hold-tangential-based volumetric modulated arc therapy (DIBH-TVMAT) and FB-TVMAT; free-breath-tangential-based volumetric modulated arc therapy (FB-TVMAT) plans. □ DIBH-TVMAT, Δ FB-TVMAT

Table 2. Patient characteristics

Characteristics		N= 43 (100%)
Median age (range)		44 (29-78)
Menopausal status	Premenopausal	27 (62.8%)
	Postmenopausal	16 (37.2%)
Histopathological type	Ductal invasive	38 (88.4%)
	Lobular invasive	2 (4.7%)
	Other	3 (6.9%)
Molecular subtype	Luminal A	3 (7%)
	Luminal B	22 (51.2%)
	HER2+	14 (32.6%)
	Triple negative	4 (9.3%)
Histopathological grade	G1	2 (4.7%)
	G2	30 (69.8%)
	G3	11 (25.6%)
Stage	2B	22 (51.2%)
	3A	12 (27.9%)
	3B	9 (20.9%)
Surgical Nodal Staging	AD	17 (39.5%)
	SLND	26 (60.5%)
Neoadjuvant Chemotherapy	Yes	19 (44.2%)
	No	24 (55.8%)

HER2: Human epidermal growth factor 2; SLND: sentinel lymph node dissection ; AD: axillary lymph node dissection

The average heart V25 was 1.3% in DIBH-TVMAT and 6.5% in FB-TVMAT plans ($p < 0.001$). A dose reduction of 78.4% was achieved. Moreover, an average dose reduction of 9.7 Gy, corresponding to a percentage of 19.8%, was obtained in the maximum heart dose by the DIBH-TVMAT plan ($p < 0.001$).

The mean LADCA dose for DIBH-TVMAT and FB-TVMAT plans were 13.7 Gy and 21 Gy, respectively ($p < 0.001$). A decrease of 7.3 Gy at a rate of 34.7% was found in the DIBH-TVMAT plan. A 43.2% and 18.3% reduction were achieved by the DIBH-TVMAT plan in V25 and Dmax of LADCA, respectively ($p < 0.001$; $p < 0.001$) (Table 3).

There was no statistically significant difference between the two plans regarding the average V10 and V20 of the left lung ($p=0.8$; $p=0.9$). However, a 6.2% reduction was encountered in V5 by the DIBH-TVMAT plan compared with the FB-TVMAT plan ($p=0.01$). The mean doses of the right lung in the DIBH-TVMAT and FB-TVMAT plans were 3.2 Gy and 4.6 Gy, respectively. These results indicated a decrease of 1.3 Gy at a percentage of 28% by the DIBH-TVMAT plan ($p < 0.001$). The mean right breast dose was lower by 0.7 Gy in the DIBH-TVMAT

plan. This difference indicated a 12.2% reduction and was statistically significant ($p < 0.001$) (Table 3).

DISCUSSION

This study has demonstrated that the DIBH-TVMAT technique reduces organ at-risk doses without missing target volume coverage in patients who received CW and RLN irradiation after mastectomy. However, a dose reduction was obtained in the V5 value of the left lung, whereas there is no impact on the V20 and V10. To the best of our knowledge, this is the first study that compared DIBH-TVMAT and FB-TVMAT techniques in cases irradiated to the CW and RLN after mastectomy. Besides, this study has the most significant number of patients among similar studies.

In recent years, many studies have been conducted to demonstrate the advantage of the DIBH technique regarding the distribution of doses applied to all OAR, primarily the heart and LADCA, in patients with left breast cancer (18-20). There is only a small number of studies that have analyzed the patients irradiated

Table 3. The dosimetric parameters and differences (Δ) for the organs-at-risk from dose-volume histogram in DIBH-TVMAT and FB-TVMAT plans

Structure	Parameter	DIBH-TVMAT	FB-TVMAT	Δ (DIBH-FB)	p
Heart	V5 Gy (%)	33±10.6	62.3±10.5	-29.2 (46%)	0.000
	V10 Gy (%)	8.7±4	24.6±6	-15.9 (64%)	0.000
	V25 Gy (%)	1.3±1.4	6.5±3	-5.1 (78%)	0.000
	V30 Gy (%)	0.7±0.8	4.3±2.3	-3.6 (83%)	0.000
	Dmean (Gy)	5.4±0.9	8.9±1.5	-3.4 (38%)	0.000
	Dmax (Gy)	39±7.7	48.8±8	-9.7 (19%)	0.000
LADCA	V5 Gy (%)	76.6±16.8	90.4±13.5	-13.7 (15%)	0.000
	V10 Gy (%)	42.5±20.6	57.4±21.7	-14.8 (25%)	0.000
	V25 Gy (%)	21±18.9	37.2±22.2	-16.1 (43%)	0.000
	V30 Gy (%)	15.4±16.3	30.2±20.9	-14.7 (48%)	0.000
	Dmean (Gy)	13.7±6.1	21±8.2	-7.3 (34%)	0.000
	Dmax (Gy)	37.9±10.4	46.4±10.3	-8.5 (18.3%)	0.000
	D25 % (Gy)	20±11	30±12.5	-10 (33%)	0.000
Left Lung	V5 Gy (%)	67.3±8.4	71.8±11.5	-4.5 (6%)	0.01
	V10 Gy (%)	34.6±4	34.4±6.3	-0.1 (0%)	0.8
	V20 Gy (%)	20.1±1.7	20.1±3.4	-0 (0%)	0.9
Right Lung	Dmean (Gy)	3.2±0.6	4.6±1.1	-1.3 (28%)	0.000
	D2 % (Gy)	10.6±3.2	13.9±4.1	-3.2 (23%)	0.000
Right Breast	Dmean (Gy)	5±1.3	5.7±1.2	-0.7 (12%)	0.000
PTV	V98 Gy (%)	98±1.4	98±0.8	-0 (0%)	0.9

PTV: planning target volume, DIBH-TVMAT: deep inspiration breath hold – tangential volumetric modulated arc therapy, FB-TVMAT: free breath – tangential volumetric modulated arc therapy, LADCA: left anterior descending coronary artery.

to the chest wall and regional LNs after mastectomy. Dumane et al. have compared DIBH-TVMAT and FB-TVMAT plans that underwent implant reconstruction after mastectomy and received irradiation to the CW and RLN. The Dmean value of the heart was 8.2 Gy for DIBH-TVMAT and 5.3 Gy for FB-TVMAT plans. An average heart dose reduction of 2.9 Gy was encountered. Similar to this study, we detected an average dose reduction of 3.4 Gy in the mean heart dose after DIBH-TVMAT. We also showed a decrease in Dmax of LADCA by 8.5 Gy in DIBH plans, indicating a decline of approximately 18%. In addition, we have also noted a reduction in V5-30, D25, and Dmean values of heart and LADCA in DIBH-TVMAT plans. Dumane et al. found no significant difference between the plans regarding V20 of the left lung, whereas the reduction in V10 and V5 was significant ($p < 0.05$). Besides, the V5 value of the right lung was evaluated to be significant, whereas no statistically significant difference could be noted in the Dmean of the right breast. Also, in our

study, we encountered a decrease in the V5 of the left lung in the DIBH-TVMAT. However, there was no statistically significant difference between the two plans regarding V20 and V10 values. Differently from this study, we have determined a significant reduction in the Dmean of the right lung and right breast with the DIBH-TVMAT plan (21).

Darapu et al. compared DIBH and FB techniques in patients planned for CW and SCLN irradiation with a single isocentric 3D conformal field-in-field technique. The chest wall and SCLN were assigned as the target volumes. This study monitored a statistically significant reduction in V5-30 and Dmean value of the heart with the DIBH technique. The decrease in V5, V10, V25, and Dmean of the LADCA were also found to be statistically significant. Besides, V5, V20, V30, and Dmean of the left lung were found to be decreased in the DIBH plan. Contrarily, the decrease in the Dmean of the right lung in the DIBH plan was considered non-significant. Even though our study's heart and LADCA doses were

correlated with this study, dosimetric analysis of left and right lung doses revealed different outcomes. We found a significant decrease only in the V5 of the left lung. We have identified a 28% statistically significant decline in the Dmean of the right lung. Darapu et al. found a statistically significant decrease in the Dmean of the right breast in the treatment plans generated using the DIBH-FIF technique, precisely like our plan using the DIBH-TVMAT technique. The differences between dosimetric evaluations may result from the differences between target volume and dose-volume definitions. Unlike our study, Darapu et al. reported that IMLN and ALN were not involved in the treatment field in their research (22).

Quirk et al. evaluated 1221 patients with LBC who received whole breast or CW irradiation in another study. In the study, dosimetric analysis was performed in a subgroup treated with DIBH and tangential-based techniques, which included IMLN. The critical result of this study was that the LADCA dose was reduced by adding the DIBH technique to the treatment in patients diagnosed with advanced breast cancer and receiving IMLN irradiation. However, the number of patients with postmastectomy was not specified in the study, and the CW irradiation group was not evaluated separately (23).

On the other side, a treatment planning based on target volume and treatment volume is mainly generated to involve chest wall, Level I, II, and III axillary, supraclavicular, and internal mammary lymph nodes in postmastectomy patients with advanced-stage breast cancer. It is challenging to design accurate treatment planning and achieve dosimetric targets because of the large size and irregular geometry of the target volume with proximity to the OAR. Therefore, some studies have compared 3D conformal, intensity-modulated RT, and VMAT plans. The advantages and disadvantages have been comprehensively analyzed (24,25). Zhang et al. evaluated the patients who have undergone left mastectomy, detected with metastatic lymph nodes, and irradiated to the chest wall and RLN in their study. They have compared IMRT and VMAT plans. However, they have planned the treatment regimen with FB for all the patients. According to the results, they determined that the VMAT plan provided better coverage of the target volume. A reduction was

encountered in V5-20 and the Dmean value of the right lung in VMAT plans. Mean right lung and right breast doses were also lower in VMAT planning. V10, V30, and Dmean of the heart decreased compared with IMRT. However, no statistical significance was identified (26). In our study, we have adapted the DIBH technique to TVMAT to improve organ-at-risk protection in this patient group. We have preferred the TVMAT technique over other techniques to increase total target volume coverage, shorten treatment duration, and minimize secondary cancer risk. The study of Lang et al. included 11 postmastectomy patients with right or left breast cancer. The chest wall and RLNs were irradiated in all patients. DIBH technique was applied in their study. They have compared the FB technique with traditional VMAT and hybrid VMAT plans, similar to tangential-based RT involving four partial arcs and optimal angles. Hybrid and traditional VMAT plans were compared in the patients diagnosed with LBC. A 0.7 Gy reduction was encountered in mean heart doses in hybrid VMAT plans after, although no statistical significance was determined. Surprisingly, the mean heart dose declined in the patients who received right breast irradiation. The most crucial changes were in V5, V10, V20, and contralateral lung V20 for the total lung. A better PTV coverage was identified after hybrid VMAT planning. In this study, they stated that hybrid, namely VMAT plans similar to tangential-based techniques, may be an alternative treatment option for IMRT (27). The main limitation of our study is that no intravenous contrast agent was used during simulation CT. Vennarini et al. have administered intravenous contrast agents to more accurately monitor LADCA during treatment planning in breast cancer patients. They have reported that only one-third of LADCA became clear after contrast agent administration and that contrast agent administration did not contribute to imaging (28). However, another study on interobserver differences has reported that interobserver differences may emerge in contouring performed after treatment without contrast agent administration (29).

CONCLUSION

In our study, the doses delivered to the heart, LADCA, left lung, right lung, and right breast in patients irradiated to the chest wall and RLNs with the DIBH

technique were lower than those delivered with the FB technique. The treatment method in which DIBH is integrated with TVMAT provides a regular dose distribution and reduces the doses applied to the OAR. The irregular geometry and large size of the target volume and its proximity to the organ at risk necessitate the application of new treatment techniques in advanced-stage patients with mastectomy. Therefore, DIBH-TVMAT can be considered as a standard treatment option in advanced-stage breast cancer after mastectomy. However, further studies are needed to clarify its clinical validity and safety.

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EFFECTS OF HEALTHY EATING HABITS AND DIET QUALITY ON QUALITY OF LIFE AND JOB PERFORMANCE IN MIDDLE-AGED (45-65) HEALTHCARE WORKERS

Sağlık Kurumlarında Çalışan Orta Yaş (45-65) Personelinin Sağlıklı Yeme Alışkanlıkları ve Diyet Kalitesinin Yaşam Kalitesi ve İş Performansı Üzerine Etkisi

Eda PARLAK¹, Emine Ozlem KOROGLU², Betül GULSEN¹, Abdullah CALISKAN³

ABSTRACT

Objective: Job performance (JP) among healthcare workers is vital for patient safety and the overall efficiency of healthcare services. Research exploring how dietary habits and quality of life influence JP in healthcare workers remains limited. This study aimed to assess the impact of healthy eating habits, diet, and quality of life factors on JP in middle-aged healthcare workers.

Material and Methods: A total of 333 healthcare workers took part in the study. The study utilised 24-hour recall method (24hDR), the Healthy Diet Indicator (HDI-2020), the Attitude Scale for Healthy Nutrition (ASHN), the 36-item Short Form Health Survey (SF-36), and the Job Performance Scale (JPS). All surveys were conducted through face-to-face interviews.

Results: The average JP score was 4.27±0.72 and no significant difference was observed between the JP scores of men and female participants. However, male healthcare workers had higher mean physical health scores (SF-36-PCSc) than female participants. There was no significant difference in the mean mental health scores (SF-36-MCSc) between genders. In women, positive correlations were found between JP and HDI-2020, ASHN, and SF-36-PCSc and SF-36-MCSc from SF-36. Logistic regression analysis revealed that factors influencing JP included education level, occupation, ASHN, and fibre consumption.

Conclusion: This study is the first to demonstrate the positive impact of dietary fibre, healthy diet quality, and eating habits on JP. These findings highlight the importance of promoting healthy eating habits that include a sufficient fibre diet to enhance JP in healthcare workers.

Keywords: Job Performance; Dietary Fiber; Healthy Eating; Healthcare Workers; Middle Age

ÖZET

Amaç: Sağlık çalışanlarında iş performansı, hasta güvenliği ve sağlık hizmetlerinin genel verimliliği açısından hayati öneme sahiptir. Sağlık çalışanlarında beslenme alışkanlıklarının ve yaşam kalitesinin iş performansı üzerindeki etkisini araştırılan çalışmalar sınırlıdır. Bu çalışmada, orta yaşlı sağlık çalışanlarında sağlıklı beslenme alışkanlıklarının, diyetin ve yaşam kalitesi faktörlerinin iş performansı üzerindeki etkisi değerlendirilmiştir.

Gereç ve Yöntemler: Çalışmaya toplam 333 sağlık çalışanı katılmıştır. Veriler, 24 saatlik besin tüketim kaydı, Sağlıklı Beslenme Göstergesi (HDI-2020), Sağlıklı Beslenme İlişkin Tutum Ölçeği (SBİTÖ), 36 maddelik Kısa Form Sağlık Anketi (SF-36) ve İş Performansı Ölçeği kullanılarak toplanmıştır. Tüm anketler yüz yüze görüşmelerle uygulanmıştır.

Bulgular: Ortalama iş performansı puanı 4,27±0,72 bulunmuş, kadın ve erkek katılımcıların puanları arasında anlamlı bir fark gözlenmemiştir. Ancak, erkek sağlık çalışanlarının fiziksel sağlık puanı kadınlara göre daha yüksek bulunmuştur. Zihinsel sağlık puanlarında cinsiyetler arasında anlamlı fark saptanmamıştır. Kadınlarda iş performansı ile HDI-2020, ASHN, fiziksel sağlık ve zihinsel sağlık arasında pozitif korelasyon tespit edilmiştir. Lojistik regresyon analizine göre, iş performansını etkileyen faktörler arasında eğitim düzeyi, meslek, SBİTÖ ve lif tüketimi yer almaktadır.

Sonuç: Bu çalışma, diyet lifi, sağlıklı beslenme kalitesi ve yeme alışkanlıklarının iş performansı üzerindeki olumlu etkisini ortaya koyan ilk çalışmadır. Bulgular, sağlık çalışanlarının iş performansını artırmak amacıyla yeterli lif içeren sağlıklı beslenme alışkanlıklarının teşvik edilmesinin önemini vurgulamaktadır.

Anahtar Kelimeler: İş Performansı; Diyet Lifi; Sağlıklı Beslenme; Sağlık Çalışanları; Orta Yaş

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INTRODUCTION

Due to technological advances, tremendous progress has been made in human health protection, disease diagnosis, and treatment, which led to increased quality of life and life expectancy. World Health Organization (WHO) stated that the rate of chronic diseases could be reduced via proper diet and lifestyle changes in developing and developed countries. It is crucial for public health that healthcare workers, particularly those working in healthcare institutions, know the importance of adequate and balanced nutrition. This awareness can enhance their attitudes and behaviors toward promoting healthy eating (1).

The health sector is vital in preventing health issues and improving overall well-being, more so than many other service sectors (2). The WHO defined healthcare workers as people who fundamentally accept the improvement of human health as their main target (3). Organization of Economic Cooperation and Development (OECD) Health Data for 2022 and the EUROSTAT database showed that there were 1470 health workers per 100000 people in OECD countries and 1442 health workers in European Union (EU) countries in 2020 (4).

Healthcare workers' job performance (JP) is significant for the safety of patients and the effectiveness of health services (5). However, only a few studies investigated the effect of healthy nutrition habits and diet quality on the JP of healthcare workers. Nevertheless, it is necessary to understand the potential relationship between the nutrition habits of workers working in health institutions and JP to improve health institutions' efficiency. Job performance is defined as the ability of workers to accomplish their duties and functions (6). A combination of different factors shapes JP, and it can be changed under the influence of individuals' knowledge, talents, motivation, health conditions, and environmental factors (7). A good JP is related to high efficiency, customer happiness, and profitability (8).

The OECD anticipated that in 2050, 27% of the world population will be above 65 years old, and at least 10% will be older than 80 (4). If human resources, which is probably the most complex resource to manage, are not directed correctly and effectively, it may cause a decline in performance and, consequently, failure. Organizations can reach their targets and have an

advantage over their rivals provided they have workers with high job performance, are talented, accomplish their duties effectively, and contribute to organizational success (9). Thus, a healthy nutrition style, one of the factors positively affecting healthcare workers' life quality, gains importance (2). The present study aimed to assess the impact of healthy eating habits, diet, and quality of life factors on JP in middle-aged healthcare workers.

MATERIAL AND METHOD

This is a descriptive, cross-sectional study. The study sample was determined using a random sampling method. The study was conducted with healthcare workers at a university hospital between February and April 2023.

The sample size was calculated using the E-PICOS AI Smart Biostatistics Software version 21.3 (E-PICOS Inc., New York, NY, USA; <https://www.epicos.ai/>). In this study, for determining the sample size, a power analysis was performed with G*Power 3.1 (Heinrich-Heine University, Düsseldorf, Germany; <http://www.gpower.hhu.de/>) software using alpha (α) = 0.05, power ($1 - \beta$) = 0.95, and $d = 0.87$ (medium effect size), which indicated that at least 139 individuals (10). Inclusion criteria consisted of consenting to participation in the study, being in the 45-65 age group, and working as a healthcare worker (doctors, nurses, dentists, pharmacists, as well as other healthcare sector employees such as cleaners, support staff, and administrative workers).

The questionnaire form used for the study was filled out by the dietician working in a health institution during face-to-face interviews with the study participants. The questionnaire form consists of four parts. The first part has items about the participants' demographic and clinical data, such as age, gender, educational background, occupational information, comorbidities, and physical activity status. The same researcher also measured and recorded the participants' body weights (kg) and heights (cm). For height measurement, the head was kept on the Frankfurt horizontal plane while the horizontal line from the ear canal to the lower border orbit was parallel to the floor. The body weight was measured on an empty stomach in the morning, with light clothing and without shoes. For further

analysis, the Body Mass Index (BMI) values were calculated using the formula: Body weight (kg)/(height (m²)) (11).

The second section of the questionnaire included the Attitude Scale for Healthy Nutrition (ASHN) and HDI-2020 to evaluate participants' dietary habits and overall diet quality. A retrospective 24-hour dietary recall (24hDR) was also conducted to gather detailed nutritional data, as it is one of the most widely used and validated dietary assessment methods, especially in individual interviews (12, 13).

HDI-2020, developed by the WHO, assesses adherence to healthy dietary guidelines. It consists of 11 components- five measuring consumption of recommended food groups (e.g., fruits and vegetables, legumes, nuts, whole grains, and dietary fibre) and six evaluating the intake of foods to be limited (e.g., total fat, sodium, added sugars, processed meats). Each component is scored from 0 and 1, with higher scores indicating better dietary adherence (14, 15).

The ASHN is as a 5-point Likert scale measuring attitudes toward healthy nutrition, categorized as "weak" (0-24), "moderate" (25-49), "good" (50-74) or "very good" (75-100) (16).

The third part of the questionnaire used the 36-item Short Form Health Survey (SF-36). The original SF-36 stemmed from the Medical Outcome Study, MOS, conducted by the RAND Corporation (17). Demiral et al. (2006) translated this form into Turkish and validated it (18). It is a questionnaire consisting of 36 items which measure 8 health-related subscales: Physical functioning (PF, 10 items), role limitation due to physical health (RP, 4 items), bodily pain (BP, 2 items), general health perception (GH, 5 items), vitality (VT, 4 items), social functioning (SF, 2 items), role limitation due to emotional problems (RE, 3 items), and perceived mental health (MH, 5 items). Correlated physical health and mental health scores (SF-36-PCSc and SF-36-MCSc) were calculated using the algorithm introduced by the developers:

$$SF-36-PCSc=(PF+RP+BP+GH)/4,$$

$$SF-36-MCSc=(VT+SF+RE+MH)/4.$$

The SF-36-PCSc and SF-36-MCSc scores were constructed by multiplying each SF-36 scale z-score by its respective scoring coefficient from the obliquely rotated two-factor solution. The summary scores

ranged between 0 and 100: While 0 indicates poor health status, 100 implies good health status (18).

In the final part of the questionnaire, the Job Performance Scale (JPS) developed by Çalışkan and Köroğlu (2022) for measuring JP was applied (9). This 11-item questionnaire included questions depending on a 5-point Likert scale and consisted of 2 subscales: Task performance (TP) and Contextual Performance (CP). In this questionnaire, higher scores indicated higher JP (9).

This study was conducted in accordance with the principles of the Declaration of Helsinki and ethical approval was obtained from Toros University Ethics Committee (Date: 24/01/2023, Decision No: 12). Informed consent forms were obtained from all participants who agreed to participate in the study.

Statistical Analysis

The Statistical Package for Social Sciences software (SPSS v22, IBM Corp., Armonk, NY, US) was used for data analysis. Data were expressed as numbers (n), percentages (%), means, and standard deviations (SD). The conformity of variables to normal distribution was analyzed using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The non-parametric Mann-Whitney U test was used to compare two independent groups regarding continuous variables. On the other hand, the non-parametric Spearman rank correlation was used to analyze the correlation between quantitative variables. Logistic regression analysis was performed to expose the variables affecting JP. A difference was considered statistically significant if the calculated p-value was lower than 0,05.

RESULTS

Overall, 333 healthcare workers (140 women and 193 men) aged 45 to 65 participated in the study. The mean age of the participants was 49.25±4.08 years. Healthcare workers had different duties: while 74.4% were healthcare professionals, 25.6% were other healthcare workers. The percentage of the workers who stated that they had a chronic morbidity (such as hypertension, diabetes mellitus, anemia, arthritis) was 27.3% (n=91). Ten (3.0%) participants were on a diet due to their chronic disease. Approximately 16%

of the study participants were on a specific diet after consulting with a dietitian (n=23; 7%) or a physician (n=30; 9%). Nearly 34.1% (n=113) of the participants regularly exercised. The demographic and descriptive data of the subjects are shown in Table 1.

The mean JP score of the healthcare workers was 4.27±0.72, and there was no significant difference between male and female participants. The participants' mean SF-36-PCSc and SF-36-MCSc scores were 74.04±17.86 and 64.14±21.14, respectively. The

mean SF-36-PCSc scores of men were significantly higher than women (p=0.01). On the other hand, there was no significant difference between men and women regarding SF-36-MCSc scores. The mean BMI was 26.05±4.14 kg/m²; the mean BMI of the male subjects was higher than female subjects (27.55±3.71 vs 25.46±4.17 kg/m²; p=0.005). Data regarding HDI-2020, SF-36, ASHN, and JP assessments are shown in Table 2.

The analysis results regarding the correlation between

Table 1. Demographic and descriptive data (n=333)

Variable	Value
Age, (±SD), years	49.25±4.08
Gender (M/F), n (%)	193 (58.0) / 140 (42.0)
Education	
Primary school	25 (7.6)
High school	58 (17.3)
Undergraduate/Graduate/Doctorate	250 (75.2)
Job, n(%)	
Healthcare professional	248 (74.4)
Other healthcare workers	85 (25.6)
Smoking, n(%)	
Yes	128 (38.5)
No	166 (50.0)
Quit smoking	39 (11.5)
Alcohol consumption, n(%)	
Yes	7 (2.2)
No	213 (64.0)
Social drinker	113 (33.8)
Regular physical activity, n (%)	
Yes	113 (34.1)
No	220 (65.9)

SD: standard deviation, M: male, F: female

Table 2. Data regarding HDI-2020, SF-36, ASHN and JP (n=333)

Variable, (±SD)	All workers	Men	Women	p
Job performance	4.27±0.72	4.25±0.95	4.28±0.61	0.51
Task performance	4.36±0.79	4.35±0.99	4.37±0.70	0.42
Contextual performance	4.19±0.77	4.16±0.96	4.20±0.69	0.67
SF-36-PCSc	74.04±17.86	79.06±16.62	71.96±18.04	0.01*
SF-36-MCSc	64.14±21.14	69.96±16.82	61.82±22.30	0.08
HDI-2020	4.82 ± 1.29	4.75±1.44	4.85±1.23	0.51
ASHN	75.32±7.96	73.43±8.00	76.05±7.86	0.130
BMI (kg/m ²)	26.05±4.14	27.55±3.71	25.46±4.17	0.005**

JP: Job Performance; SF-36-PCSc: Short Form 36 Physical Health Score; SF-36-MCSc: Short Form 36 Mental Health Score; HDI-2020: Healthy Diet Indicator 2020; ASHN: Attitude Scale for Healthy Nutrition; BMI: Body Mass Index. Mann-Whitney U test, *p<0.05, **p<0.001.

HDI-2020, SF-36, ASHN scores, and the JP scale are displayed in Table 3. A positive correlation was found between male subjects' TP and SF-36-MCSc scores ($r=0.364$, $p=0.03$). There were also significantly positive correlations between female healthcare workers' JP and HDI-2020 ($r=0.214$, $p=0.04$), ASHN ($r=0.256$, $p=0.01$), SF-36-PCSc ($r=0.222$, $p=0.04$) and SF-36-MCSc ($r=0.279$, $p=0.009$) scores.

Significant positive relationships were observed between TP and HDI-2020 ($r=0.290$, $p=0.005$), ASHN ($r=0.235$, $p=0.02$), SF-36-PCSc ($r=0.209$, $p=0.05$), and SF-36-MCSc ($r=0.237$, $p=0.02$). Additionally, positive significant relationships were found between CP and ASHN ($r=0.208$, $p=0.04$) and SF-36-MCSc ($r=0.317$, $p=0.003$) (Table 3).

According to logistic regression analysis, education level, occupation group, ASHN, and HDI-2020 "adequate fibre consumption (>25 g)" affected JP (Table 4).

DISCUSSION

In this cross-sectional study, 333 healthcare workers (140 women and 193 men) aged 45 to 65 participated. This study assessed the impact of healthy eating habits, diet, and quality of life factors on JP. There was

no significant difference in the mean JP and mental health scores between genders. In women, positive correlations were found between JP and HDI-2020, ASHN, and the physical and mental health scores. This study is one of the first to suggest the sufficient dietary fibre intake is positively associated with job performance among healthcare workers, particularly in women.

Job performance is defined as the worker's contribution to his/her workplace and work accomplished under set conditions (19, 20). It is also a qualitative and quantitative summary of how much the worker reached the target (21). From another point of view, JP depends on the institutional mission, functional needs, and particular goals related to institutional values and beliefs (22).

The concept of JP is evaluated within the frame of Vroom's expectation theory and Kahneman and Tversky's expectation-value theory (23, 24). According to Vroom's theory, a staff member's performance relies on how much he/she desires the result of his/her efforts and his/her belief in the effect of an action on this result. In this theory, a staff member's effort depends mainly on value and expectation (24). A thorough JP evaluation is essential for institutions. This

Table 3. Data regarding correlation between diet and nutrition indices, physical and mental health scores and job performance based on gender (n=333)

Variables	Men		Women	
	r	p	r	p
Job Performance				
HDI-2020	0.054	0.75	0,214	0.04*
ASHN	0.019	0.91	0.256	0.01*
SF-36-PCSc	0.007	0.96	0.222	0.04*
SF-36-MCSc	0.269	0.11	0.279	0.009**
Task performance				
HDI-2020	-0.046	0.79	0.290	0.005**
ASHN	0.188	0.26	0.235	0.02*
SF-36-PCSc	0.081	0.63	0.209	0.05*
SF-36-MCSc	0.364	0.03*	0.237	0.02*
Contextual performance				
HDI-2020	0.039	0.82	0.149	0.15
ASHN	-0.051	0.76	0.208	0.04*
SF-36-PCSc	-0.045	0.79	0.158	0.14
SF-36-MCSc	0.197	0.25	0.317	0.003**

JP: Job Performance; HDI-2020: Healthy Diet Indicator 2020; ASHN: Attitude Scale for Healthy Nutrition; SF-36-PCSc: Short Form 36 Physical Health Score; SF-36-MCSc: Short Form 36 Mental Health Score. Spearman correlation analysis, * $p<0.05$, ** $p<0.001$.

Table 4. Regression analysis between JP, HDI-2020, SF-36 and other variables (n=333)

Variables	Regression analysis (R ² value=0.337, p=0.001**)		
	Coeff.	%95CI	p
Gender, n (M: 193/F:140)	0.222	-0.125 to 0.569	0.20
Number of children, n	0.117	-0.044 to 0.278	0.15
Education level, n Primary school (25) High school (58) Undergraduate/Graduate/Doctorate(250)	0.319	0.123-0.515	0.002**
Smoking, n No (166) Yes (128) Quit smoking (39)	-0.104	-0.259 to 0.052	0.19
Alcohol consumption, n No (213) Yes (7) Social drinker (113)	0.123	-0.034 to 0.281	0.12
Job, n Healthcare professional (248) Other healthcare worker (85)	0.509	0.169 to 0.849	0.004**
BMI (kg/m ²), (±SD)	0.026	-0.012 to 0.065	0.18
ASHN, (±SD)	0.021	0.003 to 0.039	0.02*
HDI-2020, (±SD) Vegetable-Fruit consumption ≥400 g	-0,138	-0.435 to 0.160	0.36
HDI-2020, (±SD) Beans and Legume, > 0 g	-0,173	-0.451 to 0.104	0.21
HDI-2020, (±SD) Dietary fibre, >25 g	0,606	-0.014 to 1.226	0.05*
SF-36-MCSc, (±SD)	0.007	-0.003 to 0.016	0.16
SF-36-PCSc, (±SD)	0.004	-0.007 to 0.015	0.15

M: male, F: female, JP: Job Performance; HDI-2020: Healthy Diet Indicator 2020; ASHN: Attitude Scale for Healthy Nutrition; BMI: Body Mass Index; SF-36-PCSc: Short Form 36 Physical Health Score; SF-36-MCSc: Short Form 36 Mental Health Score. Significant difference was set at *p<0.05, **p<0.01.

process helps determine the worker's strengths and weaknesses (25). A worker's JP is evaluated under two main categories: TP and CP (26). Task performance is related to actions that support the staff in reaching set targets or meeting the main requirements of the work (27, 28). On the contrary, CP reflects positive behavior, which is not defined in job descriptions but is encouraged by the institution and supports the general functions (29).

Forming and maintaining a healthy workforce are the fundamentals of a health system's performance. If the welfare of the health workers is not preserved, absenteeism at work due to health issues may

impact both patient care and the welfare of the other healthcare worker. Consequently, the general functioning of the health institution may be impaired (30). Several studies investigated the relationship between JP and life quality using standardized tools such as SF-36. These studies reported that individuals with high life quality are more motivated at work and, as a result, show better JP. A meta-analysis conducted by Faragher et al. (2005) reported that job dissatisfaction increases the risk of mental illnesses, adversely affects the general health state, and reduces life satisfaction (31).

Moreover, other studies showed a weak but statistically

significant relationship between JP and physical health. These studies stated that job satisfaction considerably affects individuals' general health conditions (32). In our study, the JP of female healthcare staff was positively correlated with SF-36-PCSc and SF-36-MCSc scores. Besides, the SF-36-PCSc scores of female workers were lower than those of male workers. On the contrary, no statistically significant differences were found between the JP, TP, and CP of male and female healthcare workers. According to the existing literature, the workers' physical and mental health conditions tremendously affect their JP (32, 33). It was observed that individuals with high scores in role limitation due to emotional problems, mental health, and social functioning dimensions of life quality scale accomplish their duties more efficiently (32). Individuals with high SF-36-PCSc scores also had higher JP (33).

Poor nutrition quality, excess energy intake, physical inactivity, obesity, and cardiovascular diseases pave the way for several non-infectious diseases, including type 2 diabetes, metabolic syndrome, and cancer. Epidemiological research on overweight or obese workers identified common characteristics such as long working hours, shift work, and job stress, revealing that these conditions affect all healthcare workers and increase their vulnerability to weight gain (34).

In present study, most participants were overweight according to WHO classification, and the mean BMI value of men was higher than women. Analysis of the relationship between JP and the diet quality of female healthcare workers revealed a positive correlation between the HDI-2020 values and JP. Specifically, it was observed that the individuals with higher HDI-2020 scores had a higher JP. These results comply with the research implying the importance of nutrition on cognitive functions, energy levels, and general welfare (35-37). Nutrition and health are two significant concepts that are mentioned together. Healthy nutrition, characterized as consuming nutrient-rich foods and avoiding excess unhealthy ones, can provide daily energy and macro and micronutrients needed by individuals for accomplishing their duties. Although research regarding the relationship between HDI-2020 and JP is scarce, the limited data indicate that healthy nutrition is closely related to improvement in cognitive

functions, increase in energy levels and concentration, emotional state and stress management, productivity, and therefore, the JP (38, 39).

In this study, the logistic regression analysis revealed that being a health professional, having a high education level, a high ASHN point, and HDI-2020 compliant fibre consumption (>25g/day) positively affects the JP. Although there is no specific research about the relationship between dietary fibre intake and JP, it is widely accepted that foods with high fibre content positively affect general health and energy balance and, therefore, the JP of healthcare workers. Dietary fibre and whole grains include a unique mixture of bioactive compounds such as resistant starches, vitamins, minerals, phytochemicals, and antioxidants. In recent years, research about the potential health benefits of dietary fibre has gained attention. It has been postulated that the beneficial effects of dietary fibres on general health are related to the changes in intestinal viscosity and hormone production, nutrient absorption, intestinal motility, and production of short-chain fatty acids (40). On the other hand, this study is the first to report the favorable effects of dietary fibres, diet quality, and healthy nutrition habits on JP.

This study has several limitations that should be considered when evaluating its findings. First, as it is a cross-sectional study, it cannot establish a cause-and-effect relationship. Second, the study sample was relatively small and heterogeneous. Third, it did not include a control group. Therefore, these findings must be validated through randomized controlled trials with larger and more diverse participant samples.

CONCLUSION

In present study, a positive correlation has been found between JP and healthy eating habits, particularly those involving sufficient fibre intake. These results highlight the importance of promoting and maintaining healthy nutrition to enhance JP. Further research should be conducted to identify potential interventions to improve nutritional habits and develop strategies to enhance the dietary quality of healthcare workers.

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IMAGING PREDICTORS OF CONTRACTURE IN DUPUYTREN'S DISEASE: MULTIMODAL ULTRASONOGRAPHIC PERSPECTIVE

Dupuytren Hastalığında Kontraktür Gelişiminin Görüntüleme Yöntemleriyle Öngörülmesi: Multimodal Ultrasonografik Değerlendirme

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ABSTRACT

Objective: To investigate ultrasonographic (US), color Doppler ultrasonographic (CDUS), and strain elastography (SEL) characteristics of Dupuytren's disease (DD) and assess their relationship with clinical findings and lesion morphology.

Material and Methods: A total of 226 patients (153 males, 73 females; mean age: 61.5 ± 9.9 years) and 226 lesions were retrospectively analyzed. Lesions were evaluated using B-mode US, CDUS, and SEL for echogenicity, morphology, dimensions, vascularity, stiffness, and anatomical relationships. Flexion deformity and extension of flexor tendons and/or muscular structures were recorded. Statistical comparisons were performed using chi-square, Mann-Whitney U, and Spearman correlation tests.

Results: Lesions were most frequently located in the 4th (74.3%) and 5th (23.9%) finger. Cord-like morphology was observed in 62.8%, and 83.6% were hypoechoic. Flexion deformity was detected in 42.9% of cases and was significantly more frequent in lesions with tendon and/or muscular extension (81.3% vs. 0%; $p < 0.001$). The deformity was also more common in cord-like than nodular lesions (66.2% vs. 3.6%, $p < 0.001$). Iso-hyperechoic lesions were more likely to be associated with deformity compared to hypoechoic ones (59.5% vs. 39.7%, $p = 0.026$). In SEL, 52.7% of lesions were stiff, 41.2% moderate, and 6.2% soft. Lesions with deformity had significantly greater anterior-posterior (AP) diameter ($p = 0.001$). A moderate correlation existed between transverse and AP size ($p = 0.631$, $p < 0.001$).

Conclusion: Flexion deformity in DD is strongly associated with tendon/muscular extension and lesion morphology. US and SEL parameters offer significant value in clinical evaluation, enabling early identification of severe disease and aiding therapeutic planning.

Keywords: Dupuytren Contracture; Ultrasound; Elastography; Flexion Deformity

ÖZET

Amaç: Bu çalışmada Dupuytren hastalığında ultrasonografi (US), renkli Doppler US (RDUS) ve strain elastografi (SEL) bulgularının değerlendirilmesi ve bu bulguların klinik bulgular ve lezyon morfolojisiyle ilişkilerinin araştırılması amaçlandı.

Gereç ve Yöntemler: Toplam 226 hasta (153 erkek, 73 kadın; ortalama yaş: 61,5 ± 9,9 yıl) ve 226 lezyon retrospektif olarak analiz edildi. Lezyonlar, B-mod US, RDUS ve SEL ile ekojenite, morfoloji, boyutlar, vaskülarite, sertlik ve anatomik komşuluk açısından değerlendirildi. Fleksiyon deformitesi ve fleksör tendon ve/veya kas yapılarına uzanım kaydedildi. Karşılaştırmalarda ki-kare testi, Mann-Whitney U testi ve Spearman korelasyon analizi kullanıldı.

Bulgular: Lezyonlar en sık 4. (%74,3) ve 5. (%23,9) parmaklar düzeyinde lokalizeydi. Morfolojik olarak lezyonların %62,8'i kord şeklindeydi ve %83,6'sı hipoekoikti. Fleksiyon deformitesi vakalarının %42,9'unda saptandı ve tendon ve/veya kas yapılarına uzanımı olan lezyonlarda belirgin olarak daha sık görüldü (%81,3 vs. %0; $p < 0,001$). Ayrıca, deformite kord morfolojisine sahip lezyonlarda (%66,2) nodüler olanlara (%3,6) kıyasla daha yaygındı ($p < 0,001$). İzo-hiperekoik lezyonlarda deformite görülme oranı hipoekoik lezyonlara göre anlamlı derecede fazlaydı (%59,5 vs. %39,7; $p = 0,026$). SEL ile yapılan değerlendirmede lezyonların %52,7'si sert, %41,2'si orta sertlikte, %6,2'si yumuşak olarak sınıflandırıldı. Deformitesi olan lezyonların anterior-posterior (AP) çapları daha geniştir ($p = 0,001$). Transvers ve AP çapları arasında orta düzeyde korelasyon saptandı ($p = 0,631$, $p < 0,001$).

Sonuç: Dupuytren hastalığında fleksiyon deformitesi, özellikle tendon veya nörovasküler yapılarına uzanımı olan ve kord morfolojisine sahip lezyonlarla yakından ilişkilidir. Ultrasonografi ve elastografi bulguları, hastalığın ciddiyetini öngörmeye ve tedavi planlamasında değerli bilgiler sunabilir.

Anahtar Kelimeler: Dupuytren Kontraktürü; Ultrasonografi; Elastografi; Fleksiyon Deformitesi

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INTRODUCTION

Dupuytren's disease (DD) is a long-standing fibroproliferative disorder of the hand, marked by a gradual thickening and contraction of the palmar fascia, eventually leading to permanent flexion deformities, most often affecting the fourth and fifth digits (1). Dupuytren's disease is considered the most common type of superficial fibromatosis, with an estimated prevalence of 1–2% in the general population, increasing significantly with age (2). It predominantly affects men and often presents bilaterally (2). Previous research suggests that DD has a multifactorial etiology, involving both genetic predispositions and environmental influences (3). Well-known risk factors for DD are older age, male sex, and a family history of the condition (4). In addition, several comorbidities such as diabetes mellitus, epilepsy, liver diseases, hyperlipidemia, and adhesive capsulitis have also been associated with an elevated risk of developing DD. Lifestyle elements like smoking, heavy alcohol use, and repetitive manual labor have likewise been linked to a higher susceptibility to DD (5). It is believed that the pathogenesis of DD is mediated by fibrogenic cytokines, including TGF- β , FGF, and the Wnt signaling pathway (a key regulator of cell proliferation, differentiation, and fibrogenesis), all of which can be triggered by diverse biological stimuli (6).

While commonly known as palmar fibromatosis, the designation 'Dupuytren's contracture' is generally used when flexion deformities of the fingers are clinically present (7). Clinically, the disease is characterized by firm, non-tender nodules located beneath the palmar skin, which gradually progress and may cause retraction of the tendons, eventually leading to flexion deformities of the fourth and fifth fingers (8). Despite characteristic lesion localization and clinical findings pointing toward DD, imaging is essential to rule out differential diagnoses such as tenosynovitis, trigger finger, ganglion cysts, and other soft tissue pathologies. In addition, imaging techniques allow for accurate assessment of lesion size and its anatomical relationship with adjacent tendons and muscular structures (9). B-mode ultrasonography (US) is the principal and most commonly utilized imaging technique for assessing superficial soft tissue lesions. It facilitates distinguishing solid structures from cystic

components within a lesion. Color Doppler US (CDUS) is useful for evaluating the vascular supply within the lesion. Sonoelastography (SEL) is a modern technique that provides additional diagnostic value when assessing tendons, ligaments, muscles, and superficial soft tissue lesions in the musculoskeletal system (10). SEL is broadly categorized into two types: shear wave and strain elastography. Shear wave elastography provides quantitative data on tissue stiffness in kilopascals, whereas strain elastography uses color mapping to qualitatively represent tissue hardness as soft or stiff. Strain (compression) elastography is more practical and user-friendly for evaluating superficial lesions like those observed in DD.

At present, no curative treatment exists for DD. Conservative management strategies, such as modifying daily activities, applying topical agents, or administering corticosteroid injections, can be used in certain patients to reduce symptoms or delay disease progression (11). Flexion contractures may be improved using methods like percutaneous needle fasciotomy, collagenase derived from *Clostridium histolyticum*, or limited fasciectomy, yet these interventions are not curative. The recurrence rate after surgical intervention ranges from 21% to 85% within five years, depending on the treatment modality and how recurrence is defined (12). In light of these factors, treatment plans should be tailored according to individual patient characteristics. Within this framework, imaging (especially ultrasonography) serves a key function in informing therapeutic choices and guiding procedural strategy. Furthermore, ultrasonography supports the application of minimally invasive techniques like intralesional injections and aids in efficient post-treatment follow-up (9).

Although ultrasonographic findings of Dupuytren's disease have been described previously, studies directly correlating these imaging parameters with flexion deformity severity remain limited. This study aims to fill this gap by providing a systematic multimodal ultrasonographic assessment.

MATERIAL AND METHODS

This retrospective descriptive study was approved by the Clinical Research Ethics Committee of our institution (Decision No: E2-23-5833, dated December 6, 2023)

before commencement. We retrospectively reviewed ultrasonographic reports and corresponding sonographic image sequences of patients preliminarily diagnosed with DD between May 2020 and October 2023. A radiologist with 14 years of experience in musculoskeletal US re-evaluated all examinations. Cases with unilateral involvement were included, and in patients with multiple lesions, the most prominent lesion was selected for analysis. Clinical and physical examination data were also evaluated. Exclusion criteria included a history of rheumatologic disease, malignancy, prior hand surgery, or trauma to the hand. All ultrasound evaluations were conducted with the patient seated and the examined hand placed in a supinated position resting on the anterior surface of the thigh. Lesion size was recorded in both transverse and longitudinal planes. Each lesion was assessed using B-mode US, CDUS imaging, and strain SEL, all performed independently by the same radiologist. All evaluations were carried out using a high-frequency linear probe (5–11 MHz) with the GE Logiq S7 Expert system (GE Healthcare, Milwaukee, WI, USA). Color Doppler ultrasonography was employed to evaluate vascularity within each lesion. Strain SEL was carried out simultaneously, utilizing the same transducer and identical patient positioning as in the B-mode and Doppler evaluations. Tissue elasticity was assessed by applying light manual compression and decompression with the transducer, relying on real-time elastographic color maps superimposed on B-mode images. In elastographic mapping, soft areas appeared red, moderately stiff tissues were displayed in yellow, and firm regions were depicted in green or blue. We assessed whether DD-related nodules or cords were present, recorded their affected digit localization, measured their size and echogenicity, and noted their extension to flexor tendons (flexor digitorum superficialis and profundus). Additional evaluations included intralesional vascularity on CDUS and tissue elasticity on strain elastography. In the color-coded elastograms, red indicated soft tissue, green represented intermediate stiffness, and blue denoted firm consistency. Lesion size was measured in both transverse and longitudinal axes using B-mode US. Lesion echogenicity was evaluated in comparison to the adjacent tendon and classified as hypoechoic,

isoechoic, or hyperechoic.

All statistical analyses were carried out using IBM SPSS Statistics software (Version 22.0; Armonk, NY, USA), applying a 95% confidence interval. The distribution of numerical variables was assessed for normality using the Shapiro–Wilk test. As the data did not follow a normal distribution, comparisons were performed using the chi-square test or Mann–Whitney U test. Anatomical variation differences were specifically analyzed using the Mann–Whitney U test. A p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 226 patients were enrolled in the study, including 153 males (67.7%) and 73 females (32.3%). The mean age of the study population was 61.46 ± 9.9 years, ranging from 23 to 81 years. Female patients had a slightly greater mean age (62.12 ± 10.96 years) than male patients (61.15 ± 9.40 years).

The right hand was affected in 59.3% of cases ($n=134$), whereas the left hand was involved in 40.7% ($n=92$). Right-hand lesions were more frequently observed in female patients (71.2%) than in male patients (53.6%). Analysis of etiological factors associated with DD revealed diabetes mellitus as the most frequently encountered comorbidity (34.1%, $n=77$), followed by tobacco use (17.7%, $n=40$). Epilepsy and alcohol consumption were identified as rare etiological factors. The majority of lesions (83.6%, $n=189$) demonstrated hypoechoic characteristics on B-mode US. Morphological assessment revealed that 62.8% of lesions ($n=142$) exhibited a cord-like configuration, while 37.2% ($n=84$) presented with nodular morphology.

Color Doppler ultrasonography evaluation demonstrated vascularity in only 3 lesions (1.3%) (Figure 1). Sonoelastographic (SEL) assessment revealed that 52.7% of lesions ($n=119$) were characterized as stiff, 41.2% ($n=93$) as moderately stiff, and 6.2% ($n=14$) as soft (Figure 2). Comparative analysis between genders revealed that males had significantly larger anterior-posterior (AP) dimensions compared to females ($p=0.043$), while no significant difference was observed in transverse dimensions ($p=0.229$).

Mean lesion dimensions were 10.99 ± 6.05 mm in the transverse plane and 4.80 ± 2.91 mm in the AP dimension.

Anatomical distribution showed that 74.3% of lesions (n=168) were localized to the 4th finger, 23.9% (n=54) to the 5th finger, with 3rd finger being uncommon (1.8%, n=4). Extension to flexor tendons or muscle structures was present in 52.4% of patients (n=118).

Flexion deformity was observed in 42.9% of patients (n=97) (Figure 3).

Demographic, clinical, and lesion characteristics are described in table 1.

A significant positive correlation was identified

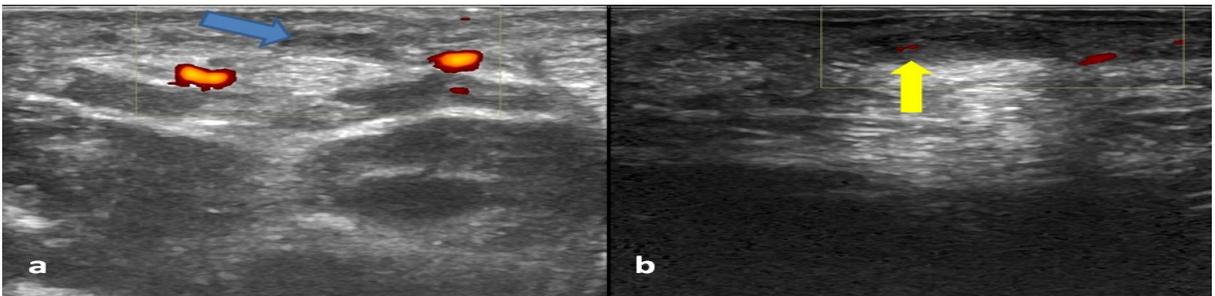


Figure 1. Gray-scale and power Doppler ultrasound (US) image of a superficial hypoechoic lesion (blue arrow) located on the palmar aspect of the right hand in one patient, showing no vascular flow (a). In a different patient, a hypoechoic lesion (yellow arrow) in the left third finger demonstrates mild internal vascularity on power Doppler US (b).

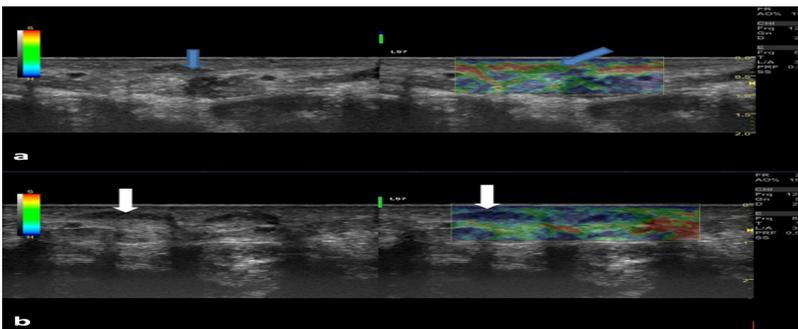


Figure 2. Strain elastography image demonstrating a superficial lesion (blue arrows) on the palmar aspect of the right hand, exhibiting predominantly green coloration suggestive of intermediate stiffness (a). A separate case shows a hypoechoic lesion (white arrows) in the third ray of the left hand with predominantly blue coloration on strain elastography, consistent with increased stiffness (b).

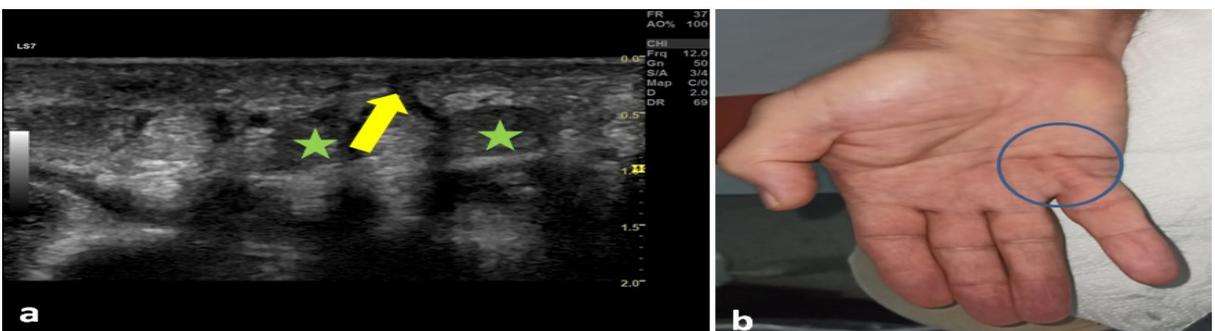


Figure 3. Gray-scale ultrasound image showing nodular lesions (green stars) on the palmar aspect of the hand with spiculated extensions toward the skin (yellow arrow) (a). A flexion contracture caused by the lesion is demonstrated in the same patient (blue circle) (b).

Table 1. Demographic, Clinical, and Lesion Characteristics of Patients with Dupuytren's Disease

Parameter	Category	n (%)
Sex	Female	73 (32.3%)
	Male	153 (67.7%)
Age (mean ±SD) years	Female	62.12 ± 10.96
	Male	61.15 ± 9.40
	Overall	61.46 ± 9.9
Side	Right	134 (59.3%)
	Left	92 (40.7%)
Diabetes	No	149 (65.9%)
	Yes	77 (34.1%)
Smoking	No	186 (82.3%)
	Yes	40 (17.7%)
Epilepsy	No	225 (99.6%)
	Yes	1 (0.4%)
Alcohol use	No	225 (99.6%)
	Yes	1 (0.4%)
Lesion Localization	3 rd finger	4 (1.8%)
	4 th finger	168 (74.3%)
	5 th finger	54 (23.9%)
Lesion Echogenicity	Hypoechoic	189 (83.6%)
	Iso-hyperechoic	37 (16.4%)
Lesion Type	Nodular	84 (37.2%)
	Cord shape	142 (62.8%)
Flexor tendon/muscle relation	Absent	107 (47.6%)
	Present	118 (52.4%)
Flexion deformity	Absent	129 (57.1%)
	Present	97 (42.9%)
CDUS feature	Absent	223 (98.7%)
	Present	3 (1.3%)
SEL feature	Stiff (hard)	119 (52.7%)
	Moderately stiff	93 (41.2%)
	Soft	14 (6.2%)

CDUS: Color Doppler Ultrasound; SEL: Sonoelastography

between the presence of flexor tendon or muscular extension and AP dimension ($p=0.017$), indicating that lesions with anatomical extension exhibited larger AP measurements.

A robust relationship was established between lesion morphology and dimensions. Cord-shaped lesions demonstrated significantly larger dimensions in both transverse and AP planes compared to nodular lesions ($p<0.001$ for both dimensions).

The relationship between lesion size and radiological

findings and clinical data is summarized in table 2.

The strongest associations with the development of flexion deformity were observed with flexor tendon or muscle involvement and lesion morphology. Among lesions with such structural extension, 81.5% demonstrated flexion deformity, whereas none of the lesions without extension developed any deformity. This association was statistically significant ($\chi^2 = 149.49$, $p < 0.001$). Additionally, cord-shaped lesions exhibited a significantly higher rate of flexion deformity (66.2%)

compared to nodular lesions (3.6%) ($p < 0.001$). Male patients demonstrated significantly higher rates of flexion deformity compared to females (49.0% vs 30.1%, $p = 0.007$). Furthermore, patients with flexion deformity presented with significantly larger AP dimensions and advanced age ($p = 0.001$ and $p = 0.008$, respectively).

A significant relationship was established between lesion localization and flexion deformity development ($p = 0.006$). The highest rate of flexion deformity was observed in the 4th finger (59.3%), while the lowest rate occurred in the 3rd finger (0.0%). Lesions in the 4th

finger demonstrated a flexion deformity rate of 38.7%. Iso-hyperechoic lesions exhibited significantly higher rates of flexion deformity compared to hypoechoic lesions (59.5% vs 39.7%, respectively, $p = 0.026$).

Other comparative findings are summarized in table 3. 4th finger demonstrated a flexion deformity rate of 38.7%.

Iso-hyperechoic lesions exhibited significantly higher rates of flexion deformity compared to hypoechoic lesions (59.5% vs 39.7%, respectively, $p = 0.026$).

Other comparative findings are summarized in table 3. A strong positive correlation was identified between

Table 2. Lesion Dimensions by Clinical and Sonographic Characteristics

Lesion Dimension	Variable	Group	Mean ± SD (mm)	Mean Rank	p-value
Transverse	Sex	Female	10.94 ± 6.83	105.47	.229
		Male	11.02 ± 5.66	116.62	
Anterior-Posterior		Female	4.49 ± 3.06	96.32	.043*
		Male	4.95 ± 2.83	114.59	
Transverse	Lesion Echogenicity	Hypoechoic	11.35 ± 6.21	116.73	.053
		Iso-hyperechoic	9.21 ± 4.87	94.07	
Anterior-Posterior		Hypoechoic	4.90 ± 3.08	108.84	.855
		Iso-hyperechoic	4.25 ± 1.66	106.71	
Transverse	Lesion Type	Nodular	9.28 ± 4.84	91.70	<.001*
		Cord shape	12.01 ± 6.47	125.69	
Anterior-Posterior		Nodular	4.02 ± 2.92	85.04	<.001*
		Cord shape	5.29 ± 2.80	123.43	
Transverse	Flexor Tendon/Muscle Extension	No extension	10.44 ± 5.13	108.57	.331
		Extension present	11.50 ± 6.76	117.02	
Anterior-Posterior		No extension	4.56 ± 3.22	98.03	.017*
		Extension present	5.02 ± 2.58	118.41	
Transverse	Flexion Deformity	No	10.31 ± 5.03	107.03	0.111
		Yes	12.48 ± 7.22	121.02	
Anterior-Posterior		No	4.47 ± 3.10	96.68	<0.001*
		Yes	5.30 ± 2.55	125.37	
Transverse	Vascularization in CDUS	No	10.91 ± 5.90	112.48	0.304
		Yes	17.60 ± 13.55	110.75	
Anterior-Posterior		No	4.80 ± 2.92	108.48	0.959
		Yes	4.40 ± 2.26	110.75	
Transverse	SEL	Stiff (Hard)	11.59 ± 6.1	111.83	0.118
		Moderately Stiff and Soft	10.43 ± 5.7	98.61	
Anterior-Posterior		Stiff (Hard)	4.66 ± 2.59	100.59	0.797
		Moderately Stiff and Soft	5.00 ± 3.24	102.73	

CDUS: Color Doppler Ultrasound; SEL: Sonoelastography; SD: Standard deviation Note: Mean ± SD values are calculated per group based on actual lesion measurements. Mean Rank values are derived from Mann-Whitney U tests. Statistically significant p-values are shown in bold.

Table 3. Associations Between Patient and Lesion Characteristics and the Presence of Tendon/Muscle Involvement and Flexion Deformity

Comparison	Group/Category	Positive Finding Rate (%)	χ^2 / p value
Sex vs Tendon/Muscle Involvement	Female	43.8	3.364 / 0.067
	Male	56.9	
Affected Side vs Tendon/Muscle Involvement	Right Hand	51.5	0.178 / 0.673
	Left Hand	54.3	
Lesion Localization vs Tendon/Muscle Involvement	3 rd finger	25.0	4.004 / 0.135
	4 th finger	50.0	
	5 th finger	63.0	
Vascularization vs Tendon/Muscle Involvement	Absent	52.9	0.455 / 0.500
	Present	33.3	
Echogenicity vs Tendon/Muscle Involvement	Hypoechoic	50.3	2.646 / 0.104
	Iso-hyperechoic	64.9	
Sex vs Flexion Deformity	Female	30.1	7.193 / 0.007*
	Male	49.0	
Affected Side vs Flexion Deformity	Right Hand	40.3	0.924 / 0.337
	Left Hand	46.7	
Lesion Localization vs Flexion Deformity	3 rd finger	0.0	10.119 / 0.006*
	4 th finger	38.7	
	5 th finger	59.3	
Echogenicity vs Flexion Deformity	Hypoechoic	39.7	4.940 / 0.026*
	Iso-hyperechoic	59.5	
Vascularization vs Flexion Deformity	Absent	43.0	0.114 / 0.736
	Present	33.3	
Tendon/Muscle Involvement vs Flexion Deformity	Absent	0.0	149.49 / <0.001*
	Present	81.5	
Lesion Morphology vs Flexion Deformity	Nodular	3.6	84.493 / <0.001*
	Cord-like	66.2	

χ^2 : Chi-square; %: Percentage; p: p-value; Tendon/muscle involvement refers to lesion extension to adjacent flexor tendons or muscle structures.

transverse and anterior-posterior lesion dimensions (Spearman's $\rho=0.631$, $p<0.001$). This finding indicates that larger lesions tend to demonstrate growth in both dimensional planes, suggesting uniform expansion patterns in advanced disease stages.

DISCUSSION

This study analyzed various sonographic features of DD lesions (echogenicity, lesion size, flexor tendon or muscle extension, strain elastography-based stiffness, and CDUS vascularity) to explore their associations with the occurrence of flexion contractures. Demographic variables, including age, sex, and relevant etiologic factors, were also examined in relation to the imaging

characteristics observed.

Our findings showed a male predominance (male/female ratio = 2.1:1), which aligns with previous studies. Literature reports indicate that men are affected approximately twice as often as women, with a more aggressive disease course in males. Some publications indicate that male predominance is less pronounced than previously thought and that this ratio changes with age (13). Furthermore, earlier disease onset is associated with increased severity of disease progression (14).

The observation that AP lesion dimensions were significantly greater in male patients carries clinical relevance ($p=0.043$). This finding supports the

hypothesis that the disease exhibits a more aggressive course in males. According to existing literature, DD in males tends to have earlier onset, advances more rapidly, and recurs more frequently (15). The notably higher frequency of flexion deformity in male patients observed in our study may represent a clinical manifestation of the disease's more severe course in this group ($p=0.007$). Hormonal mechanisms are thought to contribute significantly to these sex-based differences in disease severity. It has been suggested that estrogen exerts a protective influence in females, whereas testosterone may promote fibrous tissue proliferation in males (16). The increase in DD prevalence among women in the postmenopausal period further supports the hormonal hypothesis.

Moreover, the significantly older age of patients presenting with flexion deformity reflects the chronic and progressive character of DD ($p=0.008$). This observation suggests that age may serve as an independent prognostic indicator and underscores the value of early recognition and treatment.

A notable finding in our study was that lesions with cord-like morphology were significantly larger in both transverse and anteroposterior dimensions than those with a nodular pattern ($p<0.001$ for both). This result highlights the potential prognostic value of lesion morphology in staging the disease and anticipating its progression. Vanek et al. reported that identifying cord morphology on ultrasound may assist in predicting post-treatment outcomes (17). Aligned with their findings, our study also revealed a strong prognostic association between lesion morphology and contracture, with a 66.2% deformity rate in cord-shaped lesions versus just 3.6% in nodular ones ($p<0.001$). This disparity likely reflects distinct phases in the disease's underlying pathogenesis. The nodular phase is dominated by myofibroblast activity and TGF- β signaling, whereas the cord phase is characterized by mature collagen deposition and contracture formation (6, 18). Thus, the high rate of flexion deformity in cord-like lesions suggests that this morphological transformation serves as a strong marker of functional compromise.

One of the strongest findings of our study is that while flexion deformity was observed in 81.3% of lesions with tendon and/or muscular extension, no deformity was detected in any lesions without extension

($p<0.001$). This dramatic result demonstrates that anatomical proximity is the most critical factor determining the clinical course of the disease. Consistent with our findings, previous anatomical and ultrasonographic studies have suggested that the close spatial relationship between Dupuytren lesions and flexor tendons may mechanically contribute to the development of flexion deformities (8, 19). Therefore, evaluating tendon involvement via preoperative ultrasonography may provide valuable insight for surgical risk stratification and for informing patients.

Analysis based on lesion localization revealed that flexion deformity occurred in 59.3% of cases involving the 5th finger and 38.7% of those affecting the 4th finger ($p=0.006$), indicating that anatomical site plays a prognostic role. This difference may be attributable to anatomical features of the fourth intermetacarpal space, which may predispose to flexor tendon compression. Prior studies have shown that DD most commonly and severely affects the 4th and 5th digits (20). Our finding supports this knowledge while also demonstrating that US determination of localization has prognostic value.

Our finding of no statistically significant correlation between lesion stiffness on SEL and lesion size ($p > 0.05$) is particularly notable. Currently, no studies in the literature have demonstrated a direct correlation between elastographic stiffness and lesion size; existing reports primarily focus on using SEL to characterize lesion consistency and morphology, such as nodular versus cord types (21). Variations in technique and patient selection criteria may account for these inconsistent results. Despite these limitations, we consider our findings to offer original insights that may enrich the current literature. Future multicenter studies with larger patient populations could further validate these results.

The more frequent occurrence of flexion deformity in iso-hyperechoic lesions suggests a relationship between echogenicity and disease activity ($p=0.026$). Molenkamp et al. found that hypoechoic nodules observed on ultrasound correlate with increased myofibroblast content on histopathologic examination ($r \approx -0.4$; $p = 0.002$) (22). This finding suggests that echogenicity may be an imaging biomarker reflecting nodule activity.

The very low number of patients with vascularization detected by CDUS (1.3%) and the lack of significant relationship with clinical findings suggest that CDUS has limited value in this disease. This aligns with existing knowledge that the contracture phase of DD is dominated by avascular fibrous structures (23). Nonetheless, increased vascularity has been reported during the early nodular stage of the disease (23). This discrepancy may be attributed to the fact that most patients in our study were in more advanced disease stages.

In contrast to previous studies primarily describing the descriptive sonographic features of Dupuytren's disease, our research focuses on quantifying the associations between imaging findings and the development of flexion deformity. This approach provides practical prognostic information that may aid clinicians in stratifying patients based on deformity risk.

Our study has several limitations. Its retrospective design, absence of follow-up data, and lack of standardization in elastographic evaluation are the main constraints. Additionally, the low positivity of CDUS makes interpretation of results related to this modality challenging.

CONCLUSION

Ultrasonography and elastography offer significant prognostic insight in the management of Dupuytren's contracture. Among the evaluated variables, flexor tendon involvement stands out as the most reliable predictor of contracture development. In addition, cord-like lesion morphology, male sex, and localization to the fourth finger were found to be relevant clinical risk factors. These results may serve as a foundation for more accurate risk stratification and individualized treatment planning, allowing clinicians to make better-informed decisions regarding surgical strategies and patient communication. Routine incorporation of standardized ultrasound protocols into clinical workflows is recommended to improve patient outcomes in the treatment of this condition.

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LATERAL EPICONDYLITIS OR FIBROMYALGIA TENDER POINT? DIAGNOSTIC PITFALLS AND THE RISK OF UNNECESSARY ESWT

Lateral Epikondilit mi, Yoksa Fibromiyalji Hassas Noktası mı? Tanısal Yanılgılar ve Gereksiz ESWT Uygulama Riski

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ABSTRACT

Objective: This study aimed to determine the frequency of fibromyalgia syndrome (FMS) in patients with lateral epicondylitis (LE) receiving Extracorporeal Shock Wave Therapy (ESWT).

Material and Methods: All patients who received ESWT in the City Hospital Physical Therapy Unit between January 2017 and December 2023 were retrospectively reviewed, and those diagnosed with LE were included. Demographic data such as age, gender, side of epicondylitis, number of ESWT sessions, invoice amount, cost, and presence of FMS were recorded.

Results: A total of 2810 patients were included; 1851 had unilateral and 959 bilateral LE. Among unilateral cases, 71.3% were women, while in bilateral cases, 79.4% were women, showing a significant gender difference ($p<0.001$). The mean ages of unilateral (46.30 ± 12.73) and bilateral (46.54 ± 11.83) groups did not differ significantly ($p=0.626$). FMS was found in 0.6% of unilateral and 19.2% of bilateral cases, indicating a significant difference ($p<0.001$). Both LE and FMS were more common in women and middle-aged patients.

Conclusion: This study is the first to investigate FMS frequency in LE. Bilateral LE patients showed a higher FMS rate compared to the general population. The lateral epicondyle, a common pain site in fibromyalgia criteria, may cause diagnostic confusion, leading to misdiagnosis of LE and unnecessary ESWT. Clinicians should consider FMS, particularly in bilateral cases, and prioritize multidisciplinary fibromyalgia management, including medication, exercise, and lifestyle modification to prevent unnecessary and costly ESWT treatments.

Keywords: Lateral Epicondylitis; Extracorporeal Shock Wave Therapy; Fibromyalgia Syndrome; Prevalence

ÖZET

Amaç: Bu çalışmanın amacı, Ekstrakorporeal Şok Dalga Tedavisi (ESWT) alan lateral epikondilitli hastalarda fibromiyalji sendromu sıklığını belirlemektir.

Gereç ve Yöntemler: Ocak 2017–Aralık 2023 tarihleri arasında Şehir Hastanesi Fizik Tedavi Ünitesi'nde ESWT tedavisi gören hastalar geriye dönük olarak tarandı ve lateral epikondilit tanısı alanlar çalışmaya dahil edildi. Hastaların yaş, cinsiyet, epikondilit tarafı, ESWT seans sayısı, fatura tutarı, maliyet ve fibromiyalji sendromu tanısı kayıt altına alındı.

Bulgular: Toplam 2810 hasta incelendi; 1851'i tek taraflı, 959'u bilateral epikondilit tanısı aldı. Tek taraflı olguların %71,3'ü, bilateral olguların %79,4'ü kadındı ve cinsiyet açısından anlamlı fark bulundu ($p=0,000$). Yaş ortalamaları benzerdi ($p=0,626$). Fibromiyalji sendromu tek taraflı olgularda %0,6, bilateral olgularda %19,2 oranında saptandı ve fark anlamlıydı ($p=0,000$). Her iki hastalığın da kadınlarda ve orta yaşta daha sık olduğu görüldü.

Sonuç: Bu çalışma, lateral epikondilitte fibromiyalji sendromu sıklığını inceleyen ilk çalışmadır. Bilateral olgularda fibromiyalji sıklığı normal popülasyona göre artış göstermiştir. Lateral epikondilit, fibromiyalji tanı kriterlerindeki yaygın ağrı bölgelerinden biridir ve bu durum tanısal karışıklığa yol açabilir. Bazı hastalara fibromiyalji yerine yanlışlıkla lateral epikondilit tanısı konularak gereksiz ESWT uygulanmış olabilir. Klinik değerlendirmede, özellikle bilateral olgularda fibromiyaljinin eşlik edebileceği akılda tutulmalı ve uygun multidisipliner tedavi yaklaşımları öncelikli olarak düşünülmelidir.

Anahtar Kelimeler: Lateral Epikondilit; Ekstrakorporeal Şok Dalga Tedavisi; Fibromiyalji Sendromu; Prevalans

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INTRODUCTION

Lateral epicondylitis (LE) is one of the most common causes of non-traumatic elbow pain, which develops as a result of repetitive stresses due to overuse of the forearm muscles, and is also called tennis elbow (1, 2). It is characterized by pain in the lateral epicondyle of the humerus to which the extensor muscles of the wrist attach, and on the extensor surface of the forearm. This condition occurs as a result of excessive and misuse of the extremity, repetitive wrist movements and microtraumas due to gripping activities (3). It has a prevalence ranging from 1-3% in the general population, and the age of onset is generally between 35-55 years. It is seen in women and more often on the dominant hand side. Typical symptom duration is between 6 and 24 months (4).

Although conservative and surgical treatment methods can be used in the treatment, conservative treatment methods provide improvement in 95% of the cases (5). The main aim of treatment is to relieve pain, regain lost functions and return to normal occupational and daily life activities. Rest, patient education, behavior modification, non-steroidal anti-inflammatory drugs (NSAID), splint and orthosis use, ice application, electrotherapy, massage, manual therapy, stretching and strengthening exercises, Extracorporeal Shock Wave Therapy (ESWT), dry needling, taping, balneotherapy, cryotherapy, steroid injections, platelet-rich plasma (PRP), hyaluronic acid injections and prolotherapy applications are available conservative treatment alternatives include (5).

ESWT is a treatment method for applying high-intensity pressure waves created outside the body to the desired area of the body through an ellipsoid-shaped head. ESWT has been applied in the field of medicine since the 1980s. It is thought that it stimulates angiogenesis by increasing the diffusion of cytokinin from the vessels, and provides an effect by creating neovascularization in the tendon-bone region. It is mentioned that it is an effective treatment for the treatment of patients with resistant LE in many studies (6, 7).

Fibromyalgia syndrome (FMS) is a disease in which widespread pain in soft tissues is the leading role, accompanied by other somatic symptoms, especially fatigue, sleep disorders and tenderness in soft tissues (8). Although it is more common in

women, its prevalence in Turkey was found to be 3.9-5.6% (9, 10). The etiology and pathogenesis of the disease have not been clearly explained yet, and it is thought to be multifactorial. FMS causes physical and emotional deterioration in the patient's quality of life and difficulty in performing activities of daily living. Along with pain, which is the main symptom of the disease, other symptoms also contribute to this condition. Diagnostic criteria for the diagnosis of the disease have changed and developed over the years, but a gold standard diagnostic method has not been established yet. Until the pathophysiology is better elucidated and biomarkers are identified, diagnosis will remain dependent on patient reporting and clinical assessment (11).

The lateral epicondyle region, which is one of the 18 tender points in the ACR (American Rheumatology Society) 1990 FMS Classification Criteria and one of the common pain areas in the ACR 2016 Diagnostic Criteria, may cause diagnostic confusion (12, 13). The diagnostic difficulties of FMS and its potential to be confused with other musculoskeletal diseases were evaluated in a review published in 2014; it was reported that FMS is characterized by widespread pain and tenderness points and can be confused with other localized pain syndromes, which can lead to misdiagnosis and unnecessary treatments (14). Similarly, it was emphasized that the widespread pain and tender points of FMS can be confused with other localized pain syndromes like LE in 2016 (12). It has been reported that myofascial pain syndrome and FMS may cause LE-like symptoms, which increases the risk of misdiagnosis. It has been reported that the risk of failure increases when underlying systemic pain syndromes such as FMS are ignored in evaluating the effectiveness of methods such as ESWT in the treatment of LE (15). Similarly, it has been suggested that the effectiveness of ESWT in LE is limited and that lack of response in some patients may be due to underlying systemic factors such as FMS (16). As a result, patients may have been mistakenly diagnosed with LE and unnecessarily received ESWT treatment, although they actually had FMS. There is no data in the literature on the frequency of FMS in LE. Both FMS and LE are common in middle-aged and women, and therefore they can be seen frequently together. The aim

of this study was to determine the frequency of FMS in patients with LE receiving ESWT treatment and to raise awareness that FMS may cause patients to receive ESWT treatment unnecessarily and cause a very large cost unnecessarily. In addition, this study aimed to contribute to a better understanding of the relationship between lateral epicondylitis and fibromyalgia and to provide a basis for future prospective research.

MATERIAL AND METHODS

Study Design: This retrospective study was undertaken between January 2017 and December 2023. Since the City Hospital where the study was conducted was opened in January 2017, the scanning of the study data started from this date; since the ethical approval was received in January 2024, the data up to December 2023 were scanned. This study was conducted with the approval of the City Hospital No. 2 Clinical Research Ethics Committee (E.Kurul-E2-24-6084) and with the Chief Physician's retrospective study permit letter, in accordance with the Declaration of Helsinki.

Patients: Since the study was retrospective, no sample calculation was made; all patients diagnosed with LE and treated with ESWT in the specified date range were screened. Patients who were examined in the City Hospital Physical Therapy Unit with the diagnosis of LE, who were treated with ESWT, whose contact information could be accessed in the hospital information system, and who regularly attended their sessions were included in the study. Patients whose contact information could not be reached in the hospital data system, who did not attend their sessions regularly, and whose file data were missing were excluded from the study.

Demographic information of patients such as age and gender, epicondylitis side, number of ESWT sessions, invoice amount, cost and whether have diagnosis of FMS were recorded. Patients were classified as those with unilateral LE (group 1); those with unilateral LE plus FMS syndrome (group 2); those with bilateral LE (group 3); and those with bilateral LE plus FMS syndrome (group 4). After obtaining ethical approval and the Chief Physician's retrospective study permit letter, patients' electronic patient card information was accessed; patients who were diagnosed with FMS at repeated intervals by Physical Medicine and

Rehabilitation Polyclinics and who had a drug report issued for FMS treatment were accepted as FMS. Since it was a retrospective study, no consent was obtained from the patients and no contact was made with the patients, but permission was obtained from the chief physician to access the retrospective data. Only patients who received ESWT treatment were included in the study, and it was not evaluated whether the patients received any other physiotherapy or medical treatment. In patients diagnosed with fibromyalgia, the American College of Rheumatology criteria were used, and the diagnosis was confirmed during repeated outpatient follow-up visits. Specifically, the 2016 revised ACR diagnostic criteria were applied for the diagnosis of fibromyalgia.

ESWT: Radial shock wave therapy was applied to the patients with the EMS Swiss DolorClast Master ESWT Device in our study. The treatment was applied to the lateral epicondyle and the painful points around it, at 10 Hz, 1.6 - 1.8 bar, 2000 beats, 2 sessions a week, total of 5 sessions. Ultrasound gel was used to ensure conductivity during the treatment. The application was performed with the patient in a sitting position, shoulder abduction 45, elbow flexed, while supporting the forearm. The use of the same standardized protocol for all patients minimized potential methodological differences in treatment application

Statistical Analysis

All analyses were carried out with SPSS 26.0 (IBM, USA). The findings of the study are expressed as frequency and percentages. Parametric tests were used for normally distributed continuous variables, while non-parametric tests (Mann-Whitney U) were applied for variables that did not meet normality assumptions. Normality analysis was carried out using Kolmogorov-Smirnov test. The variables that did not normally distribute are presented as the median and interquartile range (IQR) with 25-75th percentiles. Descriptive statistics mean and standard deviation (mean±SD) were used for normally distributed variables, mean and minimum-maximum values were used for non-normally distributed variables. Numeric dependent variables with abnormal distribution were compared with the Mann-Whitney U test. Categorical variables were compared using the Chi-Square test.

P< 0.05 was accepted for statistical significance.

RESULTS

A total of 3170 patients were treated with ESWT due to LE between January 2017 and December 2023; 200 of these patients were excluded from the study because they did not complete the ESWT treatment sessions and this would add to the cost expense, and 160 patients were excluded because their past clinical information and electronic patient card could not be accessed. A total of 2810 patients who received ESWT treatment with the diagnosis of LE were included in the study.

While 1851 patients were diagnosed with unilateral epicondylitis, 959 patients were treated with the diagnosis of bilateral epicondylitis. While 1319 (71.3%) of the patients with unilateral epicondylitis were women, 761 (79.4%) of the patients with bilateral epicondylitis were women and there was a significant gender difference between groups, and female gender was more common in bilateral epicondylitis (p: 0.000). The mean age of patients with unilateral epicondylitis was 46.30±12.73 years, while the mean age of patients

with bilateral epicondylitis was 46.54±11.83 years, and there was no significant difference between the groups in terms of mean age (p:0.626). (Table 1).

While 11(0.6) of unilateral epicondylitis patients had FMS, 184(19.2%) of bilateral epicondylitis patients had FMS and there was a significant difference between the groups in terms of FMS frequency, and FMS was more common in bilateral epicondylitis (p: 0.000) (Table 2).

DISCUSSION

We found FMS more common in diagnosed of bilateral epicondylitis patients treated with ESWT compared to unilateral epicondylitis patients and to the general population in our study. We found both LE and FMS more common in women and middle age. This result suggests that fibromyalgia assessment should be considered an integral part of the clinical evaluation, particularly in cases of bilateral epicondylitis.

LE and FMS are two common diseases in women. While no significant difference was found in terms of prevalence in some studies, it was shown that LE is more common in women in some studies (10, 17). 74.02% of the patients participating in our study were

Table 1. Demographic features of unilateral /bilateral lateral epicondylitis alone (group 1, 3) and lateral epicondylitis plus fibromyalgia syndrome patients (group 2, 4)

	Unilateral		Bilateral		p
	LE alone patients Group 1	LE plus FMS patients Group 2	LE alone patients Group 3	LE plus FMS patients Group 4	
Frequency (%)	1840(99.4)	11(0.6)	775(80.8)	184(19.2)	
Gender N (%) Female/N Male (%)	1319(71.3) /532(28.7)		761 (79.4) / 198(20.6)		p<0,0001
Age(mean±SD)	46.30±12.73		46.54±11.83		0.626
Invoice amount (TL) (mean±SD)	83.71±59.756		167.81±67.885		p<0,0001
Cost (TL) (mean±SD)	81.26±41.537		164.45±53.739		p<0,0001
Number of ESWT therapy sessions (mean±SD)	2.97±1.375		3.35±1.109		p<0,0001

LE: Lateral Epicondylitis, FMS: Fibromyalgia Syndrome, SD: Standard Deviation, TL: Turkish Lira, ESWT: Extracorporeal Shock Wave Therapy

Table 2. Distribution of patients according to the presence of fibromyalgia syndrome and lateral epicondylitis

	FMS	
	Alone N (%)	Plus N (%)
Unilateral LE	99.4	0.6
Bilateral LE	80.8	19.2
P value	p<0,0001	

LE: lateral epicondylitis, FMS: Fibromyalgia Syndrome, N: number

women consistent with the literature. After the age of 30, the incidence of LE increases with the decrease in water content and loss of flexibility in the joint capsule, tendon and soft tissues, and the general age of onset is between 35-55 years (4, 18). The age of the patients was between 21 and 65, and the mean age was 46.40 consistent with the literature.

The prevalence in the general population has been reported as 1-3% for LE and 2-3% for FMS (1, 9). While the prevalence of LE in the general population is 1-3%, the prevalence of bilateral epicondylitis is not exactly known, but it constitutes 5-10% of all LE cases. Its prevalence in the general population is between 0.1% and 0.3% and is usually associated with systemic diseases (e.g. diabetes, rheumatoid arthritis, FMS) or heavy occupational loads (19, 20). Contrary to literature, we found that 65.8% of 2810 LE patients who received ESWT treatment had unilateral epicondylitis, 34.2% had bilateral epicondylitis. This difference may be due to the fact that some of the patients diagnosed with bilateral epicondylitis did not have LE and had FMS tender points that mimicked LE.

There is no data in the literature on the frequency of FMS in LE. The one of the basic pathological mechanisms of the disease is enthesitis, inflammation at the points where muscles and tendons attach to bones in ankylosing spondylitis (AS). LE is also considered an enthesopathy, and this common pathological mechanism may contribute to the development of chronic pain in both diseases. FMS is characterized by widespread pain and central sensitization. Chronic pain caused by enthesitis may lead to the development of central sensitization, creating a predisposition to FMS in AS. Similarly, central sensitization may develop in cases where LE becomes chronic, and this may increase the frequency of FMS. Therefore, AS studies examining the relationship between chronic pain caused by enthesitis and FMS provide a good comparison point for investigating the frequency of FMS in patients with LE. Sayın et al., looked at the frequency of FMS in 127 patients with axial spondyloarthropathy and 73 age- and sex-matched control patients and found the frequency of FMS 43 (33.9%) in the axial spondyloarthropathy group and 22 (30.1%) in the control group ($p : 0.58$) (21). Macfarlane et al., investigated the association of FMS in patients

with axial spondyloarthritis from the British Society of Rheumatology Biology Registry in the Ankylosing Spondylitis cohort and found FMS in 311 (20.7%) of 1504 patients who met the 2011 research criteria (22). Both LE and temporomandibular disorders (TMD) are chronic musculoskeletal pain syndromes that begin localized but can eventually cause widespread pain and functional limitations. Studies examining the frequency of FMS in TMD patients provide a meaningful scientific basis for comparison when investigating the frequency of FMS in LE patients, as they reveal common mechanisms such as chronic musculoskeletal pain, myofascial dysfunction, and central sensitization. Erbaşar et al., found the frequency of FMS 60% in patients with temporomandibular joint dysfunction in 2019 (23). They may have found the frequency of FMS to be high because the number of patients was only 25. The prevalence of temporomandibular disorders and FMS was examined in the meta-analysis published in 2023; almost one third of individuals with temporomandibular disorders (32.7%, 4.5%-71.0%) were reported to have FMS (24). Similarly to Macfarlane study, since our patient numbers were similar, we found the frequency of FMS was 19.2% in 959 patients with bilateral epicondylitis who received ESWT treatment in our study. The large sample size in our study and the focus on patients receiving only ESWT can be regarded as methodological strengths compared to similar studies in the literature.

Özçakır found the frequency of FMS to be 25.45% in the presence of clinical carpal tunnel syndrome, and 26% in the presence of carpal tunnel syndrome both clinically and electrophysiologically in her study which she investigated the frequency of FMS in patients presenting with carpal tunnel syndrome symptoms in 2020 (25). The reason for the low frequency of FMS in the study with chronic Achilles tendinopathy, unlike our study, may be the low average age and the low ratio of female. Unlike our study, the reason for the low frequency of FMS in shoulder diseases is the low female gender, shorter average complaint duration, and the fact that FMS tender points are on the trapezius above the shoulders instead of the shoulder head, so it may cause more back pain than shoulder complaints. Similarly to Özçakır's study, we found the frequency of FMS 19.2% in 959 patients with bilateral epicondylitis

who received ESWT treatment in our study. Carpal tunnel syndrome, like bilateral epicondylitis, can mimic FMS, both because it is more common in middle age and women, and because numbness, pain, and weakness mimic FMS symptoms. In our study, we think that the frequency value is more valid because the number of patients is high.

Although there is no data in the literature on the frequency of FMS in LE; Genç et al., investigated the effects of FMS on pain severity, disability and treatment outcomes in patients with chronic LE in 2012. Seventy-eight patients with chronic unilateral epicondylitis and 30 healthy people were included in their study. They found that LE patients with FMS had less improvement and less pain relief at the controls 2 weeks and 3 months after corticosteroid injection compared to those without (26).

The number of sessions and costs of ESWT applications in the treatment of LE vary in the literature. It is seen that ESWT is applied with different protocols in various studies. Bayram and his colleagues applied ESWT for a total of 3 sessions, once a week (27). A total of 4 sessions of ESWT were applied, 2 sessions per week in another study, (28). A total of 3 sessions of ESWT were applied once a week in a study comparing deep transverse friction massage with ESWT (29). These differences show that treatment protocols can vary according to the clinical situation and the preference of the practitioner. We found that the average ESWT session was 3.35 in patients with bilateral epicondylitis, while it was 2.97 in unilateral epicondylitis in our study. This difference may be due to the fact that some patients with bilateral epicondylitis actually had pain related to FMS rather than LE, and received more sessions because their pain did not go away. The cost of ESWT varies depending on the number of applications and the devices used. For example, in one study, the cost of ESWT was stated as 124 TL (29). However, it should not be forgotten that this cost is specific to the period and region in which the study was conducted. In general, it is stated that ESWT is a less invasive and more cost-effective option than surgical interventions (30). In conclusion, the number of sessions and cost of ESWT may vary depending on the applied protocol, clinical situation and regional factors. We found that the average ESWT bill was 167.81 TL in patients with

bilateral epicondylitis, while it was 83.71 TL in unilateral epicondylitis in our study. This difference was caused by patients with bilateral epicondylitis receiving more ESWT sessions, and therefore there was a greater cost loss. Nevertheless, the present findings indicate that fibromyalgia may be an important explanatory factor for treatment failures in lateral epicondylitis.

The limitations of the study include the lack of a healthy control group, the retrospective nature of the study, the lack of specification of the duration of FMS, lack of knowledge of other comorbidities, medications used, smoking and alcohol use, etc., lack of knowledge of the severity of pain, and the inability to evaluate the effect of FMS diagnosis on the effectiveness of ESWT treatment in patients with LE. Future prospective and multicenter studies are required to confirm these findings and to explore causal relationships.

CONCLUSION

Our study is the first to investigate the FMS in LE. While the prevalence of LE in the general population is 1-3%, the prevalence of bilateral epicondylitis is not exactly known, but it constitutes 5-10% of all LE cases, its prevalence in the general population is between 0.1% and 0.3% and is usually associated with systemic diseases (e.g. diabetes, rheumatoid arthritis, FMS or heavy occupational loads (19, 20). We found that 65.8% of 2810 LE patients who received ESWT treatment had unilateral epicondylitis, 34.2% had bilateral epicondylitis, and the frequency of FMS in patients with bilateral epicondylitis was 19.2%, in our study. This difference may be due to the fact that some of the patients diagnosed with bilateral epicondylitis did not have LE and had FMS tender points that mimicked LE. The lateral epicondyle region, one of the common pain areas included in the Fibromyalgia Syndrome Diagnostic Criteria, can lead to diagnostic confusion and patients may have been mistakenly diagnosed with LE despite actually having FMS and may have received unnecessary ESWT treatment. It should be kept in mind that FMS may accompany patients with bilateral LE in particular, patients should first receive a comprehensive multidisciplinary management approach for fibromyalgia, including medication, exercise, lifestyle modification, and supportive therapies, and awareness should be raised about not

using the costly ESWT treatment unnecessarily. Therefore, routine screening for fibromyalgia in patients diagnosed with lateral epicondylitis is recommended in clinical practice.

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EFFECT OF MESENCHYMAL STEM CELLS ON UTERUS AND PLACENTA

Mezenşimal Kök Hücrelerin Uterus ve Plasenta Üzerine Etkisi

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ABSTRACT

Objective: This study investigated the effects of mesenchymal stem cell (MSC) application on the expression of extracellular matrix proteins fibronectin, matrix metalloproteinase-2 (MMP-2), and matrix metalloproteinase-9 (MMP-9) at the implantation site in pregnant Wistar Albino rats.

Material and Methods: Thirty-two adult female Wistar Albino rats were divided into two groups (control, n=8; stem cell, n=8) on the 10th and 21st days of gestation. The stem cell group received MSCs derived from rat bone marrow, while the control group received Phosphate Buffered Saline (PBS). Implantation sites and placentas were collected, and fibronectin, MMP-2, and MMP-9 expressions were evaluated using immunohistochemistry.

Results: On day 10 of gestation, fibronectin reactivity in the decidual structure was similar in both control and stem cell groups, with no significant difference (p>0.05). On day 21, fibronectin expression was significantly elevated in the labyrinth area and spongiotrophoblasts of the stem cell group compared to the control group (p=0.02). MMP-2 immunoreactivity was reduced around trophoblastic giant cells in the stem cell group but remained consistent in decidua cells, gland epithelium, and vessel walls. MMP-9 levels were higher in trophoblastic giant cells in the stem cell group, though the difference was not statistically significant (p>0.05). On day 21, both MMP-2 and MMP-9 activities were less intense in both groups.

Conclusion: MSC administration significantly increased fibronectin expression in the labyrinth area and spongiotrophoblasts on day 21 of gestation, suggesting a role for MSCs in enhancing extracellular matrix remodeling at the implantation site. However, MSC treatment did not significantly alter MMP-2 or MMP-9 immunoreactivity, indicating that their effects may be specific to fibronectin-mediated processes during placental development.

Keywords: *Implantation; Mesenchymal Stem Cell; Fibronectin; MMP-2; MMP-9*

ÖZET

Amaç: Bu çalışmada, mezenkimal kök hücre (MKH) uygulamasının gebe Wistar Albino sıçanlarda implantasyon bölgesinde hücre dışı matriks proteinleri fibronectin, matriks metalloproteinaz-2 (MMP-2) ve matriks metalloproteinaz-9 (MMP-9) ekspresyonu üzerindeki etkileri araştırılmıştır.

Gereç ve Yöntemler: Otuz iki yetişkin dişi Wistar Albino sıçan gebeliğin 10. ve 21. günlerinde iki gruba ayrılmıştır (kontrol, n=8; kök hücre, n=8). Kök hücre grubuna sıçan kemik iliğinden elde edilen MKH'ler verilirken, kontrol grubuna Fosfat Tamponlu Salin (PBS) verilmiştir. Implantasyon bölgeleri ve plasentalar toplandı ve fibronectin, MMP-2 ve MMP-9 ekspresyonları immünohistokimya kullanılarak değerlendirildi.

Bulgular: Gebeliğin 10. gününde, desidual yapıdaki fibronectin reaktivitesi hem kontrol hem de kök hücre gruplarında benzerdi ve anlamlı bir fark yoktu (p>0,05). 21. günde, fibronectin ekspresyonu kontrol grubuna kıyasla kök hücre grubunun labirent alanında ve spongiotrofoblastlarında önemli ölçüde artmıştır (p=0,02). MMP-2 immünoaktivitesi kök hücre grubunda trofoblastik dev hücrelerin çevresinde azalmış, ancak desidua hücrelerinde, bez epitelinde ve damar duvarlarında sabit kalmıştır. MMP-9 seviyeleri kök hücre grubundaki trofoblastik dev hücrelerde daha yüksekti, ancak fark istatistiksel olarak anlamlı değildi (p>0.05). 21. günde, hem MMP-2 hem de MMP-9 aktiviteleri her iki grupta da daha az yoğundu.

Sonuç: MSC uygulaması, gebeliğin 21. gününde labirent bölgesinde ve spongiotrofoblastlarda fibronectin ekspresyonunu önemli ölçüde artırarak MSC'lerin implantasyon bölgesinde hücre dışı matriks yeniden şekillenmesini arttırmada rol oynadığını düşündürmüştür. Bununla birlikte, MSC tedavisi MMP-2 veya MMP-9 immünoaktivitesini önemli ölçüde değiştirmemiştir, bu da etkilerinin plasental gelişim sırasında fibronectin aracılı süreçlere özgü olabileceğini göstermektedir.

Anahtar Kelimeler: *İmplantasyon; Mezenşimal Kök Hücre; Fibronectin; MMP-2; MMP-9*

INTRODUCTION

Successful reproduction requires the blastocyst to implant into the endometrium, a process involving complex physiological, biochemical, and structural interactions between blastocyst trophoblasts and the uterine epithelium (1, 2). During the preimplantation period, the endometrial luminal epithelium and stroma undergo significant changes, including apposition, adhesion, and invasion (3). In rodents, the initial attachment response, observed by late day 4 in mice, coincides with increased stromal vascular permeability at the blastocyst attachment site (4). This triggers decidualization, a progesterone- and cAMP-driven transformation of endometrial stromal cells into decidual cells, which supports embryonic development (5, 6). In rats and mice, decidualization begins at the antimesometrial pole, where stromal cells form the primary decidual zone (PDZ) with an epithelial-like morphology. As implantation progresses, the PDZ regresses, giving way to the secondary decidual zone (SDZ), a layer of proliferating and differentiating stromal cells peaking around day 8 in mice (7, 8). This process facilitates epithelial-mesenchymal transition and immune adaptation critical for successful implantation (8).

The extracellular matrix (ECM) plays a pivotal role in implantation by mediating blastocyst-ECM interactions that maintain tissue architecture and regulate cell growth and differentiation (5). Matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, are key regulators of ECM remodeling, activating cell surface receptors, growth factors, cytokines, and adhesion molecules (9). These gelatinases degrade ECM components such as collagen IV, V, VII, XI, fibronectin, laminin, elastin, proteoglycans, and entactin, facilitating trophoblast invasion (10, 11). Studies highlight MMP-2's dominant role in early trophoblast invasion, while MMP-9 deficiency in mouse embryos impairs invasion, underscoring their importance in maternal-fetal communication (12-14). Fibronectin, a critical ECM protein, serves as a key adhesion molecule in connective tissue, promoting cell migration during embryogenesis and implantation (15-17).

This study aims to investigate the effects of mesenchymal stem cell (MSC) administration on the

expression of fibronectin, MMP-2, and MMP-9 at the rat implantation site using immunohistochemistry, elucidating their roles in ECM remodeling and implantation success.

MATERIALS AND METHODS

In our study, 32 adult Wistar albino female rats weighing between 180-200 grams were used. The ethical approval of this study was granted by Adnan Menderes University (ADÜ) Animal Experiments Local Ethics Committee (ADÜ-HADYEK) (NO:64583101/2014/070-11.06.2014). The rat experiments were performed in ADÜ Animal Experiments Research Laboratory. The cell culture was performed in the ADÜ-BİLTEM laboratory, and the histology and immunohistochemical staining phases were performed in ADÜ Histology-Embryology Laboratory. All rats were maintained in plastic cages under 12:12 h day/night cycle at 23±2 temperature °C and 45±5% humidity with intake of water and food ad libitum. For the experiment, animals were divided into 2 groups of 16 rats, then the experimental procedure was performed as follows: 1. Control group (n=16): It was divided into 2 groups of 8 rats each on days 10 and 21. Female rats were kept in the same cage with male rats overnight, and those with spermatozoa found in vaginal smears the next morning were considered as day 0 of pregnancy and Phosphate Buffered Saline (PBS) was administered through the tail vein of the rats on the same day. 2. Stem Cell Group (n=16): The rats were divided into 2 groups of 8 rats each on days 10 and 21. Female rats were kept in the same cage with male rats for one night and those with spermatozoa in vaginal smears the next morning were considered as day 0 of pregnancy and 1x10⁶ mesenchymal stem cells expressing Green Fluorescent Protein (GFP) were injected from the tail vein of the rats in 0.4 mL PBS on the same day. On days 10 and 21, all subjects were sacrificed under intraperitoneal anesthesia with 60 mg/kg ketamine and 5 mg/kg xylazine, after which the implantation site and placentas were removed and tissues were fixed in 10% neutral formalin.

Five female rats weighing 180-200 grams were used as donors to obtain mesenchymal stem cells. The rats were sacrificed by ketamine and xylazine administration and the femurs were removed after the hind and forelimbs were sterilized with 70% alcohol. The removed femurs

were cleaned from soft tissues and placed in 25 mL Hank's Buffered Slat Solution falcon tubes and kept for a period of time. In order to obtain stem cells, femurs were cut from both ends and placed vertically in tubes containing Minimum Essential Medium (MEM). After the bone marrow was transferred from the bones to the medium, it was centrifuged, 10 mL of medium was added to the pellet, pipetted and distributed into T25 flasks. The flasks were placed in the CO₂ incubator and the medium was changed every three days and checked under light microscope (18).

In this study, retrovirus-mediated gene transfer was performed for permanent labeling of MSCs with Green Fluorescent Protein (GFP) before. For this, the retroviral mammalian expression vector MSCV (The Murine Stem Cell Virus) -IRES-GFP (6500 bp) carrying the cDNA of GFP was used. For this purpose, ecotropic Phoenix (gag+, pol+) packer cells were transfected with MSCV-IRES-GFP vector by calcium precipitation method. MSCs were infected with viral supernatant produced in transfected Phoenix cells for 2 days at 12-hour intervals. Then, cells were stained with Trypan blue (Sigma 93595, Germany) at a ratio of 1/1 for viability testing and cell counting was performed using a Neubauer slide.

MSCs were identified by flow cytometry analysis using mesenchymal stem cell lineage surface expression markers (CD11b, CD29, CD45 and CD90) from passage number three. Cells attached to the surface of the culture dish were removed with 0.25% Trypsin-EDTA (Sigma T4049, Germany) centrifuged and the pellet was suspended with PBS. Cells were then incubated with fluorescein isothiocyanate (FITC)-conjugated monoclonal CD11b, CD29, CD45, and CD90 (BD, Biosciences, USA) antibodies specific for the identified cell surface markers for 45 minutes in the dark. After incubation and washing, the cell suspension was read on FACS Calibur Flow Cytometry (BD Biosciences) and analyzed with the BD CellQuest™ software program. The tissue samples were embedded in OCT (Optimal Cutting Temperature) compound and kept overnight at +4°C and then 5 µm sections were taken in a frozen (Cryostat A650) device. The sections were washed 3 times with PBS after 10 minutes in the dark with a drop of methanol and the sections were treated with the nuclear stain DAPI (Sigma-Aldrich D9542). Imaging

was then performed under a fluorescence microscope (Leica DMI 4000).

For histologic follow-up, all tissues were fixed in 10% neutral formalin and then dehydrated in various alcohol series to prepare the tissues for microscopic examination. After transparency and paraffin blocking, serial sections of 5 µm thickness were taken with a microtome (Leica RM 2265, Germany). After deparaffinization, the tissue sections were stained with Hematoxylin-Eosin (H&E) and Alcian Blue stain (Sigma-Aldrich, 123657). The specimens obtained were subjected to general histopathologic evaluation under light microscope (Olympus-BX50). In immunohistochemical analysis, the immunoreactivity of Fibronectin, MMP-2 and MMP-9 proteins in the implantation site and placental tissues of the experimental groups were determined by Avidin-Biotin peroxidase method (19). Briefly, after deparaffinization of 5 µm thick sections, they were kept in citrate buffer 2 × 4 times (pH: 6.0) in a 300 W microwave oven to open epitopes and then kept in 3% hydrogen peroxide for endogenous peroxidase activity. To prevent unwanted staining, tissue sections were kept in Ultra V block and incubated with primary antibodies at +4°C for 1 night. Biotinylated streptavidin-HRP and DAB secondary chromogens were then applied and sections were counterstained with hematoxylin Gill. They were dehydrated by passing through a series of ascending alcohol series and sections were covered with entellan. Sections were examined under an Olympus CX-31 light microscope. In all groups, the number of cells positive for Fibronectin (Abcam, ab32419), MMP-2 (Abcam, ab97779) and MMP-9 (Abcam, ab228402) immunoreactivity was evaluated by H-SCORE (Histologic scoring). Three sections were randomly selected for each group and four regions in each section were evaluated for analysis of immunohistochemical staining. Severity expression scoring: -(0): Negative, +(1): Weak, ++ (2): Moderate, +++ (3): Strong. Intensity expression scoring: 0,1: < %25, 0,4: < %26-50, 0,6: < %51-75, 0,9: < %76-100 (20). Immunoreactive score: the degree of intensity of positively stained cells multiplied by the scores obtained from the staining intensities H-SCORE for all groups was evaluated by three independent observers.

Statistical analysis was performed using the IBM SPSS

Statistics 15.0 software package (SPSS Inc., Chicago, IL, USA). Due to the relatively small sample size and the ordinal nature of the immunohistochemical scoring, a non-parametric approach was adopted. Comparisons between the control and stem cell groups were conducted using the Mann-Whitney U test. Descriptive statistics are presented as median values with interquartile ranges (25th–75th percentiles). A p-value of less than 0.05 was considered statistically significant (Table 1).

RESULTS

Immunophenotyping of MSCs was performed after the 3rd passaging. Immunophenotypic characterization of MSCs was determined by flow cytometry technique; CD45 and CD11b markers were negative and CD29 and CD90 markers were positive. Stromal markers: CD29 FITC (66.68%), CD90 (99.94%), CD45 PE (2.79%) and CD11b FITC (17.48%).

Experimental animals that were previously treated with MSCs transfected with GFP gene were sacrificed on days 10 and 21 and tissue sections were taken. Tissue sections were then labeled with DAPI and

visualized with a fluorescence microscope (Leica DMI 4000). Day 10 and 21, the presence of MSCs in the implantation site of the rat uterus was demonstrated by the presence of GFP positive (Figure 1).

On the 10th day of gestation, the uterus mainly consists of 2 parts: antimesometrial region and mesometrial region (21). Towards the mesometrial region, the cryoallontic placenta was observed and fetal membranes were prominent. In the antimesometrial region, stromal cells were dense but small in size compared to decidual cells (Figure 2A). Trophoblastic giant cells with large cytoplasm and abundant intensely stained granules with vacuoles in their cytoplasm were observed (Figure 2B). As the trophoblastic giant cells progressed towards the myometrium layer, they were observed to transform into stromal cells and the cytoplasm became smaller and differentiated as multinucleated cells with clear borders (Figure 2B). In the mesometrial region, stromal (decidua) cells differentiated into glycogen-rich cells to enable the formation of a glycogenic zone (Figure 2C). The stromal cells in the enlarged decidual area were shown to have multiple nuclei with a clear border with Alcian

Table 1. Group mean immunoreactivity scores and statistical evaluation (S: Severity, I: Intensity, NA: not available)

Day 10	Fibronectin				MMP-2				MMP-9				
	Control Group		Stem Cell Group		Control Group		Stem Cell Group		Control Group		Stem Cell Group		
	S	I	S	I	S	I	S	I	S	I	S	I	
Vascular Wall	2	0.4	1	0.1	2	0.4	2	0.4	2	0.4	2	0.4	
Gland Epithelium	2	0.4	2	0.1	2	0.1	2	0.1	2	0.1	2	0.1	
Trophoblastic Giant Cells	1	0.1	2	0.4	0.6	2	0.4	2	0.4	2	0.4	2	0.4
Stromal Decidual cells	2	0.4	2	0.4	2	0.4	2	0.4	2	0.4	2	0.4	

Day 21	Fibronectin				MMP-2				MMP-9			
	Control Group		Stem Cell Group		Control Group		Stem Cell Group		Control Group		Stem Cell Group	
	S	I	S	I	S	I	S	I	S	I	S	I
Vascular Wall	2	0.1	2	0.1	2	0.1	2	0.1	2	0.4	2	0.1
Gland Epithelium	2	0.4	2	0.1	2	0.1	2	0.1	2	0.4	2	0.4
Trophoblastic Giant Cells	2	0.1	2	0.1	2	0.1	2	0.1	1	0.4	2	0.1
Spongiotrophoblasts	1	0.4	1	0.1	1	0.1	2	0.1	2	0.4	2	0.4

Severity scoring	Intensity scoring
Strong 3	Strong 0.4 ~ 0.75/100
Moderate 2	Moderate 0.6 ~ 0.8/175
Weak 1	Weak 0.4 ~ 0.25/50
Negative 0	Negative 0.1 ~ 0.25

Protein	Region	10-Day Control Group (n = 16)	10-Day Stem Cell Group (n = 16)	p-value (10-day)	Region	21-Day Control Group (n = 16)	21-Day Stem Cell Group (n = 16)	p-value (21-day)
Fibronectin	Vascular Wall	0.8 (0.8-0.8)	0.6 (0.3-0.9)	0.620	Vascular Wall	0.2 (0.2-0.8)	0.1 (0.1-0.2)	0.132
	Glandular Epithelium	0.8 (0.1-0.8)	0.5 (0.1-0.9)	0.937	Spongiotrophoblast Cells	1.2 (0.8-1.2)	0.8 (0.8-1.2)	0.394
	Trophoblastic Giant Cells	0.8 (0.1-0.8)	1.2 (0.8-1.3)	0.260	Giant Cells	0.2 (0.2-0.5)	0.2 (0.2-0.2)	NA
	Stromal Cells	0.8 (0.8-1.2)	0.8 (0.4-1.3)	0.699	Labyrinth (Stromal) Cells	NA	0.53 (0.3-0.8)	0.620
					Vascular Wall	0.2 (0.2-0.3)	0.2 (0.2-0.3)	1.000
MMP-2	Vascular Wall	0.8 (0.8-0.9)	0.8 (0.7-1.3)	0.937	Spongiotrophoblast Cells	NA	0.73 (0.4-1.0)	0.700
	Glandular Epithelium	0.2 (0.2-0.4)	0.2 (0.1-0.4)	0.818	Giant Cells	0.2 (0.2-0.3)	0.2 (0.2-0.9)	0.394
	Trophoblastic Giant Cells	1.2 (1.1-1.3)	1.2 (0.8-1.3)	0.699	Labyrinth (Stromal) Cells	NA	NA	NA
	Stromal Cells	1.2 (1.1-1.8)	0.8 (0.8-1.3)	0.190				
					Vascular Wall	NA	0.73 (0.4-1.0)	NA
MMP-9	Vascular Wall	0.8 (0.8-1.2)	0.8 (0.6-1.2)	0.818	Spongiotrophoblast Cells	0.8 (0.8-0.9)	1.0 (0.8-1.8)	0.310
	Glandular Epithelium	0.3 (0.2-0.4)	0.2 (0.2-0.9)	1.000	Giant Cells	0.4 (0.4-0.5)	0.5 (0.2-0.9)	0.937
	Trophoblastic Giant Cells	0.8 (1.2-1.2)	1.8 (1.1-1.8)	0.093	Labyrinth (Stromal) Cells	NA	0.73 (0.4-1.0)	0.221
	Stromal Cells	1.2 (1.2-0.8)	1.2 (0.8-1.8)	0.588				

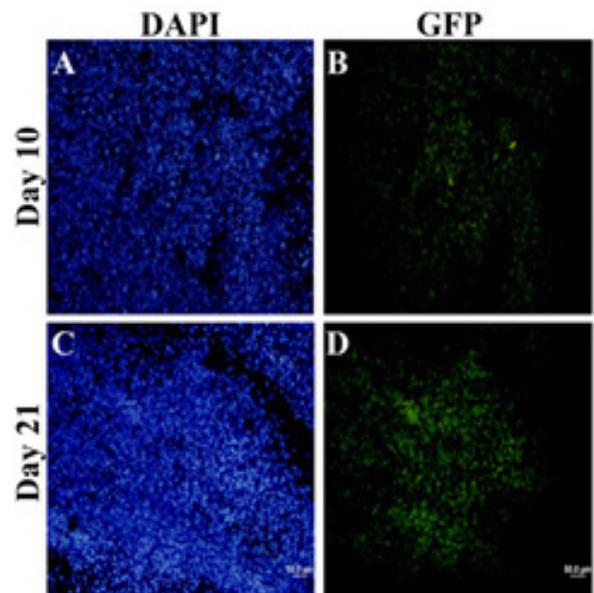


Figure 1. Demonstration of the presence of mesenchymal stem cells on days 10 and 21 by GFP positivity. A, B; Day 10 rat uterine implantation site. B: GFP positive cell line. C, D; Day 21 rat uterine implantation site. D: GFP positive cell line. Magnification: 20x, bar = 50 µm.

Blue stain (Figure 2C, D). 21-day-old rat placenta was observed to consist of 3 layers: maternal decidua area, spongiotrophoblast (basal zone) and labyrinth area (Figure 2E). Glycogen rich cells were observed in the labyrinth area, more in the spongiotrophoblast area, and their number was higher compared to 10-day-olds (Figure 2F,J). Giant trophoblastic cells were localized in the maternal decidua region, had large cytoplasm and intensely stained granule structures with vacuoles in the cytoplasm as on day 10 (Figure 2F,H). In addition, fetal and maternal blood vessels were observed in the spongiotrophoblast zone and fetal blood islets were observed in the labyrinth area (Figure 2G,J). In the day 10 control group, fibronectin expression in the implantation site of rats showed weak

immunoreactivity in giant trophoblastic cells and moderate immunoreactivity in decidual (stromal) cells (Figure 3A1,B1). Fibronectin expression was also seen in the luminal epithelium (Figure 3A1). Fibronectin immunoreactivity of the vessel wall and gland epithelium was moderate (Figure 3C1). MMP-2 immune reactivity of decidual cells was slightly more intense than in the stem cell group (Figure 3D1). Immunoreactivity of giant trophoblastic cells was moderate. (Figure 3E1). MMP-2 immunostaining showed no significant difference in immune reactivity in vessel wall and gland epithelium (Figure 3F1). In general, MMP-9 immunoreactivity examination showed intense ground staining in tissue sections. When the expression intensity for MMP-9 was analyzed, it was found to be intensely expressed in

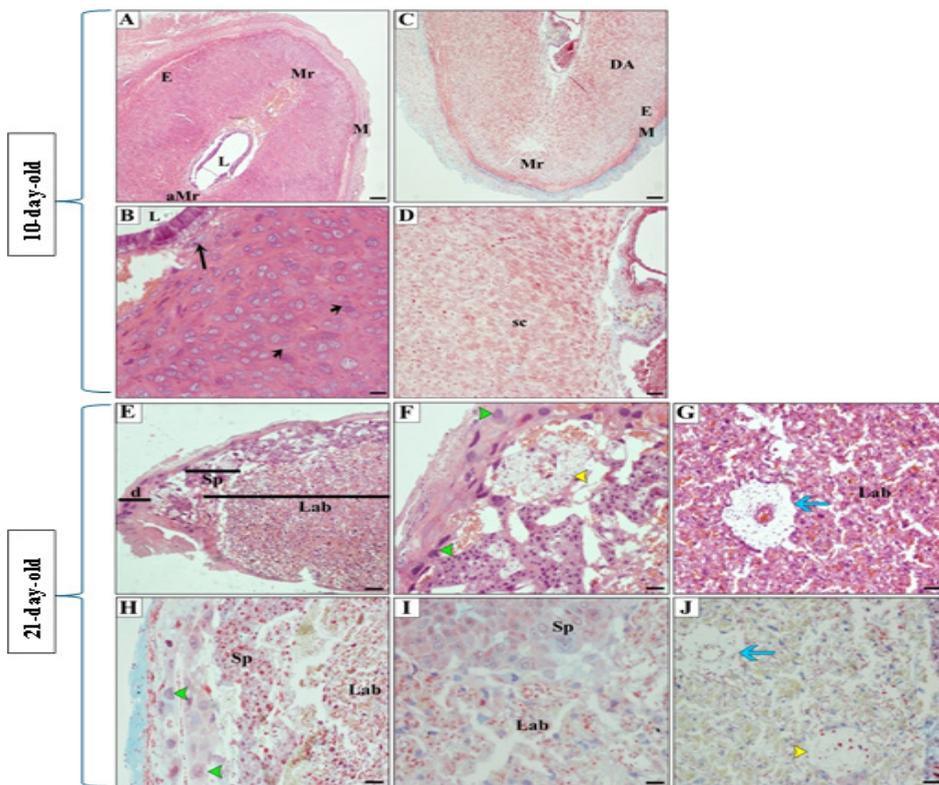


Figure 2. H&E and Alcian Blue staining images of 10-day implantation and 21-day placenta. A; General view - H&E Staining (aMr: Antimesometrial region, Mr: Mesometrial region, L: Lumen, E: Endometrium, M: Myometrium). Magnification: 10×. B; Trophoblastic Giant Cell (long arrow), L: Lumen, H&E staining, Magnification: 40×. C; Mr: Mesometrial region, DA: Decidual Area, E: Endometrium, M: Myometrium, Alcian Blue Staining, Magnification: 10×. D; sc: stroma cells, Alcian Blue Staining, Magnification: 40×. E; Lab: Labyrinth area, Sp: Spongiotrophoblast (basal zone), d: decidua area. Green arrowhead: giant trophoblastic cell. Yellow arrowhead: Glycogen cells. Blue arrow: Glycogen cells around the vessel. Figure E,F,G: H&E staining, Figure H,I,J: Alcian Blue staining. Magnification on E: 10×, Magnification H: 20×, Magnification F,G,I,J: 40×

decidual cells (Figure 3G1) and moderately expressed in giant trophoblastic cells (Figure 3H1). In the vessel wall, moderate uptake was observed (Figure 3I1). The localisation densities are given in Table 1.

In the 10-day stem cell group, fibronectin immune reactivity was low in trophoblastic giant cells (Figure 3A2), whereas immune reactivity was moderate in vessel wall endothelium (Figure 3B2) and decidual cells (Figure 3C2). Immunohistochemical evaluation of MMP-2 showed moderate MMP-2 intensity in trophoblastic giant cells (Figure 3D2) and vascular endothelium (Figure 3E2) and low expression in decidual cells (Figure 3F2). MMP-9 immunolocalisation showed that MMP-9 intensity was low in trophoblastic giant cells (Figure 3G2) and decidual cells (Figure 3I2), whereas it was localised moderately in vascular endothelium (Figure 3H2). However, when the 10-day control and stem cell groups were compared, no significant difference was found in terms of immunolocalisation densities. The localisation densities are given in Table 1.

When the immunoreactivity of fibronectin was examined in the control group on the 21st day of gestation, it was observed that the immunoreactivity of trophoblastic giant cells in the maternal decidua (Figure 4A1) was of moderate intensity and staining was also observed in the subfloor connective tissue. On the other hand, it was observed that labyrinthine

trophoblastic cells contained more than one nucleus and were larger in the transition zone from the attachment zone to the labyrinth layer (Figure 4B1). Fibronectin expression was less intense in the vessel wall (Figure 4C1). When MMP-2 immunoreactivity was analysed, immune reactivity of trophoblastic giant cells in the maternal decidua region of the rat placenta was moderate. The immunoreactivity of spongiotrophoblasts in the junctional zone was weak (Figure 4D1). Immunoreactivity of the vessel wall was moderate (Figure 4E1) and clusters of glycogen-rich cells in the labyrinth layer were detected (Figure 4B1,F1,G1,H1). When MMP-9 immunoreactivity was analysed, it was observed that the immune reactivity of trophoblastic giant cells in the maternal decidua region of the rat placenta was weak. The immunoreactivity of spongiotrophoblasts in the junctional zone was found to be moderate (Figure 4G1). MMP-9 was also localised in the vessel wall and decidua cells at medium density (Figure 4H1). At the same time, immunoreactivity of labyrinthine trophoblastic cells showed moderate intensity (Figure 5I). The localisation densities are given in Table 1.

When the immunoreactivity of fibronectin was examined in the stem cell injected group on the 21st day of gestation, it was observed that ground staining was active in the maternal decidua in the outermost

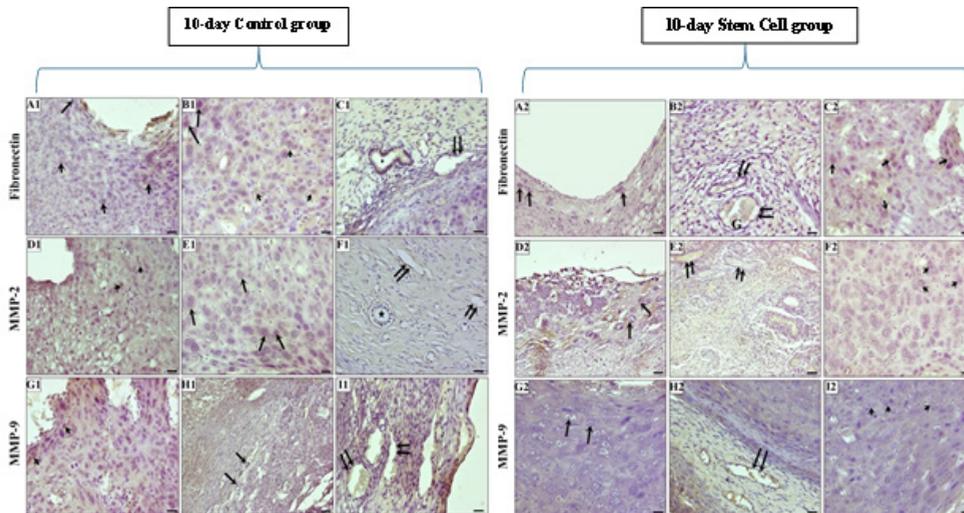


Figure 3. Fibronectin, MMP-2 and MMP-9 immunohistochemical expression images in the implantation site of control and stem cell group rats on day 10. Long arrow: Giant trophoblastic cells, Short arrow: decidual (stromal) cells, Double arrow: vascular wall (endothelium), Star: gland epithelium. Magnification A1,D1,F1,H1,I1 : 20×, Magnification B1,C1,E1,G1 : 40×. Magnification A2,B2,D2,E2,H2,I2 : 20×, Magnification C2,F2,G2 : 40×

layer, in the connecting zone just below it and the labyrinth layer (Figure 4A2). MMP-9 expression was low in trophoblastic cells (Figure 4B2), whereas the expression intensity was moderate in the vessel wall and decidua cells in the labret area (Figure 4C2). MMP-2 expression was found to be moderate in trophoblastic giant cells (Figure 4D2), moderate in labyrinth trophoblastic cells in the labyrinth layer (Figure 4E2) and in the vessel wall (Figure 4E2,F2). MMP-9 expression was moderate in trophoblastic giant cells (Figure 4G2, H2) and spongiotrophoblasts in the junctional zone (Figure 4H2) and weakly expressed in the vessel wall (Figure 4I2). The localisation densities are given in Table 1.

DISCUSSION

Embryo implantation is a critical process involving synchronized molecular and cellular interactions between the blastocyst and the endometrium, culminating in placenta formation and fetal development (3, 22). In rats, blastocyst attachment to the endometrium by late day 4 triggers stromal cell differentiation into decidual cells, forming the implantation chamber at the antimesometrial pole (23, 24). This decidualization process is essential for establishing a receptive uterine environment and

supporting trophoblast invasion.

Fibronectin, a key extracellular matrix (ECM) glycoprotein, mediates cell adhesion, migration, and tissue remodeling during implantation (25). It is highly expressed in human placental tissue and extravillous trophoblasts (26, 27). Studies using fibronectin knockdown models demonstrate that its absence impairs trophoblast migration, vascularization, and embryo implantation, highlighting its critical role at the maternal-fetal interface (27, 28). Additionally, the transition from villous to extravillous trophoblasts is marked by increased expression of fibronectin receptors ($\alpha5\beta1$) and decreased laminin receptors, influencing trophoblast morphology and behavior (29). In our study, fibronectin expression was observed in the uterus and placenta on days 10 and 21 of gestation. Notably, on day 21, fibronectin expression in the labyrinth area and spongiotrophoblasts was significantly higher in the mesenchymal stem cell (MSC)-treated group compared to the control group ($p=0.02$). This suggests that MSC administration may enhance fibronectin-mediated vascularization and ECM remodeling, potentially improving implantation success. These findings warrant further investigation into the signaling pathways, such as Src and integrin-mediated pathways, that may regulate fibronectin

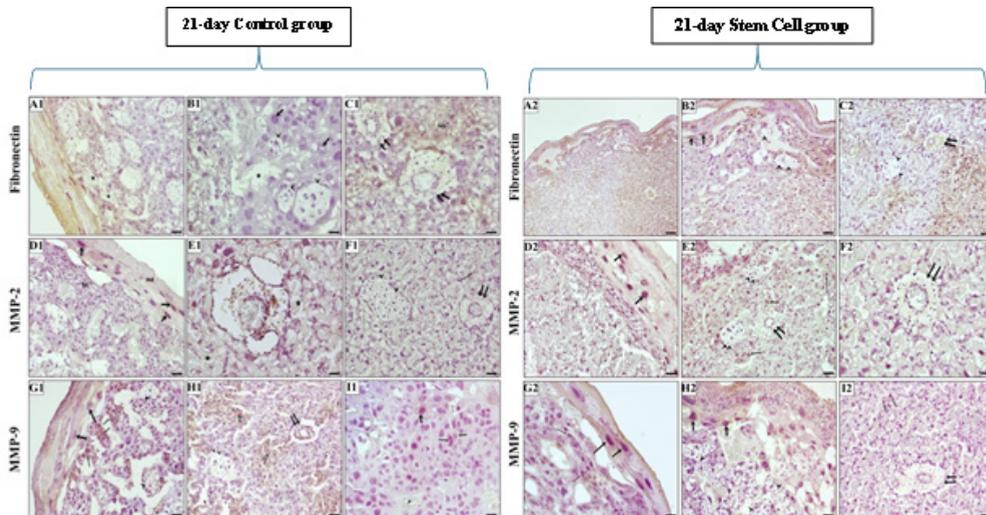


Figure 4. Fibronectin, MMP-2 and MMP-9 immunohistochemical expression images in the implantation site of control and stem cell group rats on day 21. Single long arrow: Trophoblastic giant cell, Double arrow: Vascular endothelium, Short arrow: Spongiotrophoblasts cell, Yellow star: glycogen-rich cell group. Magnification A1,-D1,F1,H11 : 20×, Magnification B1,C1,E1,G1,I1 : 40×. Magnification A2 : 10×, Magnification B2,C2,D2,E2,I2 : 20×, Magnification F2,G2,H2 : 40×.

expression in response to MSC treatment. Matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, are essential for ECM remodeling, vascularization, and trophoblast invasion during pregnancy (30, 31). MMP-9 is critical for trophoblast invasion and decidual development, with its transcripts and proteins detected in trophoblast cells and the mesometrial decidua by mid-pregnancy (31, 32). MMP-2, expressed in stromal cells and primary trophoblast giant cells from day 8 in mice, also promotes trophoblast spreading and invasion (15, 32-35). In our study, MMP-9 was expressed in decidual cells, trophoblastic giant cells, vessel walls, and gland epithelium on day 10 in both control and MSC-treated groups. However, MMP-2 expression was lower in decidual cells in the MSC-treated group. On day 21, MMP-2 expression was minimal in trophoblastic giant cells in both groups, while MMP-9 expression was moderate in trophoblastic giant cells and spongiotrophoblasts in the MSC-treated group but weak in vessel walls. No significant differences in MMP-2 or MMP-9 expression intensity were observed between groups ($p > 0.05$), suggesting that MSC treatment does not significantly alter MMP expression.

Previous studies have reported increased MMP-2 and MMP-9 expression in pregnant rat aorta, uterine artery, and myometrium from the fourth week, facilitating vascular dilation and ECM reorganization, including fibronectin degradation (36). Fibronectin has also been shown to enhance integrin-mediated adhesion and stimulate MMP-2 and MMP-9 production via Src tyrosine kinase and Ras/MAPK/PI3K signaling pathways (37). The significant increase in fibronectin expression in our MSC-treated group on day 21 may be linked to these pathways, necessitating further molecular studies. Additionally, vascular endothelial growth factor (VEGF) regulates MMP-2 and MMP-9 expression, with its inhibition reducing uterine MMP levels and impairing vascular dilation at the implantation site (38). Although vascularization increased in both groups by day 21 in our study, the lack of significant changes in MMP expression suggests that MSCs may preferentially influence fibronectin-mediated processes rather than MMP activity. Future studies should explore the molecular mechanisms, including VEGF and integrin signaling, underlying MSC

effects on ECM dynamics during implantation.

CONCLUSION

Mesenchymal stem cell (MSC) administration significantly increased fibronectin expression in the labyrinth area and spongiotrophoblasts on day 21 of gestation in rats ($p = 0.02$), suggesting a role in enhancing ECM remodeling and vascularization at the implantation site. However, MSC treatment did not significantly alter MMP-2 or MMP-9 expression, indicating that its effects may be specific to fibronectin-mediated processes rather than broad ECM degradation. These findings highlight the potential of MSCs to modulate key ECM components during implantation, which may improve pregnancy outcomes. Further research is needed to elucidate the molecular signaling pathways, such as Src, integrin, and VEGF, that mediate these effects and to explore their therapeutic implications for reproductive success.

Acknowledgements

The authors declare that they have no competing interests.

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COMPARATIVE ANALYSIS OF CBC-DERIVED INFLAMMATORY BIOMARKERS IN OPTIC NEURITIS AND NON-ARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY

Optik Nörit ve Non-Arteritik Anterior İskemik Optik Nöropatide Tam Kan Sayımından Elde Edilen İnflamatuvar Biyobelirteçlerin Karşılaştırmalı Analizi

Meryem Tuba SONMEZ¹, Selda CELIK DULGER², Duygu ARSLAN MEHDİYEV¹, Hikmet SACMACI³, Funda UYSAL TAN¹

ABSTRACT

Objective: Demyelinating optic neuritis (ON) and non-arteritic anterior ischemic optic neuropathy (NAION) represent distinct clinical entities with different pathophysiological mechanisms, yet both are believed to involve systemic inflammatory responses. This study aimed to compare systemic inflammatory indices derived from complete blood count (CBC), including the systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV), in patients with ON and NAION.

Material and Methods: Inflammatory indices (SII, SIRI, PIV, NLR, PLR, and MLR) were calculated using CBC parameters obtained before corticosteroid treatment. A total of 18 patients with demyelinating ON and 25 with NAION were included, along with age- and sex-matched healthy control groups (16 for ON, 11 for NAION). ROC analyses were performed for SII and PIV in the NAION group to assess diagnostic performance.

Results: SII ($p = 0.015$), PIV ($p = 0.004$), and SIRI ($p = 0.001$) were significantly elevated in the NAION group compared to controls. ROC analyses demonstrated AUC values of 70.1% for SII and 73.8% for PIV, indicating moderate diagnostic utility in distinguishing NAION. No significant differences in these indices were observed between the ON group and their respective controls. In the direct comparison between disease groups, patients with NAION exhibited higher SIRI and monocyte levels than those with ON.

Conclusion: The findings support the pathophysiology of NAION, which is associated with systemic inflammation, and suggest that these indices may contribute to the diagnostic process and serve as potential prognostic biomarkers. However, prospective studies with larger samples are needed to clarify the clinical validity of these results.

Keywords: Optic Neuritis; Non-Arteritic Anterior Ischemic Optic Neuropathy; Complete Blood Count; Systemic Inflammation; SII; SIRI; PIV

ÖZET

Amaç: Demiyelinizan optik nörit (ON) ve non-arteritik anterior iskemik optik nöropati (NAION), farklı patofizyolojik mekanizmalara sahip olsalar da her iki durumda da sistemik inflamatuvar yanıtın rol oynadığı düşünülmektedir. Bu çalışmada, tam kan sayımından (CBC) türetilen sistemik inflamasyon indekslerinin (SII, SIRI, PIV) ON ve NAION alt gruplarında karşılaştırmalı olarak değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Kortikosteroid tedavisi öncesinde ölçülen hemogram parametrelerine göre hesaplanan SII, SIRI, PIV, NLR, PLR ve MLR değerleri; 18 demiyelinizan ON ve 25 NAION hastasında yaş ve cinsiyet açısından eşleştirilmiş sırasıyla 16 ve 11 sağlıklı kontrol grupları ile karşılaştırıldı. Ayrıca NAION grubunda SII ve PIV için ROC analizleri gerçekleştirildi.

Bulgular: NAION grubunda SII ($p = 0,015$), PIV ($p = 0,004$) ve SIRI ($p = 0,001$) değerleri, kontrol grubuna kıyasla anlamlı şekilde yüksekti. ROC analizlerinde SII için AUC %70,1, PIV için ise %73,8 olarak bulundu; bu değerler NAION'u ayırt etmede orta düzeyde tanısal performansla işaret etmektedir. Demiyelinizan ON grubunda ise bu indeksler açısından kontrol grubuna göre anlamlı fark gözlenmedi. NAION ile ON hastaları karşılaştırıldığında, NAION grubunda SIRI ve monosit düzeylerinin daha yüksek olduğu saptandı.

Sonuç: Bulgular, NAION'un sistemik inflamasyon ile ilişkili fizyopatolojisini desteklemekte ve bu indekslerin tanı sürecine katkı sağlayabileceği ve potansiyel prognostik biyobelirteç olabileceğini düşündürmektedir. Ancak bu sonuçların klinik geçerliliğinin netleşmesi için daha büyük örneklerle yapılacak prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Optik Nörit; Non-Arteritik Anterior İskemik Optik Nöropati; Tam Kan Sayımı; Sistemik İnflamasyon; SII; SIRI; PIV

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INTRODUCTION

Optic neuropathies encompass a spectrum of disorders characterized by structural or functional impairment of the optic nerve, typically presenting with acute or subacute visual loss. Among these conditions, demyelinating optic neuritis (ON) and non-arteritic anterior ischemic optic neuropathy (NAION) are the most encountered etiologies in clinical practice (1, 2). While their characteristic clinical profiles and age distributions often facilitate differentiation, diagnostic uncertainty may arise in the early stages, particularly in younger individuals with vascular risk factors or atypical presentations (1, 2). In such cases, careful clinical evaluation becomes essential. Notably, NAION is associated with a poorer visual prognosis and generally shows minimal responsiveness to corticosteroid treatment, which underscores the importance of timely and accurate distinction between these two entities.

The complete blood count (CBC) is a low-cost and widely accessible laboratory test that has been traditionally used for hematologic evaluation. More recently, its clinical relevance has expanded to include the assessment of systemic inflammation. Inflammatory indices derived from CBC, such as the neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), monocyte to lymphocyte ratio (MLR), systemic immune inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune inflammation value (PIV), have been investigated as potential diagnostic and prognostic biomarkers in a wide array of diseases, including cardiovascular, autoimmune, and neurological conditions (3-8). Among these indices, SII and PIV have demonstrated particularly strong associations with disease activity and adverse outcomes in both systemic and neuroinflammatory disorders.

The immunopathogenesis of demyelinating optic neuritis is mediated by immune cell infiltration and cytokine-driven inflammation, which may also be reflected in peripheral blood cell profiles (9). During the acute phase, neutrophilia accompanied by relative lymphopenia is commonly observed, leading to measurable changes in systemic inflammatory indices. In contrast, NAION, although classically regarded as a microvascular ischemic event, is increasingly viewed as

a condition with an underlying component of chronic low-grade inflammation. This evolving perspective stems from its strong association with systemic comorbidities such as atherosclerosis, diabetes mellitus, and dyslipidemia, all of which are known to modulate peripheral inflammatory markers (3, 10-13). Taken together, these findings suggest that both ON and NAION may involve systemic immune activation, particularly during the acute phase, which can be assessed quantitatively through blood-based indices. Although several studies have explored conventional indices such as NLR and PLR in various forms of optic neuropathy, to the best of our knowledge, PIV has not yet been examined in the context of either ON or NAION. This represents a notable gap in current literature. As PIV integrates neutrophils, monocytes, platelets, and lymphocytes into a single composite metric, it may provide a more holistic reflection of global immune activation compared to traditional indices.

Despite the distinct pathophysiological mechanisms of ON and NAION, both conditions may exhibit systemic immune responses that are quantifiable via CBC-derived biomarkers. However, comparative studies evaluating these indices during the acute phase of optic neuropathies remain limited. Generating such data could be particularly valuable in guiding early differential diagnosis, especially in settings where advanced neuroimaging or optical coherence tomography (OCT) is not immediately accessible. Moreover, a better understanding of these biomarkers may contribute to a more comprehensive view of the systemic inflammatory landscape underlying neuro-ophthalmologic disorders.

The present study aims to evaluate and compare systemic inflammatory indices derived from CBC in patients presenting with acute demyelinating ON and NAION, with specific focus on SII and PIV. To the best of our knowledge, this is the first study to investigate PIV in the context of optic neuropathies, offering a novel perspective on systemic inflammation in neuro-ophthalmology. In our study, PIV was evaluated for the first time in ON and NAION as an additional original contribution to the literature. Furthermore, we examine the potential discriminatory value of these indices in differentiating ON from NAION, particularly in cases

with overlapping clinical features at presentation.

MATERIALS AND METHODS

This retrospective observational study was conducted at the neurology and neuro-ophthalmology outpatient clinics of a tertiary care university hospital between January 2023 and December 2024. Ethical approval (AEŞH-EK1-2023-498) was obtained from the institutional review board prior to data collection, and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

The study population consisted of three groups: patients with demyelinating optic neuritis (ON), patients with non-arteritic anterior ischemic optic neuropathy (NAION), and neurologically healthy controls matched for age and sex. Patients in the demyelinating ON group were required to be 18 years of age or older, present with acute visual loss consistent with optic neuritis, and have diagnostic confirmation based on clinical evaluation supported by cranial and/or cervical magnetic resonance imaging (MRI), oligoclonal band (OCB) analysis, and serum anti-myelin oligodendrocyte glycoprotein (MOG) or anti-aquaporin-4 (AQP4) antibody testing. To ensure that inflammatory markers were not confounded by therapeutic interventions, blood samples for complete blood count (CBC) were obtained within 72 hours of symptom onset and prior to the administration of corticosteroids. Additionally, patients who had received corticosteroid therapy within the past three months or were undergoing disease-modifying treatment (DMT) at the time of the attack were excluded. Similarly, patients in the NAION group were required to be 18 years or older and have a clinical diagnosis of NAION confirmed by a neuro-ophthalmology specialist. The diagnosis was based on typical clinical features and the exclusion of arteritic etiologies such as temporal arteritis. CBC testing had to be performed within 72 hours of symptom onset and before the initiation of any medical treatment. NAION patients with arteritic pathology, vasculitis, malignancy, chronic kidney disease, or recent corticosteroid use were excluded.

For comparative analyses, a total of 16 patients with demyelinating ON (4 males and 12 females) were selected, each matched by age (± 1 year) and sex with individuals in the control group. Similarly, 11

patients in the NAION group (4 females and 7 males) were included based on age- and sex-matching with corresponding controls. Notably, one male and one female participant were shared across both control groups.

The healthy control group consisted of individuals without neurological or systemic disease who had applied to the neurology department for purposes unrelated to illness, such as employment screening, firearm license evaluations, or immigration processes. These individuals were included if they had normal CBC parameters and could be matched with the patient groups by age (± 1 years) and sex. All demographic and clinical data were retrospectively obtained from the hospital's electronic health record system. Extracted variables included age, sex, body mass index (BMI), medical comorbidities such as hypertension, diabetes mellitus, dyslipidemia, and hypothyroidism (provided the condition had been stable and under treatment for at least one year), current medications, lifestyle habits, date of symptom onset, and date of blood collection.

Patients were excluded from the study if they had active systemic infection at the time of evaluation, a current or past history of malignancy, hematologic disorders (e.g., leukemia, clinically significant anemia or thrombocytopenia), chronic autoimmune or inflammatory diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease), untreated or recently adjusted hypothyroidism (diagnosed or modified within the previous 12 months), advanced renal or hepatic failure, or if they were pregnant or within the postpartum period. Additionally, any use of corticosteroids within the previous three months was an exclusion criterion. Initially, 29 patients diagnosed with demyelinating ON were screened. Of these, 11 were excluded due to concurrent disease-modifying treatment (n=4), active infection (n=3), recently diagnosed or medication-adjusted hypothyroidism (n=2), and hematological abnormalities (n=2). In the NAION group, 38 patients were initially evaluated, but 13 were excluded due to age over 68 years with no suitable age- and sex-matched control (n=5), malignancy (n=2), chronic kidney disease (n=2), or active infection (n=4). Ultimately, 18 patients with demyelinating ON and 25 with NAION were included in the final analysis.

Based on CBC results, several inflammatory indices were calculated using absolute cell counts. These included the systemic immune-inflammation index (SII), calculated as (neutrophils \times platelets) / lymphocytes; the systemic inflammation response index (SIRI), calculated as (neutrophils \times monocytes) / lymphocytes; and the pan-immune-inflammation value (PIV), calculated as (neutrophils \times platelets \times monocytes) / lymphocytes. Additionally, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) were computed. All calculations were validated for consistency, and patients with incomplete data or laboratory artifacts were excluded from the analysis.

Interpretations are based on previously published studies evaluating these indices in neurological and systemic inflammatory conditions as stated below: (4, 5, 8)

- 1- NLR- Neutrophil count / Lymphocyte count- Indicator of acute systemic inflammation
- 2- PLR- Platelet count / Lymphocyte count- Marker of platelet-driven inflammatory response
- 3- MLR- Monocyte count / Lymphocyte count- Reflects monocytic immune activity
- 4- SII- (Neutrophil \times Platelet) / Lymphocyte- Integrated index of neutrophilic and platelet activity
- 5- SIRI- (Neutrophil \times Monocyte) / Lymphocyte- Comprehensive index of innate immune response
- 6- PIV- (Neutrophil \times Platelet \times Monocyte) / Lymphocyte- Composite index reflecting global immune activation

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for MacOS, version 30.0 (IBM Corp., Armonk, NY, USA). All data obtained from this study were tested for goodness of fit using the Shapiro–Wilk test. Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean \pm standard deviation, median, and range (minimum–maximum) for continuous variables. Between-group comparisons for non-normally distributed continuous variables were conducted using the Mann–Whitney U test. Categorical variables were compared using Pearson’s chi-square test or Fisher’s exact test, as appropriate. Receiver operating characteristic (ROC) analysis was employed to assess the discriminatory

performance of selected indices for NAION, and the area under the curve (AUC) was calculated. A p-value $<$ 0.05 was considered statistically significant.

RESULTS

The distribution of demographic and clinical characteristics of patients diagnosed with ON and healthy controls is given in Table 1. When the table was examined, a statistically significant difference was observed between the groups in terms of smoking, alcohol use and comorbidities, while no statistically significant difference was observed between the groups in other demographic and clinical findings.

The distribution of demographic and clinical characteristics of patients diagnosed with NAION and healthy controls is given in Table 2. When the table is examined, statistically significant differences were observed between the groups in terms of smoking, comorbidities, drug use rates, and platelet, neutrophil, monocyte, MLR, SII, PIV and SIRI measurements ($p <$ 0.05, all of them). In all laboratory measurements where significant differences were observed, the measurement values of NAION patients were found to be higher than the control group.

The ROC curve results for examining the differential effect of SII and PIV measurements according to the development of NAION in patients are given in Table 3. For SII, the area under the curve was found to be 70.1%, and the cut-off value was determined to be 641.4. For PIV, the area under the curve was found to be 73.8%, and the cut-off value was determined to be 323.3. The area under the curve shows the statistical significance of the discrimination ability of the diagnostic test (Figure 1). Since the diagnostic test evaluated in our study was the presence of NAION, it was determined that the value found for SII and PIV had a moderate discrimination ability (70%-80%).

The distribution of laboratory measurements of patients with ON and patients with NAION are given in Table 4. When the table is examined, statistically significant differences were observed in monocyte, MLR and SIRI measurements between the two disease groups. In all measurements where significant differences were observed, the measurement values of the NAION group were found to be higher than the ON group ($p <$ 0.05).

Table 1. Distribution of demographic and clinical characteristics of patients with demyelinating optic neuritis (ON) and the control group.

Variables	Control ON (n=16)	ON (n=18)	p-value
Gender (n, %)			1.000
Male / Female	4 (21) / 15 (78)	4 (22) / 14 (78)	
Age (years)			0.893
Mean ± SD	29.1 ± 6.7	28.8 ± 6.8	
Median (Min-Max)	31 (19-39)	30.5 (19-39)	
How many attacks?			NA
1		14 (78)	
2		2 (11)	
3		2 (11)	
Cigarette	0 (0)	9 (50)	<0.001
Alcohol	0 (0)	0 (0)	NA
Additional disease	0 (0)	4 (22)	0.046
Hypothyroidism	-	3 (75)	
PCOS	-	1 (25)	
Medication	0 (0)	3 (17)	0.105
Thyroid medication	-	3 (100)	
ON type			NA
MS	-	16 (89)	
The others	-	2 (11)	
Attack absolute platelet (n, 10 ³ µL)			0.408
Mean ± SD	270 ± 45	280 ± 47	
Median (Min-Max)	261 (202-343)	268 (223-375)	
Attack absolute neutrophil (n, 10 ³ µL)			0.081
Mean ± SD	4.1 ± 1	5 ± 1.9	
Median (Min-Max)	4 (2.5-5.9)	4.9 (2.2-10.5)	
Attack absolute lymphocyte (n, 10 ³ µL)			0.869
Mean ± SD	2.5 ± 0.8	2.5 ± 0.7	
Median (Min-Max)	2.7 (1.5-4.6)	2.3 (1.6-3.8)	
Attack absolute monocyte (n, 10 ³ µL)			0.425
Mean ± SD	0.6 ± 0.1	0.5 ± 0.2	
Median (Min-Max)	0.6 (0.4-0.8)	0.5 (0.2-0.9)	
Neutrophil/ lymphocyte ratio			0.327
Mean ± SD	1.7 ± 0.5	2.1 ± 0.9	
Median (Min-Max)	1.7 (0.9-2.3)	1.9 (1.1-4.4)	
Platelet/ lymphocyte ratio			0.893
Mean ± SD	115 ± 30	118 ± 38	
Median (Min-Max)	128 (61-153)	115 (72-208)	
Monocyte/ lymphocyte ratio			0.142
Mean ± SD	0.2 ± 0.1	0.2 ± 0.1	
Median (Min-Max)	0.3 (0.2-0.3)	0.2 (0.1-0.5)	
Attack SII			0.425
Mean ± SD	458 ± 125	599 ± 343	
Median (Min-Max)	496 (220-638)	486 (268-1616)	
Attack PIV			0.964
Mean ± SD	261 ± 92	288 ± 151	
Median (Min-Max)	223 (106-390)	253 (88-660)	
SIRI			0.964
Mean ± SD	1 ± 0.4	1 ± 0.5	
Median (Min-Max)	1 (0.4-1.5)	1 (0.4-2.5)	

SD: standard deviation, PCOS: Polycystic ovary syndrome, MS: Multiple Sclerosis, SII: Systemic immune-inflammation index, PIV: (Neutrophils × platelets × monocytes) / lymphocytes, SIRI: Neutrophils × monocytes / lymphocytes. Results are expressed as mean ± standard deviation, median (min-max) and; p< 0.05 is statistical significant, min:minimum, max: maximum

Table 2. Distribution of demographic and clinical characteristics of patients with and without non-arteritic anterior ischemic optic neuropathy (NAION)

Variables	Control NAION (n=11)	NAION (n=25)	p-value
Gender, male (n,%)	17 (68) / 8 (32)	17 (68) / 8 (32)	1.000
Age (years) (mean ± SD)	57 ± 8	57 ± 8	1.000
Cigarette	0 (0)	10 (40)	<0.001
Alcohol	0 (0)	4 (16)	0.110
Additional disease DM, HT, Sleep apnea, Asthma, Hyperlipidemia, Heart disease, Hypothyroidism	0 (0)	21 (84)	<0.001
Medication	0 (0)	20 (80)	<0.001
Attack absolute platelet (n, 10 ³ µL) Mean ± SD	245 ± 28	285 ± 59	0.011
Median (Min-Max)	242 (206-343)	290 (165-374)	
Attack absolute neutrophil (n, 10 ³ µL) Mean ± SD	4.4 ± 0.8	5.5 ± 1.8	0.012
Median (Min-Max)	4.3 (3.5-5.7)	5 (2.5-9.4)	
Attack absolute lymphocyte (n, 10 ³ µL) Mean ± SD	2.2 ± 0.4	2.4 ± 0.6	0.484
Median (Min-Max)	2.2 (1.6-3.4)	2.3 (1.6-4.1)	
Attack absolute monocyte (n, 10 ³ µL) Mean ± SD	0.5 ± 0,1	0.7 ± 0.3	<0.001
Median (Min-Max)	0.5 (0.4-0.6)	0.6 (0.2-1.7)	
Neutrophil/ lymphocyte ratio Mean ± SD	2 ± 0.4	2.4 ± 0.9	0.252
Median (Min-Max)	2.1 (1-2.6)	2.2 (0.9-4.2)	
Platelet/ lymphocyte ratio			0.290
Mean ± SD	112 ± 12.8	122 ± 32.6	
Median (Min-Max)	113 (83-129)	125 (46-184)	
Monocyte/ lymphocyte ratio			0.041
Mean ± SD	0.2 ± 0	0.3 ± 0.1	
Median (Min-Max)	0.2 (0.2-0.3)	0.2 (0.1-0.7)	
Attack SII			0.015
Mean±SD	494 ± 98	686 ± 325	
Median (Min-Max)	513 (290-630)	653 (171-1386)	
Attack PIV			0.004
Mean ± SD	240 ± 52	494 ± 451	
Median (Min-Max)	232 (157-315)	427 (61-2253)	
SIRI			0.001
Mean ± SD	1 ± 0.2	1.7 ± 1.3	
Median (Min-Max)	1.1 (0.6-1.2)	1.3 (0.3-7)	

SD: standard deviation, DM: Diabetes Mellitus, HT: Hypertension, SII: Systemic immune-inflammation index, PIV: (Neutrophils × platelets × monocytes) / Lymphocytes, SIRI: Neutrophils × monocytes / lymphocytes. Results are expressed as mean ± standard deviation, median (min-max) and; p< 0.05 is statistical significant, min:minimum, max: maximum

Table 3. Roc analysis results regarding the measurement parameters of non-arteritic anterior ischemic optic neuropathy.

Risk Factor	AUC (%95 GA)	Cut-off	p-value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
SII	0.701 (0.542-0.859)	>617.4	0.013	64.0	88.0	84.2	71.0
PIV	0.738 (0.576-0.899)	>314.8	0.004	64.0	100.0	100.0	73.5

AUC: Area Under Curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value, SII: Systemic immune-inflammation index, PIV: (Neutrophils × platelets × monocytes) / lymphocytes

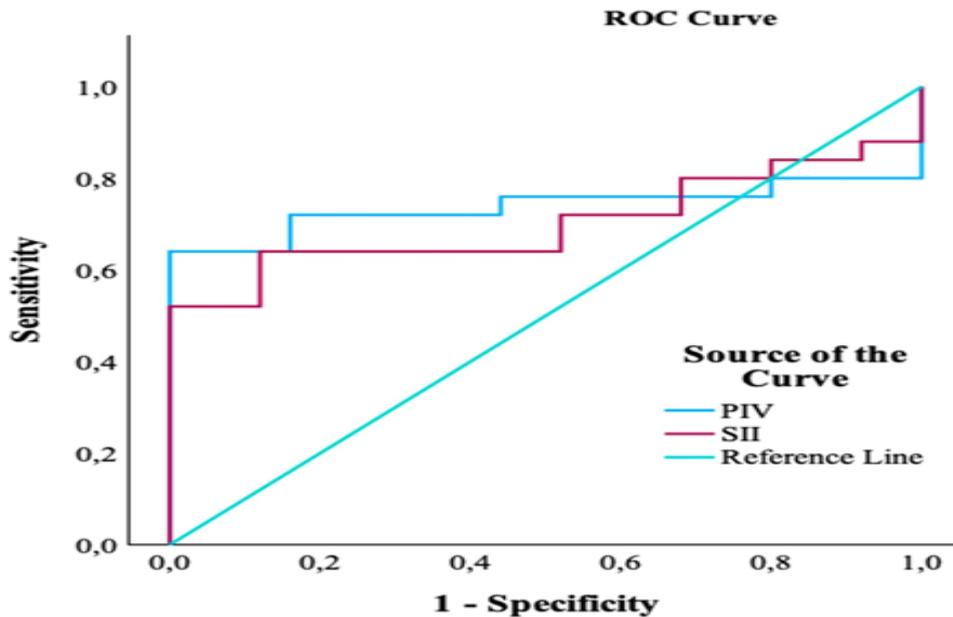


Figure 1. ROC curve of measurement parameters in Non-arteritic anterior ischemic optic neuropathy (NAION) development

To further illustrate individual variability and highlight the range of inflammatory responses, six patients with complete data were selected for descriptive comparison. This subset included four individuals with MS-associated ON and two individuals diagnosed with NAION. As shown in Table 5, the NAION cases exhibited higher values across most inflammatory indices, including SII, PIV, and SIRI, supporting the broader group-level trends observed in this study.

DISCUSSION

In this study, a comparative analysis of hemogram-derived systemic inflammatory indices was performed in patients diagnosed with ON and NAION, revealing significant indices differences between the two patient groups. In the NAION group, the composite inflammatory parameters SII (p= 0.015), PIV (p= 0.004), and SIRI (p= 0.001) were statistically significantly higher compared to age- and sex-matched healthy controls. In contrast, no significant differences were

found in the demyelinating ON group compared to the control group for these indices. Furthermore, ROC analyses performed for SII and PIV in NAION patients yielded AUC values of 70.1% and 73.8%, respectively, suggesting that these parameters may have moderate diagnostic performance in distinguishing NAION. These findings suggest that CBC-based inflammatory markers are potential biomarkers that should be considered not only in terms of accessibility and cost but also in terms of diagnostic value.

While the use of inflammatory indices for diagnostic and prognostic purposes in optic neuropathies has received increasing interest in recent years, the current literature still provides limited data on this topic. The majority of existing studies have focused on traditional ratios such as NLR and PLR, while systematic evaluation of more complex and composite formulas have been rarely included. Some studies have shown that NLR may be associated with disease activity, particularly in MS and ON patients (9). However, evidence regarding

Table 4. Distribution of measurement values in patients with non-arteritic anterior ischemic optic neuropathy (NAION) and demyelinating optic neuritis (ON)

Variables	ON (n=18)	NAION (n=25)	p-value
Attack absolute platelet (n)			0.631
Mean ± SD	280 ± 47	285 ± 59	
Median (Min-Max)	268 (223-375)	290 (165-374)	
Attack absolute neutrophil (n)			0.416
Mean ± SD	5 ± 1.9	5.5 ± 1.8	
Median (Min-Max)	4.9 (2.2-10.5)	5 (2.5-9.4)	
Attack absolute lymphocyte (n)			0.676
Mean ± SD	2.5 ± 0.7	2.4 ± 0.6	
Median (Min-Max)	2.3 (1.6-3.8)	2.3 (1.6-4.1)	
Attack absolute monocyte (n)			0.006
Mean ± SD	0.5 ± 0.2	0.7 ± 0.3	
Median (Min-Max)	0.5 (0.2-0.9)	0.6 (0.2-1.7)	
Neutrophil/ lymphocyte ratio			0.325
Mean ± SD	2.1 ± 0.9	2.4 ± 0.9	
Median (Min-Max)	1.9 (1.1-4.4)	2.2 (0.9-4.2)	
Platelet/ lymphocyte ratio			0.431
Mean ± SD	118 ± 38	122 ± 33	
Median (Min-Max)	115 (72-208)	125 (46-184)	
Monocyte/ lymphocyte ratio			0.012
Mean ± SD	0,2 ± 0,1	0,3 ± 0,1	
Median (Min-Max)	0,2 (0,1-0,5)	0,2 (0,1-0,7)	
Attack SII			0.301
Mean±SD	599 ± 343	686 ± 325	
Median (Min-Max)	486 (268-1616)	653 (171-1386)	
Attack PIV			0.061
Mean ± SD	288 ± 151	494 ± 451	
Median (Min-Max)	253 (88-660)	427 (61-2253)	
SIRI			0.014
Mean ± SD	1 ± 0.5	1.7 ± 1.3	
Median (Min-Max)	1 (0.4-2.5)	1.3 (0.3-7)	

SD: standard deviation, SII: Systemic immune-inflammation index, PIW: (Neutrophils × platelets) / lymphocytes, SIRI: Neutrophils × monocytes / lymphocytes. Results are expressed as mean ± standard deviation, median (min-max) and; p<0.05 is statistical significant, min:minimum, max: maximum

the diagnostic or prognostic value of inflammatory biomarkers in NAION-specific studies is still limited. Koçak et al. reported that neutrophil, platelet, NLR, and SII levels were significantly higher in NAION patients than in healthy controls (10). However, this study did not include more complex and multicomponent inflammatory indices such as PIV and SIRI. Similarly, the diagnostic or prognostic potential of these composite parameters in patients with ON has not been systematically addressed to date. Unlike the limited number of studies evaluating traditional parameters such as NLR and PLR, formulas such as SII, SIRI, and PIV, which also include monocytes, offer the

opportunity to assess systemic inflammation more holistically because they reflect synergistic interactions and multiplier effects among inflammatory cells. Some preliminary findings regarding the prognostic value of these multicomponent indices in vascular and neuroinflammatory diseases have been reported in the literature (3, 8, 12). However, there is no comprehensive study directly comparing these parameters in specific optic neuropathy subgroups such as NAION or MS-related optic neuritis. In this context, our study contributes significantly to the literature by being the first to examine these indices within the same methodological framework, encompassing both

Table 5. Distribution of optic neuritis (ON) and Non-arteritic anterior ischemic optic neuropathy (NAION) patients with similar age distribution according to hemogram and demographic characteristics

Variables	Patients with ON diagnosis				Patients diagnosed with NAION	
	Female	Female	Female	Male	Male	Female
Gender	Female	Female	Female	Male	Male	Female
Age (years)	35	37	36	36	36	36
Smoking	Yes	None	Yes	Yes	None	None
Alcohol	None	None	None	None	None	None
Comorbidity	None	None	None	None	Yes	Yes
Drug	Yok	None	None	None	Yes	Yes
Attack absolute platelet 10 ³ µL	298.00	261.00	272.00	266.00	362.00	261.00
Attack absolute neutrophil 10 ³ µL	4.03	5.02	7.03	4.36	5.19	4.31
Attack absolute lymphocyte 10 ³ µL	3.47	1.94	3.63	3.72	2.58	1.80
Attack absolute monocyte 10 ³ µL	0.48	0.49	0.48	0.65	0.62	0.57
Neutrophil/lymphocyte ratio	1.16	2.59	1.94	1.17	2.01	2.39
Platelet/lymphocyte ratio	85.88	134.54	74.93	71.51	140.31	145
Monocyte/lymphocyte ratio	0.14	0.25	0.13	0.17	0.24	0.32
Attack SII	346.00	675.00	526.76	311.76	727.13	625.83
Attack PIV	166.12	331.00	252.84	207.67	451.45	355.57
SIRI	0.56	1.27	0.93	0.76	1.25	1.36

SII: Systemic immune-inflammation index, PIW: (Neutrophils × platelets × monocytes) / lymphocytes, SIRI: Neutrophils × monocytes / lymphocytes

patient groups.

Neutrophils, lymphocytes, platelets, and monocytes, which form the basis of these composite formulations, play various roles at different stages of the inflammatory response. Neutrophils are the first responders of the innate immune system and play a decisive role in the initiation of acute inflammation through their ability to release cytokines and migrate into tissues (14). Lymphocytes, on the other hand, serve as key cells of the adaptive immune response; therefore, the neutrophil/ lymphocyte ratio is considered an important parameter reflecting the balance between the innate and adaptive immune systems (15). Platelets play an active role not only in hemostatic processes but also in inflammatory signaling in the vascular endothelium and interaction with immune cells (16). Monocytes, in addition to serving as proinflammatory cells in the circulation, play a key role in directing the immune response through antigen presentation and cytokine production, differentiating into macrophages or dendritic cells upon migration into tissue (17).

SII is a composite index that evaluates neutrophil and platelet activity together, balanced by lymphocytes. SIRI reflects the innate inflammatory burden derived

from neutrophils and monocytes, normalized by lymphocytes. PIV is a multicomponent index that combines neutrophil, platelet, and monocyte activity and normalized by lymphocytes; theoretically, it is the most complex formula capable of reflecting both the intensity and extent of inflammation (18). These multicomponent indices stand out as more sensitive and holistic biomarkers than classic ratios in some clinical settings because they consider not only cell ratios but also the potential multiplier effect of interactions between inflammatory cells (19).

Because the two patient groups exhibited fundamentally different demographic characteristics in terms of age and sex, the ON and NAION groups were not directly compared; instead, each was evaluated separately with an age- and sex-matched control group. While this approach does not allow for a direct statistical comparison between the two disease groups, the findings revealed some striking differences. Specifically, the systemic inflammatory response exhibited by the NAION group compared to the control group was significantly higher in terms of composite indices such as SII, PIV, and SIRI, and was more pronounced than the response observed in

the demyelinating ON group. This suggests that the underlying pathophysiological processes in ON and NAION operate differently. The baseline inflammatory burden present in NAION due to systemic vascular risk factors such as atherosclerosis, hypertension, and diabetes, combined with an acute ischemic event, may produce a more pronounced inflammatory profile in the peripheral blood. In contrast, demyelinating ON associated with MS is characterized by a more localized immune response confined to the central nervous system. Table 5, which presents individual data from a small number of ON and NAION patients matched for age and sex, supports this difference mathematically. In particular, the NAION group exhibited higher values compared to the ON group for composite inflammatory indices such as SII, PIV, and SIRI, demonstrating a clear distinction in the pathophysiological basis of these two optic neuropathies.

Although prognosis was not directly assessed in this study, it is well known in the literature that NAION may have worse outcomes compared to demyelinating ON (20). Based on this known prognostic difference, it can be suggested that the higher systemic inflammatory indices found in NAION patients may be not only diagnostic but also a prognostic biological indicator. Composite indices, such as PIV and SII, may be more sensitive in measuring the peripheral manifestations of the immune response associated with tissue damage because they reflect not only the cellular distribution but also the intensity of the inflammatory burden. Therefore, a potential relationship between the intensity of the inflammatory response and the severity of the clinical course is considered. However, prospective, long-term studies with visual outcomes are necessary to confirm this hypothesis.

One of the major strengths of this study is that CBC-derived indices, potential biomarkers for assessing the peripheral inflammatory response, were measured only in the acute phase and before systemic treatment. The exclusion of corticosteroid and disease-modifying therapies provided a valuable methodological contribution by reflecting the natural history of systemic inflammation. Furthermore, the use of age- and sex-matched control groups minimized potential demographic biases and allowed the NAION and ON groups to be assessed with their own physiological

reference values.

However, some limitations of the study should not be overlooked. First, the relatively small number of patients limits statistical power, particularly in subgroup analyses. Furthermore, the study is retrospective and lacks long-term follow-up data; therefore, potential relationships between inflammatory indices and clinical prognosis remain interpretable. Furthermore, the exclusion of classical inflammatory markers such as CRP, erythrocyte sedimentation rate, and homocysteine prevented comparison of CBC-derived indices with other biomarkers.

CONCLUSION

The findings of this study suggest that systemic inflammatory indices derived from complete blood counts may aid the clinical course of optic neuropathy subtypes, such as NAION and MS-associated optic neuritis, which can be difficult to differentiate. The significantly elevated values of composite indices such as SII, PIV, and SIRI in NAION patients support a clinical picture that is not only statistically significant but also pathophysiologically significant. It is suggested that these parameters, in addition to their contribution to the diagnostic process, can also be considered biomarkers for disease prognosis. CBC-derived indices can contribute to differential diagnosis, especially in centers where advanced examination opportunities are limited, due to their low cost and easy applicability. However, prospective and long-term follow-up studies with larger samples are needed to clarify the clinical validity of these findings and understand their potential prognostic role.

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DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH NEUROMUSCULAR DISEASES IN A REHABILITATION CLINIC OF A TERTIARY HEALTH CENTER: 5-YEAR RESULTS

Üçüncü Basamak Bir Sağlık Merkezinin Rehabilitasyon Kliniğinde Nöromusküler Hastalıklar Nedeniyle Takip Edilen Hastaların Demografik ve Klinik Özellikleri: 5 Yıllık Sonuçları

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ABSTRACT

Objective: We aimed to investigate the demographic and clinical characteristics of patients who received inpatient physical therapy and rehabilitation programs for neuromuscular diseases (NMDs) in a tertiary health center.

Material and Methods: This retrospective study examined patients who received a inpatient physical therapy program in the NMDs clinic between March 2019 and March 2024. Sociodemographic data, body mass index, muscle strength, sensory examination, presence of atrophy, presence of involuntary movements, spasticity examination, presence of dysphagia and dysarthria, history of osteoporosis, respiratory system examination findings and functional status were recorded.

Results: The highest number of patients was in the neuropathy group, followed by motor neuron disease (MND) and myopathy groups (n=146, 37, 21, respectively). The mean age was significantly lower in the myopathy group compared to the MND and neuropathy groups (p<0.001). History of fracture (p<0.001) and frequency of osteoporosis (p=0.016) were significantly higher in the MND group than in the neuropathy and myopathy groups. Upper extremity proximal muscle weakness was significantly higher in the myopathy group than in other groups (p=0.041). Sensory deficits were significantly higher in the neuropathy group compared to the MND and myopathy groups (p<0.001). Independent ambulation ratio was statistically significantly lower in the MND group than in the other two groups (p<0.01).

Conclusion: MNDs are noted for fracture risk and difficulty in ambulation, while myopathies are marked by muscle weakness and neuropathies by sensory deficits.

Keywords: Motor Neuron Diseases; Neuropathies; Myopathies; Rehabilitation; Clinical Features

ÖZET

Amaç: Üçüncü basamak bir sağlık merkezinde nöromusküler hastalıklar (NMH) nedeniyle yatarak fizik tedavi ve rehabilitasyon programı alan hastaların demografik ve klinik özelliklerini incelemeyi amaçladık.

Gereç ve Yöntemler: Çalışmamız NMH Kliniğinde 2019 Mart ve 2025 Mart ayları arasında yatarak fizik tedavi programı almış hastaların incelendiği retrospektif bir çalışmadır. Hastaların sosyodemografik verileri, vücut kitle indeksi, kas gücü, duyu muayenesi, atrofi varlığı, alt ekstremitte eşitsizliği, spastisite muayenesi, disfaji ve dizartri varlığı, osteoporoz öyküsü, solunum sistemi muayenesi ve fonksiyonel durumları kaydedildi.

Bulgular: Çalışmamıza dahil edilen 204 hastaların dağılımına bakıldığında en fazla hasta sayısı nöropati grubundaydı, motor nöron hastalığı (MNH) ve miyopati grubu sırasıyla takip etmekteydi (sırasıyla n=146, 37, 21). Miyopati grubunda yaş ortalaması MNH ve nöropati grubuna göre istatistiksel anlamlı düşüktü (p<0,001). MNH grubunda geçmişte gelişen kırık öyküsü (p<0,001) ve osteoporoz sıklığı (p=0,016), nöropati ve miyopati grubuna göre istatistiksel anlamlı yüksekti. Üst ekstremitte proksimal kas güçsüzlüğü miyopati grubunda diğer gruplara göre istatistiksel anlamlı yüksekti (p=0,041). Nöropati grubunda MNH ve miyopati grubuna göre duyu kayıplar istatistiksel anlamlı yüksekti (p<0,001). Bağımsız ambulasyon MNH grubunda diğer iki gruba göre istatistiksel anlamlı düşüktü (p<0,01).

Sonuç: NMH alt gruplarını karşılaştırdığımız bu çalışmada MNH grubu kırık riski ve ambulasyon zorluğu ile öne çıkarken miyopatiler kas güçsüzlüğü ve nöropatiler de duyu kayıplarıyla öne çıkmaktadır.

Anahtar Kelimeler: Motor Nöron Hastalıkları; Nöropatiler; Miyopatiler; Rehabilitasyon; Klinik Özellikler

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INTRODUCTION

Neuromuscular diseases (NMDs) are a group of diseases, which are genetically inherited or acquired, caused by an abnormality in the anterior horn motor cells, peripheral nerves, neuromuscular junction, or muscles (1). The damage in NMDs can be in the cell body, axons, Schwann cells, neuromuscular junction, or muscles. If the damage is in the neuron, the condition is called neuronopathy; if the damage is in the anterior horn motor neuron, it is called motor neuron disease (MND); if the damage is in the posterior root ganglion cell, it is called sensory ganglionopathy (1, 2). In our country, the NMD diagnosis and treatment guidelines established by the Ministry of Health in collaboration with neurologists were updated in 2006. (3).

The prevalence of NMDs is approximately 160 in 100,000 (4). It is known that there are over 70,000 patients with a NMDs diagnosis in Western Europe, 40,000 in the USA, and 35,000 in the UK (5). There are about 100,000 patients diagnosed with a NMDs in our country (6). NMDs can present at any age, from childhood to adulthood. Although advances in modern medicine have prolonged life expectancy in individuals with NMDs, there is still no curative treatment. These diseases generally have a progressive course and cause disability and impairment in daily living activities (5). The most common symptom of NMDs is weakness. Patients may also present with functional deficits due to weakness, including reduced grip strength, difficulty getting up from a sitting position, squatting, walking, and climbing stairs (7). Physical examination findings include sensory loss, signs of autonomic dysfunction, muscle atrophy, cramps, fasciculations, and contractures. Dysarthria and dysphagia may also occur in these patients due to dysfunction of the neuromuscular junction or muscles, upper motor neurons, lower motor neurons, or both upper and lower motor neurons (8). NMDs can cause respiratory system disorders ranging from impaired airway patency to respiratory failure. They can cause decreased exercise capacity, cardiac conduction disorders, and structural changes. In addition to muscle weakness, NMDs can cause a wide range of involvement, including sensory loss, impaired swallowing and speech, and impaired respiratory and cardiac functions (9).

There is currently no treatment that provides complete

recovery for NMDs. A literature review has shown that a well-structured physiotherapy program slows the loss of muscle strength in slowly progressing NMDs and improves the patient's secondary problems (10-12). A detailed evaluation of the patient's clinical characteristics is necessary to establish an effective physical therapy program. Studies have shown that comorbidities are seen at an earlier age and more frequently in NMDs than in the normal population. In this respect, clinical follow-up of these patients should be more careful, and all organ systems should be examined (13).

In this study, we aimed to examine the sociodemographic and clinical characteristics of patients who received inpatient physical therapy and rehabilitation programs due to NMDs, to make suggestions about the issues we should evaluate during follow-up, and to share our 5-year experience with the literature.

MATERIALS AND METHODS

Approval for the study was obtained from the, Bilkent City Hospital Ethical Review Board (Date: 12.06.2024, Number: 2-24-265). The study was conducted following the Declaration of Helsinki Principles. This retrospective study reviewed the files of patients who received inpatient physical therapy and rehabilitation programs at the NMDs Clinic between March 2019 and March 2024. Age, gender, occupation, marital status, height, weight, body mass index, disease duration (months), medications, comorbidities, smoking and alcohol use, history of fractures and falls, history of osteoporosis (OP), physical examination findings, including muscle strength, sensory examination, presence of atrophy, shortness and diameter difference in the lower extremities, presence of involuntary movements, spasticity, swallowing and speech evaluation, respiratory system examination, ambulation and functional status, were recorded.

Our study included patients aged ≥ 18 years of age who received inpatient physical therapy and rehabilitation programs in the NMD clinic between March 2019 and March 2024 for the diagnoses of MND, neuropathies, and myopathy. Patients with neuromuscular junction diseases, patients under 18, and patients with incomplete file data were excluded. Patients were divided into 3 groups: motor neuron

diseases, neuropathies, and myopathies. Poliomyelitis sequelae, spinal muscular atrophies (SMA), and amyotrophic lateral sclerosis (ALS) were evaluated in motor neuron disease group. Guillain-Barré syndrome and polyneuropathies (diabetic polyneuropathy, drug-induced neuropathies, critical illness neuropathies, inflammatory polyneuropathies) were included in neuropathies group. Myopathies and muscular dystrophies were evaluated in myopathies group.

Statistical Analysis

Recorded data were analyzed using the Statistical Package for Social Sciences, version 27.0 (SPSS Inc., Armonk, NY). The normality of numerical data distribution was examined using the Shapiro-Wilk normality test. Normally distributed continuous variables were presented as mean and standard deviation, while non-normally distributed ones were presented with median and interquartile range (IQR; 25th-75th percentiles). Qualitative data were expressed as frequencies and percentages. Categorical variables were compared using the Chi-square test, and p-values from Pearson's Chi-square test and Likelihood ratio were used, depending on the sample

and expected counts. Numeric variables were analyzed using the Kruskal-Wallis test with post hoc Bonferroni correction for multiple comparisons. The numeric variables between the two groups were analyzed using the Mann-Whitney U test. The confidence interval was set at 95%, and the accepted margin of error was 5%. Therefore, the p-value was considered significant when $p < 0.05$.

RESULTS

Two hundred and four patients were included in our study. The largest number of patients was in the neuropathy group (n=146), followed by MND (n=37) and myopathies (n=21). The sociodemographic features of the patients are presented in Table 1. The age is lower in the myopathies group than in other groups ($p < 0.001$).

Systemic diseases, medications, frequency of fractures, osteoporosis, time since diagnosis, and prophylactic or treatment for deep venous thrombosis (DVT) and pulmonary thromboembolism (PTE) are listed in Table 2. The history of falling or fracture ratio is significantly higher in the MND group than in the other groups ($p < 0.001$). OP frequency is greater in the MND group

Table 1. Sociodemographic data of the patients according to diagnostic groups

	MND (n=37)	NP (n=146)	MYP (n=21)	P
Age (median: IQR)	58.0 (17.0)	59.5 (29.0)	38.0 (17.0)	<0.001
Gender (n/%)				0.277
Female	23 (62.2)	72 (49.3)	9 (42.3)	
Male	14 (37.8)	74 (49.7)	12 (57.1)	
Marital status (n/%)				0.012
Married	18 (48.6)	79 (54.1)	6 (28.6)	
Single	11 (29.7)	35 (24.0)	13 (61.9)	
Widow	8 (21.6)	32 (21.9)	2 (9.5)	
Education (n/%)				
Retired	22 (59.5)	98 (67.1)	7 (33.3)	
Nonworking	5 (13.5)	6 (4.1)	4 (19.0)	
House-wife	1 (2.7)	4 (2.7)	1 (4.8)	
Officer	7 (18.9)	6 (4.1)	4 (19.0)	
Worker	2 (5.4)	30 (20.5)	4 (19.0)	
Self-employment	-	2 (1.4)	1 (4.8)	
BMI (median: IQR)	25.3 (6.1)	26.3 (8.4)	23.2 (6.3)	0.180
Smoking (n/%)	7 (28.0)	17 (13.1)	1 (4.8)	0.062
Alcohol (n/%)	3 (13.0)	2 (1.6)	-	

IQR: interquartile range, MND: motor neuron disease, NP: neuropathies, MYP: myopathy, BMI: body mass index

Table 2. The medical history, clinical specialties and performed tests or imaging methods of the patients

	MND (n=37)	NP (n=146)	MYP (n=21)	P
Systemic diseases (n/%)				
HT	12 (32.4)	65 (44.5)	4 (19.0)	
DM	3 (8.1)	47 (32.2)	1 (4.8)	
CAD	1 (2.7)	28 (19.2)	1 (4.8)	
Malignancy	2 (5.4)	11 (29.7)	2 (9.6)	
History of fracture (n/%)	12 (32.4)	8 (5.5)	1 (4.8)	<0.001
Osteoporosis (n/%)	8 (21.6)	16 (11.0)	-	0.016
Duration of disease (months) (median: IQR)				
Dyspnea	2 (8.7)	18 (12.3)	3 (14.3)	0.443
Cough	1(2.7)	18 (12.3)	1 (4.8)	0.152
Lower respiratory tract infection	-	15 (10.3)	1 (4.8)	0.024
Bilateral lower extremities Doppler USG imaging (n/%)	12 (32.4)	89 (54.8)	11 (52.4)	0.051
DVT diagnosis (n/%)	--	9 (6.2)	-	0.154
Prophylactic treatment for DVT (n/%)	3 (8.1)	35 (24.0)	1 (4.8)	0.019
Pulmonary embolism diagnosis	-	2 (1.4)	1 (4.8)	0.350
Echocardiography imaging (n/%)	8 (21.6)	46 (31.5)	12 (57.1)	0.019
Ejection fraction (%) (median; IQR)	60.8±3.5	57.2±7.3	58.8±5.5	0.325

IQR: interquartile range, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary arterial disease, USG: Ultrasonography, DVT: Deep venous thrombosis, MND: Motor neuron disease, NP: Neuropathies, MYP: Myopathies, BMI: Body mass index

than in neuropathies (p=0.016). The history of lower respiratory tract infections is more common in the neuropathies group compared to the MND group (p = 0.024). Prophylactic treatment for DVT was applied more commonly in the neuropathy group than in other groups (p=0.019). Echocardiography imaging was performed more frequently in the myopathies group than in the other groups (p = 0.019).

The patient's physical examination findings and ambulation status are presented in Table 3. The frequency of proximal weakness in the right and left upper extremities is higher in the myopathies group than in the other groups (p = 0.041). Proximal weakness in the right lower extremity is more frequent in the MND and myopathies group than in the neuropathies group (p < 0.001). Left lower extremity proximal weakness is more common in the MND group than in the neuropathies group (p = 0.011). The ratio of patients with loss of sensation is higher in the neuropathy group compared to the other groups (p < 0.001). Muscle atrophy is more frequent in the MND group and the myopathies group than in the neuropathies group (p<0.001). Shortness in lower extremities is more common in MND than in the neuropathies

group (p<0.01). The frequency of absence of urinary sensation is higher in the neuropathy group than in the MND group (p = 0.035). The proportion of dependent/independent ambulated patients is significantly lower in the MND group than in other groups. (p<0.01). Therefore, the frequency of patients dependent on a wheelchair is not significantly different between the groups. (p=0.075). Using a forearm crutch is more common in the MND group than in the other groups (p<0.01).

DISCUSSION

There was no significant difference in terms of gender between the three groups in our study. A study conducted in the Netherlands showed that 56% of 20,000 patients diagnosed with NMDs were male and 44% were female, and no difference was found in gender, similar to our study (14). In our study, the mean age is lower in the myopathy group compared to the neuropathy and MND groups. In a study from our country, the median age was lower in the myopathy group than in the neuropathy group, similar to our study. Neuropathies are a common neurological disorder with a prevalence of 1-3% in the normal

Table 3. Physical examination findings and ambulation status of the patients

Physical examination findings (n/%)	MND (n=37)	NP (n=146)	MYP (n=21)	P
Muscle weakness	36 (97.3)	131 (89.7)	20 (95.2)	0.272
Right upper extremity proximal weakness	18 (48.6)	68 (47.6)	16 (76.2)	0.041
Right upper extremity distal weakness	21 (56.8)	79 (55.2)	13 (61.9)	0.846
Left upper extremity proximal weakness	18 (48.6)	71 (49.7)	16 (76.2)	0.041
Left upper extremity distal weakness	18(48.6)	74(50.6)	16 (76.2)	0.709
Right lower extremity proximal weakness	34 (91.9)	97 (67.8)	20 (95.2)	<0.001
Right lower extremity distal weakness	30 (81.1)	102 (71.3)	14 (66.7)	0.401
Left lower extremity proximal weakness	33 (89.2)	97 (67.4)	18 (85.7)	0.011
Left lower extremity distal weakness	28 (75.7)	103 (72.0)	14 (66.7)	0.762
Loss of sensation	5 (13.5)	92 (63.0)	3 (14.3)	<0.001
Muscle atrophy	8 (21.6)	3 (2.1)	2 (9.5)	<0.001
Shortness in the lower extremities	5 (13.5)	2 (1.4)	-	<0.01
Involuntary movements	1 (2.7)	4 (2.7)	1 (4.8)	0.712
Spasticity	6 (16.2)	10 (6.8)	1 (4.8)	0.151
Dysphagia	6 (16.2)	20 (13.7)	1 (4.8)	0.372
Speech disorder	4 (10.8)	10 (6.8)	1 (4.8)	0.650
Absence of urinary sensation	-	14 (9.6)	2 (9.5)	0.035
Loss of urinary control	4 (10.8)	29 (19.9)	2 (9.5)	0.264
Fecal incontinence	1 (2.7)	13 (8.9)	1 (4.8)	0.326
Ambulation (n/%)				
Independent ambulation	3 (8.1)	40 (27.4)	9 (42.9)	<0.01
Dependent on a wheelchair, non-functional ambulation	13 (35.1)	27 (18.5)	6 (28.6)	0.075
Ambulation with a walker	8 (21.6)	31 (21.2)	1 (4.8)	0.118
Ambulator, dependent on the physical assistance of a single person	3 (8.1)	16 (11.0)	3 (14.3)	0.760
Ambulator, dependent on the physical assistance of two persons	1 (2.7)	16 (11.0)	1 (4.8)	0.166
Using a forearm crutch	8 (21.6)	10 (6.8)	-	<0.01
Using a cane	1 (2.7)	6 (4.1)	1 (4.8)	0.899

MND: motor neuron disease, NP: neuropathies, MYP: myopathy

population, increasing to 7% in people over 65 years of age (15). Although myopathies are genetically inherited or acquired diseases, they are mainly genetically inherited and present at a younger age (16). We think that the difference in age between the groups is attributable to these clinical features of the diseases. In this study, 24.3% of patients in the MND group, 25% in the neuropathy group, and 42.8% in the myopathy group were employed. In a study conducted in Turkey on the difficulties experienced by the families of patients with neuromuscular diseases, 126 volunteer family members of patients with NMD were interviewed, and it was concluded that 31.7% of the patients

were able to work, and 50% of them had difficulty in meeting the care needs of their disease. We believe that the sociodemographic characteristics of patients diagnosed with NMDs should be determined, and social support should be a part of the rehabilitation process in addition to the medical support. In our study, the frequency of fracture history and OP was higher in the MND group than in the neuropathy and myopathy groups. Previous studies have shown that bone mineral density decreases and fracture risk increases in SMA, amyotrophic lateral sclerosis (ALS), and Duchenne muscular dystrophy (17, 18). In a retrospective study conducted in our country,

45 patients were included, composed of only postmenopausal women and men over 50. The patients were divided into 3 groups, and a comparison was made similarly to our study. No difference was observed between the groups regarding OP and fracture risk in that study (19). We think that this difference is due to the different age range of the patient populations. A study conducted in 33 ALS patients and a control group concluded that bone density was lower than in healthy individuals, particularly females. The risk of falling is increased in patients with NMDs (20). Assessment of OP and fracture risk is an essential point to keep in mind in all patients with NMDs, especially in those with MND, as the risk of falling is increased.

Progressive loss of muscle strength seen in NMDs causes a decrease in upper airway tone, impairing the cough reflex, making it difficult to clear secretions, and may lead to recurrent respiratory tract infections and severe respiratory system symptoms that may progress to respiratory failure (21). In this study, the prevalence of dyspnea was 8.7% in the MND group, 12.3% in the neuropathy group, and 14.3% in the myopathy group, with no difference between the groups. Lower respiratory tract infection frequency was significantly higher in the neuropathy group than in other groups. The onset of respiratory problems varies according to the patient's age and the type of NMDs. Patients with SMA type 1 suffer from severe respiratory failure in childhood, and patients die before the age of 3 if adequate respiratory support is not provided (22). The evaluation of the adult patients who were followed up in the inpatient clinic and the lack of comparison with the normal population may be the reason for our study's lower frequency of dyspnea and lower respiratory tract infections.

The incidence of deep venous thrombosis (DVT) is considered to be increased in individuals with NMDs due to their older age and decreased mobility. DVT and subsequent pulmonary thromboembolism (PTE) are significant causes of death in patients with NMDs (23). PTE leads to mortality in 2% of ALS patients (24). It is thought that decreased muscle pump activity resulting from weakness and atrophy of the legs in these patients facilitates blood congestion (25). Furthermore, venous stasis associated with wheelchair use also increases the risk of DVT and consequently PTE

development. In a study conducted in stroke patients, the risk of DVT development was found to be greater in wheelchair users compared to bed-level patients (26). DVT prophylaxis is recommended for all NMDs patients who ambulate by wheelchair (27). There are very few studies regarding DVT in NMDs patients. A study in which 50 outpatients with ALS were followed up for one year found that one patient had symptomatic DVT, one patient had PTE, and two patients had asymptomatic DVT during follow-up (28).

In our study, 32.4% of the MND group, 54.8% of the neuropathy group, and 52.4% of the myopathy group were screened for DVT by Doppler ultrasonography (USG). DVT was diagnosed in nine patients in the neuropathy group, and PTE in two patients, while PTE was diagnosed in one patient in the myopathy group. The rate of receiving treatment for DVT prophylaxis was significantly higher in the neuropathy group than in the other groups. The neuropathy group had the highest number of DVT and PTE cases. In terms of mobilization, 27 patients in the neuropathy group were ambulatory with a wheelchair. The higher number of DVTs and PTEs in the neuropathy group may be because ambulation limitations were more severe in the neuropathy group compared to the other groups. One hundred twelve patients were evaluated for DVT by bilateral lower extremity venous Doppler USG, and 39 patients were receiving DVT prophylaxis. The annual incidence of DVT in the general population is 0.1%. In our study, the frequency of DVT was found to be higher, at 6.2%. We think that this is because we screened approximately 55% of the patients for DVT and detected asymptomatic cases in addition to the patient's mobilization limitations. Physicians should be cautious against DVT and PTE, which may cause mortality in patients with NMDs, and patients should be evaluated in detail for prophylactic treatment.

Cardiac pathologies, including cardiomyopathies and/or conduction disorders, may be seen in NMDs, which develop as a result of simultaneous or progressive involvement of the heart muscle as well as skeletal muscle (29). Most forms of cardiac involvement are detected from childhood to the second decade of life (DMD, myotonic dystrophy, etc.). It may also remain asymptomatic until advanced age (Becker muscular dystrophy, some forms of congenital myopathy,

etc.). Cardiac involvement is more severe when neuromuscular symptoms appear in childhood or rapidly progress during infancy (30). Patients were divided into two groups in a study investigating echocardiographic features in NMDs. MND and polyneuropathies were included in one group, and myopathies in the other group, and echocardiographic findings were compared. The results revealed lower left ventricular ejection fraction and impaired diastolic function in the myopathy group (31). Unlike this study, there was no difference in left ventricular ejection fraction between the groups in our study. We found that cardiac involvement was more frequent in the myopathy group than in the other groups. This is an expected result in the myopathy and muscular dystrophy group, where cardiac involvement is more frequent and causes severe morbidity and mortality compared to MND and neuropathies (32).

Muscle weakness is one of the most important clinical findings that affects the daily life activities and prognosis of patients with NMDs. The distribution of weakness is also critical in the diagnosis of neuropathic and myopathic diseases (33). In this study, right and left upper extremity proximal muscle weakness was significantly higher in the myopathy group than in the other groups. Muscle weakness in the proximal right lower extremity was significantly higher in the neuropathy group compared to the other groups, and in the proximal left lower extremity in the MND group compared to the neuropathy group. Muscle atrophies were also more frequent in the myopathy and MND groups than in the neuropathy group. The hallmark of MND is painless weakness and atrophy, often accompanied by cramps and fasciculations (7).

Neuropathies are neurological disorders affecting motor, sensory, or autonomic fibers and have various subtypes. The most common form is distal symmetrical polyneuropathies that start with sensory symptoms (numbness, paresthesia) or small fiber neuropathy (pain, loss of temperature perception). Loss of muscle strength in neuropathies develops after sensory losses (15). In our study, sensory losses were statistically significantly higher in the neuropathy group than in the MND and myopathy groups.

Length discrepancy in the lower extremities was statistically significantly more common in MND group

than in the other groups in our study. Leg length disparity caused by growth due to paralysis is the most common sequela in poliomyelitis patients. Many factors are involved in lower extremity discrepancies. Some of these factors are directly related to bone growth, and some are indirectly related to affecting bone development. This discrepancy in the lower extremities may cause many problems (34). Due to alterations in postural balance, musculoskeletal problems such as low back pain, scoliosis, degenerative arthritis of the hip or knee joint, and patellofemoral pain syndrome may occur (35). It is crucial to recognize limb inequalities early in clinical follow-up to prevent musculoskeletal problems that may occur secondary to the discrepancy.

Spasticity was most common in the MND group, with a rate of 16.2%, but there was no significant difference between the groups. Upper motor neuron involvement may cause spasticity, especially in ALS. In a study examining the prevalence of spasticity and spasticity-related pain in ALS, 150 patients were evaluated, and spasticity was found in 36% of patients (36). In this study, the spasticity ratio was lower because the motor neuron disease group did not consist only of ALS patients. Lower spasticity rates may be expected since post-polio or SMA-related weakness is typically flaccid rather than spastic.

In a study investigating the frequency of dysarthria and dysphagia in NMDs, 220 patients were evaluated by speech and language therapists, and dysarthria was found in 56% and dysphagia in 47% of the patients. They explained that the higher rates of dysarthria and dysphagia in this study compared to other studies were because the evaluations were made by experienced speech therapists, not by a questionnaire or an interview (37). The prevalence of dysarthria and dysphagia was lower in our study than in other studies, and we thought that this was because not all patients were evaluated by a speech and language therapist. As Simone et al. stated in their research, a detailed evaluation of patients with NMDs by speech and swallowing therapists is important to identify these patients in the early period (37).

NMDs significantly affect patients' independence in their daily activities. Functional mobility should be assessed in all patients with NMDs. The symptoms that

often occur are the biomechanical consequences of the inappropriate mobility of the patient. In these patients, the onset of movement, weight transfer, balance, and the effort required to complete the movement should be observed, and appropriate assistive devices should be used when necessary (38). Patients should also be checked for assistive devices, considering disease progression (39). In our study, independent ambulation was statistically lower in the MND group than in the other two groups, while cane use was significantly higher. Most patients in all groups (91.9%, 72.6%, 57.1%, respectively) were dependent in their ambulation through a walker, single-person support, double-person support, cane, or cane use. In a study conducted in our country, the use of assistive devices in patients with NMDs was found to be higher in the myopathy group, 22.7%, compared to the MND and neuropathy groups (40). In our study, the evaluation of ambulation with person support, not only the use of the device, may have caused different results. The studies on NMDs were generally conducted on a specific disease in the literature. The strengths of our research included 5-year data from a clinic in a tertiary health center where only NMDs were followed up, a high number of patients, multidimensional sociodemographic and clinical evaluation of patients, and comparison between subgroups. We think that it is a valuable study in these respects. The limitations of our study were its retrospective nature, lack of comparison with a healthy control group, and lack of treatment outcome data.

CONCLUSION

Our study demonstrates that each subgroup of neuromuscular disorders possesses distinct clinical features. The younger age profile observed in myopathies, the increased prevalence of osteoporosis and fractures in MNDs, and the higher rates of infections and thromboembolic events in neuropathies emphasize the need for a disorder-specific clinical approach. Differences in the distribution of muscle weakness, sensory impairment, and ambulation levels further support this heterogeneity. Therefore, early evaluation, precise identification of risk factors, and individualized rehabilitation planning are essential in the management of neuromuscular

disorders. We consider that larger and prospective studies will significantly enhance follow-up and treatment strategies for this patient population.

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KRONİK HASTALIĞI OLANLARDA BELİRSİZLİĞE TAHAMMÜLSÜZLÜK DURUMUNUN DEĞERLENDİRİLMESİ

Evaluation of Intolerance to Uncertainty in Patients with Chronic Disease

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ÖZET

Amaç: Bu çalışma, kronik hastalığı olan bireylerin belirsizliğe tahammülsüzlük düzeylerini değerlendirmeyi amaçlamıştır.

Gereç ve Yöntemler: Tanımlayıcı ve kesitsel tipte olan bu çalışmaya Yozgat Bozok Üniversitesi Tıp Fakültesi İç Hastalıkları polikliniklerine başvuran ve bilinen kronik hastalık tanısı olan 18 yaş üstü 354 birey dahil edilmiştir. Bireylerin antropometrik ölçümleri, sosyo-demografik özellikleri ve belirsizliğe tahammülsüzlük ölçekleri yüzyüze görüşme yöntemi kullanılarak toplanmıştır.

Bulgular: Bekar, yalnız yaşayan ve psikiyatrist/psikolog desteği alan bireylerde belirsizliğe tahammülsüzlük, ileriye dönük kaygı ve engelleyici kaygı daha yüksek, lisans ve yüksek lisans eğitimi alanlar ile psikiyatrik ilaç kullanımı olanlarda belirsizliğe tahammülsüzlük ve ileriye dönük kaygı daha yüksek, şehir ve büyük şehirlerde yaşayanlarda ileriye dönük kaygı düzeyinin daha yüksek olduğunu ortaya koymuştur. Ayrıca kronik hastalıklar açısından en yüksek oran %63,6 ile HT saptanmıştır. Psikiyatrik hastalığa sahip olanlarda belirsizliğe tahammülsüzlük, ileriye dönük kaygı ve engelleyici kaygı daha yüksek iken, kronik kalp hastalıkları olan bireylerde engelleyici kaygı düzeyinin daha yüksek olduğu gösterilmiştir.

Sonuç: Kronik hastalığı olan bireylerde özellikle psikiyatrik hastalık ile kalp hastalığı olan bireyler başta olmak üzere, eğitim düzeyi yüksek, bekar, yalnız ve kentsel yaşantısı olan bireylerle sağlanacak psikososyal destek ile belirsizliğe tahammülsüzlük, ileriye dönük kaygı ve engelleyici kaygıyı azaltmayı amaçlayan müdahalelerin önemi vurgulanmıştır.

Anahtar Kelimeler: Kronik Hastalık; Belirsizliğe Tahammülsüzlük; BTÖ-12

ABSTRACT

Objective: This study aimed to evaluate the intolerance of uncertainty levels of individuals with chronic diseases.

Material and Methods: This descriptive and cross-sectional study included 354 individuals over the age of 18 who applied to the Yozgat Bozok University Medical Faculty Internal Medicine outpatient clinics and had a known chronic disease diagnosis. Individuals' anthropometric measurements, socio-demographic characteristics and intolerance of uncertainty scales were collected using the face-to-face interview method.

Results: It was revealed that intolerance of uncertainty, anticipatory anxiety and inhibitory anxiety were higher in individuals who were single, living alone and receiving support from a psychiatrist/psychologist, intolerance of uncertainty and anticipatory anxiety were higher in those who received undergraduate and graduate education and those using psychiatric medication, and anticipatory anxiety levels were higher in those living in cities and big cities. In addition, the highest rate in terms of chronic diseases was determined as HT with 63.6%. While intolerance of uncertainty, anticipatory anxiety and inhibitory anxiety were higher in those with psychiatric diseases, it was shown that inhibitory anxiety levels were higher in individuals with chronic heart diseases.

Conclusion: The importance of interventions aimed at reducing intolerance of uncertainty, anticipatory anxiety and inhibitory anxiety through psychosocial support to be provided to individuals with chronic diseases, especially those with psychiatric illnesses and heart diseases, as well as individuals with a high level of education, who are single, lonely and live in urban areas, has been emphasized.

Keywords: Chronic Disease; Intolerance of Uncertainty; IUS-12

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GİRİŞ

Dünya Sağlık Örgütü (DSÖ)'den edinilen bilgiye göre; kronik hastalıklar en sık ölüm nedenleri arasında bulunmaktadır (1). Türkiye'de ise nüfusun yaklaşık %88'inde kronik hastalıklar nedeni ile ölüm bildirilmiştir (2). Kronik hastalıklar genellikle tedavi edilemez veya uzun süreli tedavi gerektirebilir. Avustralya Sağlık ve Refah Enstitüsü (AIHW) kronik hastalık olarak artrit, sırt ağrısı, kardiyovasküler hastalık, kronik obstrüktif akciğer hastalığı, kanser, kronik böbrek hastalığı ve ruh sağlığı bozuklarını içeren hastalıkları tariflemiştir (3). Başka çalışmalarda ise obezite, diyabet, karaciğer hastalıkları, HIV (Human Immunodeficiency Virus) gibi kronik enfeksiyonları ve inflamatuvar barsak hastalıkları (yani Crohn hastalığı ve ülseratif kolit) da kronik hastalıklar olarak tanımlanmıştır (4). Belirsizliğe tolerans, kişinin belirsizliği anlama, psikolojik olarak bunlarla başa çıkma durumu ifade eder (5). Belirsizlik, bir olayın veya davranışın sonucunun ne olacağını tahmin edememe, başka deyişle olumsuz tepkilere direnememe olarak tanımlanmıştır (6,7). Belirsizliğin insan psikolojisini olumsuz etkilediği bilinmektedir. Bu süreç devam ettiği takdirde kişide endişe, kaygı ve korku oluşturmaktadır (8). Bir başka açıdan bakıldığında, belirsizliğe tahammülsüzlük kişilerde duygusal, bilişsel olumsuz tepki oluşturmaktadır (9). Bilindiği kadarıyla belirsizliğe tahammülsüzlük, başlangıçta yaygın anksiyete bozukluğu (GAD) ile ilişkilendirilmiştir (10). Belirsizliğe Tahammülsüzlük Ölçeğinin Kısa Formunun (BTÖ-12), ilk olarak 2007 yılında geliştirilmiş, 2014 yılında ise Türkçe versiyonu sunulmuştur. Ölçek, toplam 27 madden oluşan 5'li likert tipinde bir ölçektir. 12 maddeden oluşan ölçekte alınan puan 12 ile 60 arasındadır. Ölçekten alınan puan yükseldikçe belirsizliğe tahammülsüzlük artmaktadır (11). Ölçeğin özelliklerinden biri de ters kodlama bulunmamasıdır. Bu ölçeğin iki alt sınıfı vardır. Bunlar, ileriye dönük belirsizliğe tahammülsüzlük ve engelleyici belirsizliğe tahammülsüzlüktür. Türkçe güvenilirlik analizi Cronbach alfa 0,90 olarak bulunmuştur. İç tutarlık katsayısı ölçeğin geneli için 0,79 ve 0,88 arasında değişmiştir (12). Bu rakamlar ölçeğin geneli için 0,88 iken, ileriye yönelik kaygı alt grubu için 0,84, engelleyici kaygı alt grubu için 0,77 olarak bulunmuştur (9). Ayrıca bu ölçek ile endişe ve kaygı zemini hakkında fikir edinilmektedir (13). Kronik hastalık tanısı alan

bireylerde uyum sürecini içeren bir zaman dilimine ihtiyaç vardır (14). Bu zaman dilimi hastalığın ruhsal ve bedensel değişikliklere uyum sağlamayı içeren bir süreçtir (15). Kronik hastalıkların çeşitliliğine bağlı olarak her bir hastalık farklı semptom ve bulgular verir (16). Kronik hastalıkların insan sağlığına yaptığı olumsuz etkiler bilinmektedir. Bu çalışmanın farklı bir bakış açısı geliştirmesi ve gerekli önlemlerin alınmasına katkı sağlaması beklenmektedir.

GEREÇ VE YÖNTEMLER

Bu çalışma, Yozgat Bozok Üniversitesi Tıp Fakültesi Girişimsel Olmayan Araştırmalar Etik Kurulu'ndan (2024-GOKAEK-245_2024.06.05_52) onay alındıktan sonra yürütülmüştür. Bu çalışma için analiz edilen ham veriler kişisel olarak tanımlanabilir bilgi içermediğinden, anonimlik ve gizlilik garanti edilmiştir. Bu çalışmada nicel araştırma yöntemlerinden tarama modeli kullanılmıştır. Tarama modeli, geçmişte veya şimdi var olan bir durumu olduğu gibi betimlemeyi içeren bir nicel araştırma yaklaşımıdır. Bu model kapsamında, çalışmaya Yozgat Bozok Üniversitesi Tıp Fakültesi İç Hastalıkları Polikliniklerine başvuran ve bilinen kronik obstrüktif hastalığı (KOAH), diyabetes mellitus (DM), dislipidemi (HL), hipertansiyon (HT), osteoporoz, kronik kalp hastalığı (KKH), kronik böbrek hastalığı (KBH), romatolojik hastalık (artrit vb.), hematolojik hastalık tanısı olan 18 yaş üstü 354 birey dahil edilmiştir. Bireylerin demografik bilgileri araştırmacılar tarafından hazırlanan, yaş, cinsiyet, sigara ve alkol kullanımı, medeni durum, gelir düzeyi, yaşam alanı, birlikte yaşadığı birey/bireyler, psikiyatrik hastalık öyküsü, psikolog/psikiyatrist desteği, psikiyatrik ilaç kullanımı, kronik hastalık gibi sosyodemografik bilgilerin olduğu form ile toplanmış olup, antropometrik ölçümleri, sosyo-demografik özellikleri ve belirsizliğe tahammülsüzlük ölçekleri yüzyüze görüşme yöntemi kullanılarak toplanmıştır.

Toplanan veriler SPSS 22.0 (SPSS IBM Corp., Armonk, NY, USA) paket programı kullanılarak analiz edilmiştir. Tanımlayıcı istatistikler; kategorik değişkenler için sayı ve yüzde, ölçümsel değişkenler için ortalama, standart sapma olarak verilmiştir. Verilerin normal dağılıma uygunluğa çarpıklık ve basıklık değerleri ile bakılmıştır. Verilerin doğrusal dağılımı sonucunda parametrik testlerden bağımsız örneklem t testi ve ANOVA testi

kullanılarak veriler analiz edilmiştir. Verilerin analizinde alanyazında genel kabul gören $p<0,05$ anlamlılık değeri olarak kabul edilmiştir.

BULGULAR

Araştırmada yer alan katılımcıların yaş ortalaması 57,14 yıl, vücut kitle indeksi ortalaması 28,93 kg/m², kilo ortalaması 77,4 kilogram, belirsizliğe tahammülsüzlük toplam puan ortalaması 37,25, ileriye yönelik kaygı

puan ortalaması 22,21, engelleyici kaygı puan ortalaması 15,03 saptanmıştır.

Katılımcıların %68,9'ü kadın, %74'ü evli, %49,7'si ilkokul mezunu, %48'u orta gelir düzeyine sahip, %17,8 'i sigara, %4,5'i alkol kullanmaktaydı. Katılımcılarda en sık görülen kronik hastalık HT (%63,3) idi. Katılımcıların %6,5'i psikiyatrist/psikolog desteği alıyor, %7,9'u psikiyatrik ilaç kullanıyordu (Tablo 1).

Medeni durum ile belirsizliğe tahammülsüzlük

Tablo 1. Tanımlayıcı Veriler

Değişken(N=289)	Sayı(n)	Yüzde (%)
Cinsiyet		
Kadın	210	31,1
Erkek	244	68,9
Eğitim durumu		
Okuryazar olmayan	70	19,8
İlkokul	176	49,7
Ortaokul	57	16,1
Lise	47	13,3
Lisans	4	1,1
Medeni Durum		
Evli	262	74
Bekar	45	12,7
Dul/Boşanmış	47	13,3
Gelir Düzeyi		
Düşük	145	40,9
Orta	170	48
Yüksek	39	10,1
Alkol kullanımı		
Var	16	4,5
Yok	338	94,5
Sigara kullanımı		
Var	63	17,8
Yok	291	83,2
Diyabetes mellitus		
Var	197	56,6
Yok	156	43,4
Hipertansiyon		
Var	224	63,3
Yok	130	36,7
Hiperlipidemi		
Var	78	22
Yok	276	78

Tablo 1. devamı.

Kronik Obstrüktif Akciğer Hastalığı		
Var	23	6,5
Yok	331	93,5
Astım		
Var	36	10
Yok	318	90
Kronik Böbrek Hastalığı		
Var	20	5,6
Yok	334	94,6
Kronik Kalp Hastalığı		
Var	48	13,5
Yok	306	86,5
Nörolojik Hastalık		
Var	14	4
Yok	340	96
Romatolojik hastalık		
Var	18	5,1
Yok	336	94,9
Alerjik hastalık		
Var	17	4,8
Yok	337	95,2
Psikiyatrik hastalık		
Var	14	4
Yok	340	96
Kanser		
Var	8	2,3
Yok	346	97,7
Diğer Hastalık		
Var	42	11,9
Yok	321	89,1
Psikiyatrist/psikolog desteği		
Var	23	6,5
Yok	331	93,5
Psikiyatrik ilaç kullanımı		
Var	28	7,9
Yok	326	92,1

arasında anlamlı farklılık saptandı ($p=0,001$). Medeni durum ile ileriye dönük kaygı arasında anlamlı farklılık saptandı ($p=0,002$). Medeni durum ile engelleyici kaygı arasında anlamlı farklılık saptandı ($p=0,007$). Bekarlarda toplam kaygı, engelleyici kaygı düzeyi ve ileriye dönük kaygı düzeyi daha yüksekti. Birlikte

yaşadığı kişi/kişiler ile belirsizliğe tahammülsüzlük durumunda anlamlı farklılık saptandı ($p=0,008$). Birlikte yaşadığı kişi/kişiler ile ileriye dönük kaygı arasında anlamlı farklılık saptandı ($p=0,001$). Birlikte yaşadığı kişi/kişiler ile engelleyici kaygı arasında anlamlı farklılık saptandı ($p=0,001$). Toplam kaygı, engelleyici kaygı ve

ileriye yönelik kaygı düzeyi yalnız yaşayanda daha yüksek saptandı. Eğitim düzeyi ile belirsizliğe tahammülsüzlük arasında anlamlı farklılık saptandı ($p=0,014$). Eğitim düzeyi ile ileriye yönelik kaygı düzeyi arasında anlamlı farklılık saptandı ($p=0,001$). Toplam kaygı ve ileriye yönelik kaygı eğitim düzeyi ile ters orantılı bulundu. Yaşam alanı ile ileriye yönelik kaygı düzeyi arasında anlamlı farklılık saptandı ($p=0,035$). Köy ve kasabada yaşayanlarda, şehir ve büyük şehirde yaşayanlara göre ileriye yönelik kaygı düzeyi göre daha düşüktü (Tablo 2).

Kronik kalp hastalığı ile engelleyici kaygı arasında anlamlı farklılık saptandı ($p=0,006$). Kronik kalp hastalığı olanlarda engelleyici kaygı daha yüksekti. Psikiyatrik hastalığı olanlar ile belirsizliğe tahammülsüzlük arasında anlamlı farklılık saptandı ($p=0,001$). Psikiyatrik hastalığı olanlar ile ileriye yönelik kaygı arasında anlamlı farklılık saptandı ($p=0,070$). Psikiyatrik hastalığı olanlar ile engelleyici kaygı arasında anlamlı farklılık saptandı ($p=0,032$). Psikiyatrik hastalığı olanlarda toplam kaygı, ileriye yönelik kaygı ve engelleyici kaygı daha yüksekti. Psikiyatrist/psikolog desteği ile belirsizliğe tahammülsüzlük arasında anlamlı farklılık saptandı ($p=0,001$). Psikiyatrist/psikolog desteği ile ileriye yönelik kaygı düzeyi arasında anlamlı farklılık saptandı ($p=0,001$). Psikiyatrist/psikolog desteği ile engelleyici kaygı düzeyi arasında anlamlı farklılık saptandı ($p=0,001$). Psikiyatrik ilaç kullananlar ile belirsizliğe tahammülsüzlük arasında anlamlı farklılık saptandı ($p=0,021$). Psikiyatrik ilaç kullananlarda belirsizliğe tahammülsüzlük daha yüksek saptandı. Psikiyatrik ilaç kullananlar ile ileriye yönelik kaygı düzeyi arasında anlamlı farklılık saptandı ($p=0,013$).

Psikiyatrik ilaç kullananlarda ileriye yönelik kaygı daha yüksek saptandı (Tablo3).

TARTIŞMA

Belirsizlik kaygı ve stresi tetikleyen bir durumdur. Belirsizliğe tahammülsüzlük birçok faktörün bir araya gelmesiyle önplana çıkabilir. Belirsizliğe tahammülsüzlük durumu belirlemek ve gerektiğinde müdahale için eyleme geçmek gerekir. Kronik hastalıkların psikolojik birçok etkisi olduğu bilinmektedir. Çalışmamız kronik hastalıkların belirsizliğe tahammülsüzlük durumunu ve alt gruplarını nasıl etkilendiğini araştırdı. Bu çalışma bazı kronik hastalıkların belirsizliğe tahammülsüzlüğün ortaya çıkmasında potansiyel bir neden olabileceğini göstermektedir. Bu bağlamda, tespit edilen sonuçlara göre, belirsizliğe tahammülsüzlüğün çok daha iyi anlaşılmasını ve gerekli durumlarda erken müdahale edilmesi gerektiğini ortaya koymuştur.

Bu çalışmanın sonuçları değerlendirildiğinde, psikiyatrik hastalıkların kronik hastalıklar arasında belirsizliğe tahammülsüzlük ve alt grupları olan ilerleyici kaygı ile engelleyici kaygıyı ortaya çıkaran en önemli hastalık grubu olduğu elde edilen ilk önemli sonuçtur. Bir diğer açıdan bakıldığında da belirsizliğe tahammülsüzlük diğer psikolojik sorunların tetikleyici olmaktadır. Literatüre bakıldığında bu çalışma ile tutarlılık gösteren bulguların olduğu çalışmalar bulunmaktadır. Belirsizliğe tahammülsüzlük puanlarının arttığı bireylerde obsesif-kompulsif bozukluk, sosyal fobi, depresyon, panik bozukluk, agorafobi, yeme bozuklukları, siberkondri gibi psikolojik soruna yol açabildiği gösterilmiştir (17). Benzer şekilde, belirsizliğe tahammülsüzlüğün sosyal kaygıyı anlamlı şekilde artırdığı gösterilmiştir (18). Bu

Tablo 2. Demografik Veriler

	P		
	Belirsizliğe tahammülsüzlük	İleriye yönelik kaygı	Engelleyici kaygı
Cinsiyet (erkek/kadın)	0,747	0,929	0,610
Vücut kitle indeksi	0,367	0,051	0,882
İkamet	0,279	0,035	0,821
Medeni durum (evli/bekar)	0,001	0,002	0,007
Birlikte yaşadığı kişi/kişiler	0,008	0,001	0,118
Eğitim	0,014	0,001	0,337
Gelir	0,244	0,304	0,318
Meslek	0,746	0,603	0,811

Tablo 3. Belirsizliğe Tahammülsüzlük- Kronik Hastalık İlişkisi

	P		
	Belirsizliğe tahammülsüzlük	İleriye yönelik kaygı	Engelleyici kaygı
Diyabetes Mellitus	0,381	0,209	0,377
Hipertansiyon	0,642	0,380	0,903
Kronik Obstrüktif Akciğer Hastalığı	0,924	0,837	0,960
Astım	0,916	0,692	0,804
Kronik Böbrek Hastalığı	0,516	0,588	0,065
Kronik Karaciğer Hastalığı	0,309	0,464	0,271
Kronik Kalp Hastalığı	0,339	0,416	0,006
Romatolojik Hastalık	0,467	0,336	0,723
Nörolojik Hastalık	0,790	0,874	0,745
Kanser	0,809	0,986	0,662
Allerjik Hastalık	0,701	0,249	0,569
Psikiyatrik Hastalık	0,001	0,001	0,032
Diğer Hastalıklar	0,044	0,070	0,142
Psikiyatrist/psikolog desteği	0,001	0,001	0,001
Psikiyatrik ilaç kullanımı	0,021	0,013	0,118

çalışmada literatürden farklı olarak psikiyatrik hastalıkların belirsizliğe tahammülsüzlük ilişkisinin yanında ilerleyici kaygı ve engelleyici kaygıyı içeren alt grupları da ele alınmış ve her iki alt grupta da psikiyatrik hastalıkları olan bireylerin kaygı düzeyleri daha yüksek saptanmıştır. Ayrıca çalışmanın sonucu; kronik kalp hastalığı olanlarda belirsizliğe tahammülsüzlüğün alt grubu olan engelleyici kaygının daha yüksek olduğu ortaya çıkarmıştır. Yine benzer şekilde literatürde kronik kalp hastalığı olan bireylerde belirsizliğe tahammülsüzlük ilişkisinin varlığına rastlanmamıştır. Belirsizliğe tahammülsüzlüğün, psikiyatrik hastalıkların göstergeleriyle sıkı ilişkiler gösterdiği çalışmalar bulunmakla birlikte, aslında birçok faktörün etkili olduğu tahmin edilmekte ancak yeterli çalışma bulunmamaktadır (10). Bu çalışmada cinsiyetin belirsizliğe tahammülsüzlükte etkili bir risk oluşturmadığı yönündedir. Ancak daha önce yapılan bir çalışmada yetişkin kadınlarda belirsizliğe tahammülsüzlüğün ön plana çıktığı yönündedir (19). Bu sonuç, bu çalışmadaki katılımcıların kronik hastalığı olan bir grubun seçilmiş olması nedeniyle veya katılımcıların biyolojik, fizyolojik ve sosyoekonomik özelliklerden kaynaklanıyor olduğunu düşündürmektedir. Alkol, sigara kullanımı gibi yaşam tarzının belirsizliğe tahammülsüzlük ile ilişkili olduğu

bilinmektedir. Özellikle, alkol kullanımı olan ergenlerin daha yüksek belirsizliğe tahammülsüzlük seviyeleri gösterilmiştir (20). Ancak bu çalışmadaki örnekleme alkol kullanım oranı küçük tutulmuş ve hastalar yetişkin popülasyondan seçilmiştir. Dolayısıyla alkol kullanımı bu çalışmada belirsizliğe tahammülsüzlük veya alt gruplarıyla ilişkili bulunmamıştır. Yapılan çalışmalarda, kişilik özellikleri (nevrotik, vs.), çevresel faktörler ve bilişsel faktörler gibi durumların belirsizliğe tahammülsüzlükle ilişkili olduğu gösterilmiştir. Daha önce ergenlerin olduğu popülasyonun seçilerek yapıldığı bir çalışmada örneklem grubu benzer yaşam alanına sahip olduğu için yaşama alanının belirsizliğe tahammülsüzlük için bir öngörücü değeri olup olmadığı değerlendirilememiştir (10). Bu çalışmada köy ve kasaba gibi kırsal bölgede yaşayanlarda, şehir ve büyük şehirde yaşayanlara göre ileriye yönelik kaygı düzeyi göre daha düşük saptanmıştır. Bu durum şehir hayatının getirdiği yoğun ve stresli yaşamın zorluklarına da vurgu yapmaktadır. Bu çalışmada, belirsizliğe tahammülsüzlük ölçeğinden alınan toplam puan ortalaması 37,25 olup ortalama puanın üzerinde saptanmıştır. Kronik hastalığı olan bireylerin çalışmaya alındığı bu çalışmaya benzer şekilde yine Türkiye’de yürütülen bir başka çalışmada bu ölçekten alınan toplam puan $35,16 \pm 9,42$ olarak bulunmuştur (21). Bu çalışmaya benzer sayıda katılımcı

ile yürütülen ve 310 sağlık çalışanının katıldığı bir diğer çalışmada da belirsizliğe tahammülsüzlük toplam puanı $39,14 \pm 9,31$ olarak bulunmuştur (22). Bu durum farklı evrenlerde yapılan benzer çalışmalarda belirsizliğe tahammülsüzlükten alınan toplam puanların birbirine çok yakın olduğunu işaret etmektedir.

İleriye yönelik kaygı puan ortalaması 22,21, engelleyici kaygı puan ortalaması 15,03 olduğu saptanmıştır. Diğer çalışmalardan farklı olarak belirsizliğe tahammülsüzlük alt gruplarının puanları hesaplanmış ve diğer parametrelerle ilişkisi değerlendirilmiştir. Yapılan çalışmalarda yaş arttıkça belirsizliğin tahammülsüzlüğünde daha yüksek olduğu görülmektedir (23). Benzer şekilde bu çalışmanın yaş ortalaması 57,14 olarak bulunmuştur.

Bu çalışmada en sık bulunan kronik hastalık HT idi. Türkiye’de yapılan çalışmalarda da benzer şekilde en sık kronik hastalık HT olarak gösterilmiştir (24). Katılımcıların 224’ünde (%63,3) HT olduğu görülmüştür. Daha sonra ise DM, HL, KKH, astım, KOAH, KBH, romatizmal hastalıklar, alerjik hastalıklar, psikiyatrik hastalıklar ve kanser sıralanmıştır. Literatürde yapılan diğer çalışmalarda da benzer şekilde en sık HT tanısı olduğu bildirilmiştir (25).

SONUÇ

Mevcut çalışmada, kronik hastalığı olan bireylerin belirsizliğe tahammülsüzlük ve alt grup profillerinin belirlenmesine ve belirsizliğe tahammülsüzlüğün sosyodemografik verilerine katkı sağlamakla birlikte, kronik hastalıklarda spesifik ve hedefli müdahale önlemlerinin alınmasını sağlamaktadır. Bekar, yalnız yaşayanlar ve psikiyatrist/psikolog desteği alanlarda belirsizliğe tahammülsüzlük, ileriye dönük kaygı ve toplam kaygı, lisans ve yüksek lisans eğitimi alanlar ile psikiyatrik ilaç kullanımı olanlarda ileriye dönük kaygı ve toplam kaygı daha yüksek, şehir ve büyük şehirlerde yaşayanlarda ileriye dönük kaygı ile ilişkili olduğu gösterilmiştir. Özellikle psikiyatrik ve kalp hastalığı olan bireyler başta olmak üzere, kentsel ortamda, eğitim düzeyi yüksek, bekar ve yalnız yaşayan bireylere sağlanacak psikososyal destek ile belirsizliğe tahammülsüzlük, ileriye dönük kaygı ve engelleyici kaygıyı azaltmayı amaçlayan müdahaleler yapılabilir. Gelecekteki araştırmalar, belirsizliğe tahammülsüzlük, ileriye yönelik kaygı ve engelleyici kaygı düzeylerinin

azaltılması için gerekli müdahalelere odaklanmalıdır.

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SUTURE-BUTTON FIXATION OUTPERFORMS HOOK PLATE IN FUNCTIONAL OUTCOMES AFTER ACROMIOCLAVICULAR JOINT DISLOCATION

Akromioklaviküler Eklem Çıkığı Tedavisinde Çift Düğme İmplant Fonksiyonel Sonuçlarda Kanca Plaktan Daha Fazla İyileşme Sağlar

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ABSTRACT

Objective: There is no consensus on the optimal surgical treatment for acromioclavicular joint separation (ACJD). This study aimed to compare the functional and radiological outcomes of hook plate (HP) fixation and suture-button (SB) fixation.

Material and Methods: Patients who underwent surgery for Rockwood type III and V ACJD between June 2010 and June 2023 were retrospectively reviewed. Group I included patients treated with HP and Group II included patients treated with SB. Postoperative outcomes were assessed using range of motion (ROM), Constant–Murley Score (CMS), and American Shoulder and Elbow Surgeons (ASES) score. Radiological evaluation included coracoclavicular distance (CCD) measurements and Rockwood classification.

Results: Sixty-two patients (47 men, 15 women; mean age, 29.2±16.1 years) were evaluated with a mean follow-up of 52.9±20.5 months. Anatomical reduction was achieved in 87% of cases. Both groups showed significant postoperative improvement in CMS (53.8±6.4 to 89.7±5.4) and ASES scores (40.4±7.4 to 89.0±7.8) ($p<0.01$). Group II demonstrated superior ROM in abduction (160° vs. 153°) and forward flexion (172° vs. 162°). Postoperative CCD decreased significantly in both groups. At the final follow-up, recurrence was observed in 16.6% of patients in Group I and in 9.3% of patients in Group II ($p = 0.032$).

Conclusion: Both fixation methods are effective for acute ACJD. However, SB fixation provides superior functional outcomes, greater shoulder mobility, and avoids the need for secondary implant removal, making it a favorable option, particularly for young and active patients.

Keywords: *Acromioclavicular Joint Dislocation; Hook Plate Fixation; Suture-Button Fixation; Functional Outcomes*

ÖZET

Amaç: Akromioklaviküler eklem çıkığı (AKEÇ) için en uygun cerrahi tedavi yöntemi konusunda halen bir fikir birliği bulunmamaktadır. Bu çalışmada, hook plak (HP) ve suture-button (SB) yöntemleri ile yapılan tedavilerin fonksiyonel ve radyolojik sonuçları karşılaştırıldı.

Gereç ve Yöntemler: Haziran 2010 – Haziran 2023 tarihleri arasında Rockwood tip III ve V AKEÇ nedeniyle ameliyat edilen hastalar retrospektif olarak incelendi. Grup I’de HP, Grup II’de SB ile tedavi edilen hastalar yer aldı. Postoperatif değerlendirmede eklem hareket açıklığı (EHA), Constant–Murley Skoru (CMS) ve American Shoulder and Elbow Surgeons (ASES) skoru kullanıldı. Radyolojik incelemede korakoklaviküler mesafe (KKM) ölçümleri ve Rockwood sınıflaması değerlendirildi.

Bulgular: Çalışmaya 62 hasta (47 erkek, 15 kadın; ort. yaş 29,2±16,1 yıl) dahil edildi ve ortalama takip süresi 52,9±20,5 ay idi. Anatomi redüksiyon %87 hastada sağlandı. Her iki grupta CMS (53,8±6,4’ten 89,7±5,4’e) ve ASES skorlarında (40,4±7,4’ten 89,0±7,8’e) anlamlı iyileşme görüldü ($p<0,01$). SB grubunda abduksiyon (160° vs. 153°) ve fleksiyon (172° vs. 162°) değerleri daha yüksekti. KKM her iki grupta da anlamlı olarak azaldı. Son muayenede Grup I’de bulunan hastaların %16,6’sında rekürrens gözlenirken bu oran Grup II’de %9,3 olarak bulundu ($p=0,032$).

Sonuç: Hem HP hem de SB yöntemi akut AKEÇ tedavisinde etkili olmakla birlikte, SB fiksasyonu daha iyi fonksiyonel sonuçlar, daha geniş omuz eklem hareket açıklığı ve implant çıkarma gereksiniminin ortadan kalkmasıyla öne çıkmaktadır. Bu nedenle SB yöntemi özellikle genç ve aktif hastalar için daha uygun bir cerrahi seçenek olarak değerlendirilebilir.

Anahtar Kelimeler: *Akromioklaviküler Eklem Çıkığı; Hook Plak; Suture-Buton; Fonksiyonel Sonuçlar; Omuz Eklem Hareket Açıklığı*

INTRODUCTION

Acromioclavicular joint dislocation (ACJD) occurs after direct or indirect shoulder trauma, with severity determined by the extent of acromioclavicular (AC) and coracoclavicular (CC) ligament disruption (1–3). ACJD accounts for approximately 10% of all shoulder injuries and nearly half of sports-related injuries to the shoulder girdle (4,5). The incidence is higher in males and peaks in the second decade of life (6,7).

The Rockwood classification is widely used for ACJD (8). Type I–II injuries are treated conservatively, while type IV–VI injuries are generally managed surgically (9,10). Treatment of type III injuries remains controversial and should be individualized based on functional impairment, occupational demands, activity level, and cosmetic concerns (3).

Although various surgical options exist, the optimal intervention remains debated (9,11–13). Among these, hook plate (HP) and suture-button (SB) fixation are widely used with reliable outcomes (4,11). The HP functions as a bridge between the acromion and clavicle, facilitating healing of the AC and CC ligaments, whereas the SB aims to mimic the function of the native AC and CC ligaments (13,14).

This study aimed to evaluate the functional and radiological outcomes of HP and SB fixation in ACJD. We hypothesized that SB fixation would result in superior functional outcomes, greater range of motion (ROM), and lower complication rates compared with HP fixation.

MATERIAL AND METHOD

Before the start of the study, approval was obtained from the Bilecik Şeyh Edebali University School of Medicine Ethics Committee (decision number 331994, date: 21/05/2025). Informed consent was obtained from patients who agreed to participate in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

We retrospectively examined patients who underwent surgical treatment for type III and Type V ACJD according to Rockwood classification between June 2010 and June 2023. Exclusion criteria included; 1) the presence of a metabolic bone disease, 2) osteoarthritis around the shoulder girdle, 3) infection, fracture and surgery history on the same shoulder, 4) a follow-

up period time under 2 years. The evaluation was performed by two orthopedic surgeons who did not participate in the operations and interventions at June 2025 (U.S. and Ö.C.Ç). The patients who participated were divided into two groups and evaluated: patients who operated with HP as Group I and patients who operated with SB as Group II.

Range of motion (ROM), American Shoulder and Elbow Score (ASES), Constant Murley Score (CMS) were used for functional evaluations. The ACJD were graded according to the Rockwood classification system, based on the preoperative shoulder radiographs (8). Radiographic outcomes included pre and post-operative coracoclavicular distance (CCD) measurement, development of acromial lysis, residual dislocation and/or subluxation. Postoperative wound site infection, and reoperations for hardware removal or revision and contracture release were recorded for comparing two technique.

Radiological examinations of the patients were performed after 2 weeks, 1 month, 3 months, 6 months, and annually after the first year. In addition, a radiological examination with radiographs of the shoulder was performed under the supervision of an independent orthopaedic surgeon during the examination in June 2025, during which functional assessments were made.

Surgical Technique and Rehabilitation: In both surgical methods, the patients were prepared in the beach chair position. In group I, a transverse incision was made over the AC joint. Once the AC joint was reached, the HP hook was placed as far back as possible over the AC joint. After the implantation was completed and the joint repositioning was checked under fluoroscopy, the subcutaneous tissue and skin were closed (Figure 1). In group II, a vertical incision was made starting approximately 3 cm medial to the AC joint and extending towards the coracoid process. After dissection of the soft tissue, the coracoid process and clavicle were visualized. To reduce the risk of possible fractures of the clavicle and coracoid process and implant failure, two-stage tunnels were opened under fluoroscopic control of the clavicle and coracoid process, first to the clavicle and then to the coracoid base. The SB implant was pulled with the suture retrograde from the coracoid process to the clavicle. After manual

reduction, temporary fixation was performed with a K-wire, the SB implant was tensioned and knotted, and the K-wire was removed after this phase. Soft tissue closure was then performed in a standart manner (Figure 2).

After the operation, the shoulder was immobilised with a sling for 4 weeks. Between the 2nd and 6th week, limited movement of the shoulder (90° abduction and flexion) was allowed. After the 6th week, free range of motion (ROM) was allowed. Removal of the implant (IR) was recommended at the end of the sixth month. Light resistance work was allowed after the 8th week, while heavy resistance work and sports were allowed after the 3rd months in both groups.

Statistical Analysis: Data were analyzed using SPSS Statistics (version 23.0; IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess the normality of data distribution. Categorical variables were compared using the Pearson chi-square test, Fisher’s exact test, or Fisher–Freeman–Halton test, as appropriate. Continuous variables were analyzed using the Student’s t test for parametric data and the Mann–Whitney U test for nonparametric data. For paired comparisons of non-normally distributed data, the Shapiro–Wilk and Wilcoxon signed-rank tests were applied.

A p value of <0.05 was considered statistically significant. A priori power analysis, based on previously published data, indicated that a minimum of 48 patients would be required to achieve a statistical power of 0.8. Postoperative ASES score was defined as

the primary outcome measure for the two-sample t test power calculation (15,16).

RESULTS

A total of 79 patients underwent surgery for ACJD during the study period. After excluding three patients who underwent revision surgery due to early postoperative coracoid base fractures, seven patients who declined to participate in the study, three patients with a follow-up period of less than two years, and six patients whose preoperative radiographs were unavailable, 62 patients (45M/17F) were included in the study.

The patients' mean age was 29.2±16.1 years (18–52), and the mean follow-up period was 52.9±20.5 months (24–177). Group 1 comprised 30 patients (8F/22M), and group II comprised 32 patients (7F/25M)). (Table 1) The mean period from trauma to surgery was 12.6±12.5 days (1-28) in group I and 9±7.8 days (1-17) in group II (p=0.67).

In group I, 13 of the patients were operated on for Rockwood type III ACJD and 17 patients were operated on for Rockwood type V ACJD. In group II, 17 of the patients were operated on for Rockwood type III ACJD and 15 patients were operated on for Rockwood type V ACJD (p=0.441). (Table I) Radiological evaluation at final follow-up revealed that anatomical reduction was achieved and maintained in 54 patients (87%). (Figure 1).

In group I, the CCD decreased from 18.3±3.6 mm to 10.7±1.8 mm, and in group 2, the preoperative CCD was 16.5±3.2mm and the postoperative CCD was

Table 1. Baseline demographic and clinical characteristics of patients in the hook plate (HP) and suture-button (SB) groups.

	Group I (n:30)	Group II (n:32)	p
Age (Year)	29.1±15.5	21.9±15.4	0.239
Gender (M/F)	22/8	25/7	>0.999
Follow-up period (Month)	62.2 ± 28.9	44.2±36.8	0.041
Preoperative Classification			0.441
Type III	13	17	
Type V	17	15	
Postoperative Classification			0.032
Anatomic	25	29	
Type III	4	2	
Type V	1	1	

m: male, f: female, Student’s t test / Mann–Whitney U test for continuous variables; Fisher’s exact or Chi-square test for categorical variables.

11.2±2.1 mm. There was a significant decrease pre- and postoperative CCD value in both groups. (p<0.01, p<0.01 respectively). (Table II).

Eight patients (26.6%) in Group I did not want a second operation because they had no complaints, although removal of the implant was recommended at the follow-up examination after six months.

A significant difference was noted in the pre- and postoperative CM scores between the groups. Even though group II exhibited a significantly better preoperative CM score (55.1±4.5 vs 52.2±4.7; p=0.013), group II had a significantly better postoperative CM score (94.1±5.2 vs 86.8±2.9; p=0.017). (Table III).

When ROM was compared, group II had significantly better results for abduction (153.2±5.7 vs 160.6±6.9,

p=0.019) and forward flexion (162.7±10.7 vs 172.5±5.4, p=0.032). (Table IV)

While no AC joint arthritis was observed in our patients, three patients in group I developed acromial lysis and wound infection occurred in only one patients. In Group II, three patients experienced implant failure, two patient underwent debridement and implant removal due to wound infection. After implant removal, ACJD recurred in five (16.6%) patients in Group I, while three (9.3%) patients in Group II had persistent ACJD. (p=0.032). (Table I)

DISCUSSION

Our study demonstrated that both HP and SB fixation can successfully treat acromioclavicular joint separation.



Figure 1. Shoulder X-rays of the patients in Group I and Group II taken pre- and postoperatively. Anatomical reduction achieved and maintained in both method.

Table 2. Comparison of preoperative and postoperative coracoclavicular distance in two groups

Coracoclavicular Distance				
	Overall	Group I	Group II	P
Preoperative	17.4±3.4	18.3±3.6	16.5±3.2	0.073
Postoperative	10.9±2.9	10.7±1.8	11.2±2.1	0.176
p	<0.01	<0.01	<0.01	

Paired t test/Wilcoxon signed-rank test for within-group comparisons; independent t test / Mann–Whitney U test for between-group comparisons.

Table 3. Comparison of preoperative and postoperative functional outcomes in two groups

Constant-Murley Score				
	Overall	Group I	Group II	P
Preoperative	53.8±6.4	52.2±4.7	55.1±4.5	0.013
Postoperative	89.7±5.4	86.8±2.9	94.1±5.2	0.017
p	<0.01	<0.01	<0.01	
ASES Score				
	Overall	Group I	Group II	P
Preoperative	40.4±7.4	39.7±11.9	41.0±16.2	0.407
Postoperative	89.0±7.8	87.5±8.56	94.8±6.5	0.02
p	<0.01	<0.01	<0.01	

Paired t test/Wilcoxon signed-rank test for within-group comparisons; independent t test / Mann–Whitney U test for between-group comparisons.

Table 4. Comparison of abduction and forward flexion range of motions in two groups

	Group I	Group II	p
Abduction	153.2±5.7	160.6±6.9	0.019
Forward Flexion	162.7±10.7	172.5±5.4	0.032

Independent t test / Mann–Whitney U test for between-group comparisons

However, postoperative CMS, ASES scores ($p=0.017$ and 0.02), abduction ($p=0.019$), and forward flexion ($p=0.032$) were significantly better in the SB group. Although CCD reduction was similar between the groups, SB fixation yielded superior functional outcomes. These findings are consistent with previous reports. Wang et al., in a meta-analysis of 195 HP and 204 SB patients, found better pain and functional outcomes with SB, while complication rates were comparable (13). Similarly, Lloyd et al. reported significantly higher CMS in SB patients across multiple studies (17). Güzel et al. observed faster recovery and fewer complications with SB in a comparative series of 60 patients (18). Lim et al. showed that CMS was similar at 3 months, but significantly higher with SB at 24 months (19). Ko et al. also reported better ROM in the SB group, attributing restricted forward flexion in HP patients to subacromial irritation from the hook (15). Likewise, Kim et al. noted delayed ROM recovery in HP patients due to bursal inflammation, which negatively affected early outcomes (20). Our results align with these studies, confirming that SB fixation provides better long-term function without the need for secondary surgery. The effect of preoperative ACJD type on functional outcomes has been investigated in several studies, which

have reported that as the severity of trauma increases, symptoms become more pronounced and the degree of associated soft tissue injury also rises (5,21–24). In a study conducted by Muench et al. in 2019 involving 43 patients, it was reported that those who underwent surgery for Type V ACJD had poorer functional outcomes (25). Furthermore, postoperative loss of reduction has also been shown to be associated with inferior functional results (26–28). When the functional outcomes of our patients were evaluated together with the preoperative and postoperative severity of ACJD within each group, it was observed—consistent with the literature—that patients in Group II had better functional outcomes both before and after surgery. The timing of surgery has also been linked to outcomes. Previous studies suggest that operations performed within 3 weeks of injury achieve superior reduction and functional recovery (10,29,30). In our series, all patients were operated on within the first month, with most SB patients treated within 2 weeks, which may have contributed to their superior functional results. HP fixation is frequently used in acute ACJD because of its technical simplicity and successful history in distal clavicle fractures with CC ligament injury (31). However, disadvantages include the requirement for implant

removal and complications such as subacromial erosion, osteolysis, CC ligament calcification, impingement, and rotator cuff degeneration (32–35). In our study, acromial lysis occurred in three HP patients, and ROM was more restricted than in the SB group. SB fixation avoids implant removal but is not free of complications. Loss of reduction, implant failure, coracoid fracture, and malreduction have been reported (15). Consistent with previous studies, our overall complication rates were similar between groups (17,19,36,37). In the SB group, complications included implant failure, wound infection, and persistent ACJD, while in the HP group, acromial osteolysis, wound infection, implant failure, and recurrence after implant removal were observed. This study has several limitations. Its retrospective design may have introduced selection bias. Rotator cuff pathologies were not systematically assessed, which could influence functional outcomes. Nonetheless, strengths include the use of a single implant type by one surgeon, standardized and consistently applied surgical techniques throughout the study period, in which patients in Group II underwent dynamic fixation performed by creating a single tunnel—first through the clavicle and then through the coracoid—and evaluation by independent observers using multiple scoring systems.

CONCLUSION

Both hook plate and suture-button fixation are effective options for the treatment of acute acromioclavicular joint separation. However, suture-button fixation was associated with superior functional scores, improved shoulder mobility, and avoidance of secondary implant removal. Given these advantages, SB fixation may be considered the preferred surgical option, particularly in young and active patients.

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RETROSPECTIVE ANALYSIS OF EPISTAXIS CASES: IMPACT OF COMORBIDITY AND RECURRENCE ON TREATMENT APPROACHES

Epistaksis Vakalarının Retrospektif Analizi: Eşlik Eden Hastalık ve Rekürrensin Tedavi Yaklaşımları Üzerindeki Etkisi

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ABSTRACT

Objective: This study aimed to evaluate the etiology and treatment approaches of patients who presented to our clinic with nosebleeds, in accordance with the current literature.

Material and Methods: Between January 2018 and March 2023, patients diagnosed with epistaxis who either presented to the otorhinolaryngology outpatient clinic of a tertiary university hospital or were referred from the emergency department, and whose data were accessible through the hospital information system, were retrospectively analyzed.

Results: Among 2,169 patients diagnosed with epistaxis, 658 patients aged 0–95 years who met the inclusion criteria were included in the study. The mean age was 38.4 years, and 54% were male. The highest number of admissions occurred in February. Among patients with available recurrence data, recurrent epistaxis was observed in 28.1% of cases, while a single episode occurred in 8.7%. Recurrence information was unavailable for the remaining patients. Single episodes were more frequent among females. Most patients were treated on an outpatient basis (78.9%) and received only medical therapy (90.4%). A history of surgery was present in 3.3% of cases, the majority following septorhinoplasty. Hospitalization was required in 2.6% of cases, most of whom had comorbid conditions. Recurrence rates were also higher among patients with comorbidities.

Conclusion: Epistaxis is a common otorhinolaryngologic emergency that can generally be managed effectively with outpatient medical treatment. However, recurrence and hospitalization rates are higher in elderly patients and those with comorbidities. A thorough assessment of patients' medical history and accompanying conditions is crucial for selecting the most appropriate treatment approach.

Keywords: Epistaxis; Cauterization; Surgery; Comorbidity; Recurrence

ÖZET

Amaç: Bu çalışmanın amacı, kliniğimize burun kanaması nedeniyle başvuran hastaların etyolojisini ve tedavi yaklaşımlarını güncel literatür ışığında değerlendirmektir.

Gereç ve Yöntemler: Ocak 2018 – Mart 2023 tarihleri arasında, üçüncü basamak bir üniversite hastanesinin Kulak Burun Boğaz (KBB) polikliniğine ayaktan başvuran veya acil servisten yönlendirilip verilerine hastane bilgi sistemi üzerinden ulaşılan epistaksis tanılı hastalar retrospektif olarak incelendi.

Bulgular: Epistaksis tanısı konan 2.169 hastadan dışlama kriteri bulunmayan, 0–95 yaş aralığındaki 658 hasta çalışmaya dahil edildi. Hastaların yaş ortalaması 38,4 yıl olup, %54'ü erkekti. En sık başvuru Şubat ayında gerçekleşti. Rekürrens verisine ulaşılabilen hastalarda tekrarlayan epistaksis %28,1, tek başvuru ise %8,7 oranında görüldü. Kalan olgularda rekürrens bilgisi mevcut değildi. Tek başvurular kadınlarda daha sık izlendi. Hastaların büyük kısmı ayaktan değerlendirildi (%78,9) ve medikal tedavi uygulandı (%90,4). Cerrahi öykü %3,3 oranında olup çoğunlukla septorinoplasti sonrası idi. Yatış gerektiren hastaların oranı %2,6 olup, çoğunda komorbid hastalık mevcuttu. Komorbid hastalarda rekürrens oranı daha yüksekti.

Sonuç: Epistaksis genellikle ayaktan medikal tedavi ile kontrol altına alınabilen yaygın bir KBB acilidir. Ancak ileri yaş ve komorbidite varlığı, rekürrens ve hospitalizasyon riskini artırmaktadır. Hastaların öyküsünün ve eşlik eden hastalıklarının dikkatle değerlendirilmesi, en uygun tedavi yaklaşımının belirlenmesi açısından büyük önem taşımaktadır.

Anahtar Kelimeler: Epistaksis; Koterizasyon; Cerrahi; Komorbidite; Rekürrens

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INTRODUCTION

Epistaxis is defined as spontaneous or iatrogenic bleeding within the nasal cavity that arises from vascular or coagulation disorders involving the nasal mucosa, septum, or turbinates. Epistaxis may resolve on its own or after treatment, but in exceptional instances, it can be complicated by secondary issues that can increase morbidity and, occasionally, mortality. Epistaxis is widely recognized as one of the most common otorhinolaryngologic emergencies. Epidemiological analyses consistently demonstrated a bimodal age distribution, with peak incidence among individuals aged 2–10 years and 50–80 years (1,2). Although the prevalence of epistaxis varies among populations, approximately 10% of cases require medical evaluation. Classification is based on the site of origin within the nasal cavity and is broadly categorized as anterior epistaxis—most commonly arising from Little’s area at Kiesselbach’s plexus—or posterior epistaxis, which originates from the posterior nasal segments (3,4). Epistaxis is primarily a symptom rather than a distinct diagnosis, with a multifactorial etiology. Potential causes include idiopathic factors, trauma, iatrogenic injury, infections, vascular abnormalities, neoplastic lesions, coagulopathies, medications, environmental influences, chronic systemic conditions such as hypertension, renal or hepatic insufficiency, and genetic predisposition. Although most episodes resolve spontaneously or with minimal intervention, recurrent or refractory bleeding may occur. To avert potentially life-threatening complications, timely and appropriate management is essential (5,6). To manage epistaxis optimally, it is first necessary to localize the bleeding focus with precision. The clinician subsequently performs a comprehensive evaluation of the underlying etiology.

This study aimed to evaluate and discuss our diagnostic and therapeutic algorithm for patients presenting with epistaxis—one of the most common otorhinolaryngologic emergencies and a symptom frequently encountered in clinical practice—within the context of current scientific evidence.

MATERIALS AND METHODS

Following the approval of the institutional review board for scientific ethical conduct (2023-07/05, 20.07.2023)

and written permission from the Office of the Chief Physician and the Department of Otorhinolaryngology of our tertiary university hospital, medical records were retrospectively reviewed. The study included patients who presented to the Otorhinolaryngology outpatient clinic or were referred from the emergency department with a diagnosis of epistaxis between January 2018 and March 2023. Patients with trauma-related epistaxis, postoperative bleeding, or insufficient medical records were excluded from the study. Demographic data, season of admission, lifestyle habits (smoking and alcohol use), hematological and coagulation parameters, comorbid diseases, use of high-risk medications, recurrence status, and treatment modalities were extracted from the hospital information system and analyzed.

Definitions: Recurrence was defined as rebleeding from the same site or the contralateral nasal cavity after the initial bleeding episode had been controlled. Comorbidity was defined as the presence of at least one chronic systemic disease (e.g., hypertension, diabetes mellitus, cardiovascular disease, asthma, chronic renal/hepatic disease, cerebrovascular disease, known coagulopathy, or malignancy) and/or the use of high-risk medications (anticoagulants, antiplatelet agents). Medical/conservative treatment was defined as the control of bleeding without invasive intervention, using anterior nasal compression, topical vasoconstrictors and/or local agents (e.g., adrenaline with anesthetics, topical tranexamic acid), saline irrigation, and moisturizing or antibiotic ointments. Nasal packing, chemical/electrocauterization, endoscopic hemostasis, sphenopalatine artery ligation/embolization, and blood transfusion were not classified as conservative measures but were evaluated as separate treatment categories.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as numbers (n) and percentages (%), while continuous variables were expressed as mean ± standard deviation and, when appropriate, as median (minimum–maximum). The Pearson chi-square test and Fisher’s exact test were used for comparisons of

the categorical variables. The independent samples t-test was applied for comparisons between the two independent groups, and the homogeneity of variances was assessed with Levene’s test. One-way analysis of variance (ANOVA) was used for comparisons of three or more groups. A p-value < 0.05 was considered statistically significant.

RESULTS

Between January 2018 and March 2023, 658 patients aged 0–95 years who were diagnosed with epistaxis and met the inclusion criteria were enrolled in the study. These patients were selected from a total of 2,169 individuals presenting with epistaxis to the otorhinolaryngology clinic of a university hospital (Figure 1).

Of the patients aged 0–95 years (mean 38.40 ± 26.04 years), 355 were male (54%) and 303 were female (46%), with mean ages of 37.33 ± 26.28 and 39.66 ± 25.74 years, respectively. Presentations for epistaxis peaked in February (9.59%). Recurring presentations were noted in 185 patients (28.1%), in contrast to a single presentation, which was documented in 57 patients (8.7%). None of the patients presenting with a single condition required inpatient care. Among the female patients, 38 (12.5%) had a single presentation, whereas this was observed in 19 male patients (5.4%) (p = 0.04). A total of 139 patients (21.1%) were referred

from the emergency department, whereas 519 patients (78.9%) presented directly to the outpatient clinic. Of the patients referred from the emergency department, 67.6% were successfully managed with medical therapy. In total, 595 patients (90.4%) received medical treatment on their own, with the interventions given to the other patients outlined in Table 1.

A history of surgical intervention was present in only 22 patients (3.3%), of whom 17 (77.3%) developed epistaxis following septorhinoplasty. In total, 17 patients (2.6%) required inpatient treatment. The cohort included 327 patients (49.7%) aged 10–50 years, 255 patients (38.8%) older than 50 years, and 76 patients (11.6%) younger than 10 years. The hemoglobin (Hb) levels according to age and sex groups are presented in Table 2. Mean values of INR, PT, and aPTT according to age groups are shown in Table 3. One-way ANOVA demonstrated a statistically significant difference only in the INR values among age groups (p < 0.001), while no significant differences were observed for PT and aPTT values. The effect size for this difference was small (η² = 0.024).

Research into the link between sex and recurrence found a recurrence rate of 29.9% in males and 26.1% in females. According to Pearson’s chi-square analysis, the association was found to be statistically significant (χ² = 10.886; p = 0.004). Male sex was associated with a 2.68-fold higher risk of recurrence (OR = 2.68, 95%

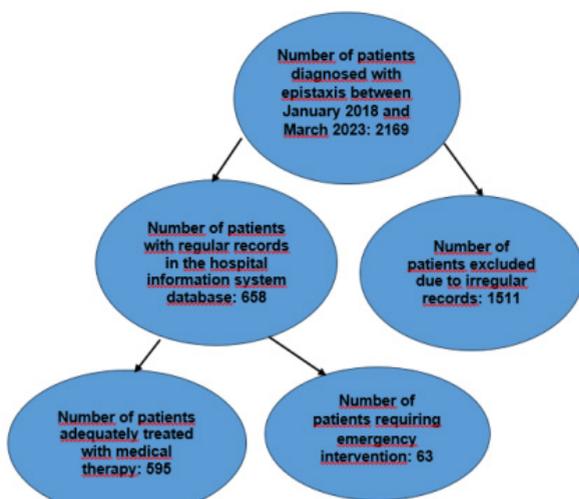


Figure 1. Flowchart illustrating the process of patient inclusion from the cohort of patients diagnosed with epistaxis.

Table 1. Interventions performed during epistaxis

Interventions performed during epistaxis	Frequency n (%)
Conservative	595(90.4%)
Anterior Nasal Packing	47(7.1%)
Chemical Cauterization	7(1.1%)
Anterior Nasal Packing + Chemical Cauterization	4(0.5%)
+Endoscopic Bleeding Control	5(0.6%)
+ Blood Product Tranfusion	2(0.3%)

Table 2. Distribution of mean hemoglobin levels gram/deciliter (g/dL) across different age and sex groups

Age ranges	Mean	N	Std.Deviation
0–6 years of age	12.23	35	1.46
6-18 years of age	15.53	182	1.23
Adult male	14.70	227	2.27
Adult female	13.00	214	1.68
Total	13.69	658	1.96

g/dL: gram/deciliter

Table 3. Comparison of INR, PT, and aPTT values according to age groups

Parameter	Age group	N	Mean±SD	Minimum-Maximum	ANOVA F	p-value
INR	0-14years	151	1.07±0.08	0.9-1.4		
	15-50years	252	1.07±0.11	0.8-2.1	8.178	<0.001*
	>50years	255	1.18±0.52	0.6-5.5		
	Total	658	1.11±0.34	0.6-5.5		
PT(sec)	0-14years	151	12.23±8.67	8.0-116.0		
	15-50years	252	11.85±1.57	7.7-19.1	1.139	0.321
	>50years	255	12.60±5.81	8.1-63.0		
	Total	658	12.23±5.59	7.7-116.0		
aPTT(sec)	0-14years	151	28.81±3.93	20.5-43.1		
	15-50years	252	28.58±4.49	0.0-42.2	0.080	0.923
	>50years	255	28.69±7.06	15.9-98.2		
	Total	658	28.68±5.52	0.0-98.2		

INR: International Normalized Ratio; PT: Prothrombin Time; aPTT: Activated Partial Thromboplastin Time, sec: second.

CI: 1.44–5.00). These results demonstrate that the incidence of recurrent epistaxis is higher among male patients than among female patients.

The prevalence of comorbid conditions was found to be 29.6%. The recurrence rate was 34.4% in patients with comorbidities, compared with 25.5% in those without ($\chi^2 = 18.162$; $p < 0.001$). These results indicate that comorbidities may constitute a significant risk factor for the occurrence of recurrent epistaxis. The recurrence rate was 25.1% in patients aged 10–50 years, increasing to 32.2% in those over 50 years.

Of the patients requiring hospitalization, 70.6% had comorbidities ($p = 0.001$), while 64.7% presented via the emergency department (Table 4). Comorbidity increased the likelihood of hospitalization nearly sixfold (OR = 5.99, 95% CI: 2.08–17.26), while emergency presentation was strongly associated with hospitalization (OR = 7.28, 95% CI: 2.64–20.05). The results indicate that comorbid conditions and emergency presentation significantly predict

hospitalization among patients with epistaxis.

Recurrent epistaxis is significantly associated with hospitalization, surgical intervention, and patient age. Recurrence was observed in 58.8% of hospitalized patients, whereas the rate was 27.8% among non-hospitalized patients, a difference that was statistically significant ($\chi^2 = 8.229$; $p = 0.016$). Surgical intervention was performed in 62.5% of hospitalized patients, whereas only 1.9% of non-hospitalized patients required surgery, a difference that was highly significant ($\chi^2 = 173.028$; $p < 0.001$). Recurrence was more frequent among patients older than 50 years, with a statistically significant association identified between age and recurrence ($\chi^2 = 11.373$; $p = 0.023$) (Table 5).

DISCUSSION

Epistaxis is a common condition, affecting nearly 60% of individuals at least once during their lifetime. In most cases, epistaxis occurs spontaneously in the absence of

Table 4. Association of comorbidity and emergency admission with hospitalization

Variable	Category	Hospitalization (+)	Hospitalization (-)	Chi-square (X ²)	p-value
Comorbidity	Present	12 (70.6%)	5 (29.4%)	13.978	<0.001
	Absent	179 (28.6)	447 (71.4%)		
Emergency admission	Yes	11 (64.7%)	6 (35.3%)	19.616	<0.001
	No	126 (20.1%)	500 (79.9%)		

Table 5. Factors Associated with Hospitalization and Recurrence in Patients with Epistaxis

Variable	Category	Group (%)	Comparison	Chi-square (X ²)	p-value
Hospitalization vs. Recurrence	No hospitalization	Recurrence: 27.8 % No recurrence: 6.9 %	Higher recurrence in hospitalized patients (%58.8)	8.229	0.016
	Hospitalization	Recurrence: 58.8 % No recurrence: 0.0 %			
Hospitalization vs. Surgical Intervention	No hospitalization	Surgery: 1.9 % No surgery: 98.1 %	Surgical intervention more frequent in hospitalized patients (%62.5)	173.028	<0.001
	Hospitalization	Surgery: 62.5 % No surgery: 37.5 %			
Age Group vs. Recurrence	<10 years	Recurrence: 27.6 % No recurrence: 3.9 %	Recurrence more frequent in patients >50 years (%32.2)	11.373	0.023
	10-50 years	Recurrence: 25.1 % No recurrence: 7.3 %			
	>50 years	Recurrence: 32.2 % No recurrence: 11.8 %			

an identifiable trigger. The etiology may involve local factors, such as trauma, mucosal dryness, intranasal medications, infection, inflammation, or neoplasms, as well as systemic factors, including hematologic disorders, leukemia, atherosclerosis, hypertension, and congestive heart failure (7). Although nearly 90% of epistaxis episodes are clinically insignificant, resolving spontaneously within minutes without the need for medical care, in patients with comorbidities, they may result in severe complications including hypotension, aspiration, hypoxia, and myocardial infarction (8). Epidemiological research on epistaxis remains relatively limited. Previous large population-based studies, which are similar to this research, have mainly relied on hospital records; nevertheless, the absence of systematic collection of patient data

remains a significant obstacle to conducting a thorough investigation of this widespread condition. The majority of studies in the literature demonstrated a higher incidence of epistaxis among males. In a cohort of 104 emergency and outpatient cases, Ruhela et al. reported that 68.3% occurred in male patients (9). Similarly, Kaygusuz et al. reported that 67.7% of the patients who were hospitalized for treating epistaxis were male. In contrast, Shaw et al., in their study of 65 cases of epistaxis, reported that 47% occurred in males and 53% in females (10). In a comprehensive analysis of 1,724 patients presenting with epistaxis, Juselius reported a male predominance of 58%. This finding aligns with the 54% observed in our series and confirms a comparable gender distribution. The slightly lower male ratio in our cohort may be

attributable to the inclusion of outpatients and the broader population base, which could have diluted the relative predominance of male cases (11).

Environmental factors such as humidity and temperature have been implicated in the occurrence of epistaxis, leading many authors to investigate its seasonal and monthly distribution. A study conducted in India in 2022 reported that 42.31% of epistaxis presentations occurred during the cold winter months (9). Similarly, Pallin et al., in their analysis of approximately 4.5 million epistaxis visits, did not identify any significant variation across different months, consistent with the findings of our study (12). Geographical differences, levels of regional development, and occupational profiles may substantially modify the environmental conditions, thereby influencing the seasonality of epistaxis presentations. Some authors have specifically reported an increased frequency of epistaxis during months characterized by hot and dry climates (13).

Recurrent epistaxis is clinically significant because it may represent the initial manifestation of an underlying systemic or neoplastic disease. The likelihood of recurrent bleeding and clinically relevant blood loss or transfusion is particularly high in patients receiving anticoagulant or antiplatelet therapy (14). In our study, the recurrence rate among patients with comorbid conditions was found to be 34.4%. Moreover, 70.6% of the hospitalized patients had comorbidities ($p = 0.001$). In a meta-analysis including 896 cases, the frequency of recurrent epistaxis was reported as 13.4%, whereas in our cohort this rate was notably higher at 28.1% (15). It has been reported that 6% of patients treated for epistaxis in emergency departments require hospitalization for the aggressive management of severe nasal bleeding (12). In contrast, our research found this rate to be 2.6%. In a study including 104 patients diagnosed with epistaxis, 79.81% of the cases were managed on an outpatient basis (9). In our study, a very similar rate of 78.9% was observed. In previous studies, medical or conservative treatment was sufficient in 69.1%–85.6% of patients (6,9). In our study, medical or conservative management proved sufficient in 90.4% of the cases. Nevertheless, arterial ligation or embolization remains an option for refractory, persistent, or recurrent episodes. Similarly, Kucur et al. reported that surgical intervention was

required in only 1.5% of patients with epistaxis, underscoring that operative approaches are reserved for a very limited subset of cases (3). In our study, 0.9% of the patients required surgical intervention in the form of endoscopic hemostasis or sphenopalatine artery ligation. This technique is effective in controlling recurrent, intractable bleeding in approximately 98% of cases (16).

A history of previous surgical intervention was present in only 22 patients (3.3%) in our cohort, of whom 17 (77.3%) experienced epistaxis following septorhinoplasty. This rate is comparable to the incidence of postoperative epistaxis reported in the literature after septorhinoplasty (2–4.5%) (17,18). As rhinoplasty procedures become more common, it is likely that the rates of such surgeries will continue to increase.

Notably, 67.6% of the patients transferred from the emergency department required only medical treatment. This outcome may suggest either the general practitioner's inability to handle initial and emergency nosebleed cases or a preference for referring patients due to medicolegal concerns in university hospitals that have residents or specialists available in the relevant field. Future studies and targeted training programs for emergency physicians should be planned to address this issue.

The limitations of this study include its retrospective, single-center design, irregular data, the broad categorization of comorbidities, and the absence of information on the localization of bleeding and hospital stay. Validation of these findings requires future prospective, multicenter studies.

CONCLUSION

Epistaxis is a common condition that should not be underestimated. Careful evaluation of the patient's medical history and comorbidities is crucial, and recurrent episodes must be recognized as potential indicators of underlying systemic or local disease. Future large-scale cohort studies with systematic data collection are warranted to provide more robust insights into its clinical significance.

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İNFERTİL HASTALARDA UYGULANAN VARİKOSELEKTOMİNİN SPERMİOGRAM PARAMETRELERİNE ETKİSİ

The Effect of Varicocele on Semen Parameters in Infertile Patients

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ÖZET

Amaç: Varikozel erkek infertilitesinin tedavi edilebilir en önemli nedenlerinden biridir. Varikozel çeşitli mekanizmalarla infertiliteye sebebiyet vermekte olup en çok suçlanan mekanizmalar yüksek ısı ve oksidatif strestir. Varikoselektomi ile bu etkilerin önüne geçilerek fertilitate katkı sağlanmaktadır. Çalışmamızda infertil hastalarda yapılan varikoselektominin semen parametrelerinde iyileşmeye katkısı olup olmadığını değerlendirmek amaçlanmıştır.

Gereç ve Yöntemler: Primer infertilite nedeniyle üroloji polikliniğine başvuran ve en az grade 2 varikozeli olup varikoselektomi yapılmış olan 18-40 yaşları arasında hastaların sistemde kayıtlı olan verileri retrospektif olarak değerlendirildi. Hastaların semen analizlerinde semen hacmi, total sperm sayısı, sperm konsantrasyonu, ileri hareketli sperm yüzdeleri ve toplam hareketli sperm oranları semen parametreleri olarak kayıt altına alındı. Hastaların spermioqram değerleri preoperatif ve postoperatif olarak karşılaştırıldı.

Bulgular: İncelenen 110 hastanın operasyon öncesi ve sonrası bakılan semen parametrelerinde toplam sperm sayısı ($p<0,001$), sperm konsantrasyonu ($p<0,001$), ileri hareketli sperm oranları ($p=0,007$) ve total hareketli sperm oranlarında ($p=0,044$) postoperatif anlamlı artış vardı. Semen volümlerinde anlamlı değişiklik yoktu ($p=0,150$).

Sonuç: Yapılan çalışmaların çoğu varikoselektominin olumlu sonuçlarından bahsederken varikozelin infertilite üzerine etkisi ve tedavisinin fertilitate katkısı olmadığını savunanlar da vardır. Çalışmamız varikoselektominin primer infertil hastalarda semen parametreleri ve sperm kalitesi üzerinde anlamlı ve klinik açıdan değerli etkileri olduğunu desteklemektedir. Bu veriler, hem yardımcı üreme tekniklerine hazırlık hem de doğal yolla gebe kalma şansının artırılması bağlamında klinik kararları desteklemektedir.

Anahtar Kelimeler: Varikozel; Varikoselektomi; Infertilite; Semen Analizi; Spermioqram

ABSTRACT

Objective: Varicocele is one of the most significant treatable causes of male infertility. It contributes to infertility through various mechanisms, the most frequently implicated being elevated scrotal temperature and oxidative stress. Varicocele aims to mitigate these effects and thereby enhance fertility potential. This study aimed to evaluate whether varicocele in infertile patients leads to improvements in semen parameters.

Material and Methods: The study retrospectively evaluated data from patients aged 18–40 years who presented to the urology outpatient clinic with primary infertility and underwent varicocele for at least grade 2 varicocele. Recorded semen parameters included semen volume, total sperm count, sperm concentration, percentage of progressively motile sperm, and total motile sperm percentage. Preoperative and postoperative semen analysis results were compared.

Results: Analysis of 110 patients revealed statistically significant postoperative improvements in total sperm count ($p<0.001$), sperm concentration ($p<0.001$), percentage of progressively motile sperm ($p=0.007$), and total motile sperm percentage ($p=0.044$). No significant change was observed in semen volume ($p=0.150$).

Conclusion: While many studies emphasize the positive effects of varicocele, some argue that varicocele has no substantial impact on fertility and that its treatment may not contribute to improved fertility outcomes. Our study supports the notion that varicocele yields statistically and clinically significant improvements in semen parameters and sperm quality in patients with primary infertility. These findings have important implications for clinical decision-making, both in preparing patients for assisted reproductive techniques and in enhancing the potential for natural conception.

Keywords: Varicocele; Varicocele; Infertility; Semen Analysis; Spermioqram

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Giriş

Varikozel, testisin venöz drenajında görevli üç daldan oluşan (A.spermatice interna, A.deferenstialis, A.kremasterica) pampiniform pleksusun dilatasyonu olarak tanımlanmaktadır (1). İnfertilite ise Dünya Sağlık Örgütü (WHO) tarafından 12 ay veya daha uzun süreli düzenli korunmasız cinsel ilişki sonrası klinik gebelik elde edilememesiyle sonuçlanan üreme sisteminin bir hastalığı olarak tanımlanmaktadır (2). Dünya Sağlık Örgütü (WHO), varikozelin erkek infertilitesinin önemli bir nedeni olduğunu ve tedavi edilebilir en önemli nedenlerden olduğunu belirtmiştir.

Genel popülasyonda varikozel prevalansının % 8-15 olduğu tahmin edilmektedir; ancak primer infertilitesi olan erkeklerde prevalans %35 ve sekonder infertilitesi olan erkeklerde %80 düzeyindedir (3).

Varikozel öncelikle fiziksel muayene sırasında teşhis edilir ve Dubin ve Amelar sistemine göre derecelendirilir: Subklinik varikozel: varikozel fizik muayenede palpe edilemez ancak USG ile tanı konulabilir; 1.Derece varikozel: skrotumdaki varikoz damarlar ancak Valsalva manevrası ile palpe edilebilir; 2.Derece varikozel: pampiniform pleksus Valsalva manevrası olmadan palpe edilebilir; 3.Derece varikozel: herhangi bir manevra veya manipülasyon olmaksızın skrotumda damarlar inspeksiyonla gözlemlenebilir (4).

Avrupa Üroloji Derneği kılavuzlarında anormal semen parametreleri/DNA fragmentasyon indeksi ve başka sebeplerle açıklanamayan infertilitesi olan yetişkin hastalarda varikosektomi önerilmektedir (5).

Varikozelin infertilite üzerine etkisinde yüksek ısı, adrenal hormon reflüsü, gonadotoksik metabolit reflüsü, değişen testis kan akımı, antisperm antikor oluşumu, hipotalamus-hipofiz-gonadal ekseninde değişiklikler ve oksidatif stres gibi pek çok teori öne sürülmekte olup en çok suçlanan ve en kabul görmüş teoriler yüksek ısı ve oksidatif stres teorileridir (6). Sağlıklı erkeklerde skrotal sıcaklık, vücut iç sıcaklığından 2°C daha düşüktür (7). Vücut içi sıcaklığına eşit olan testis sıcaklığı, sperm sayısında ve kalitesinde azalma ile ilişkilidir. Isı artışının spermatogenez üzerine etki mekanizması tam olarak bilinmemekle birlikte, en çok suçlanan mekanizma, Leydig hücrelerinin ve/veya spermatik tübül hücrelerinin çekirdeğindeki DNA ve proteinlerde termal hasar olmasıdır (7, 8). Varikozel ve bozulmuş sperm kalitesi olan erkeklerde skrotal

sıcaklıkların yükseldiği ve varikosektominin normal skrotal sıcaklığa yol açtığı bildirilmiştir (7-9).

Literatürdeki varikosektominin infertilite üzerindeki etkisiyle ilgili güncel verilerde tutarsızlıklar vardır, bunun başlıca nedeni tanı, tedavi ve sonuç parametrelerindeki farklılıklardır. Örneğin; bazı çalışmalarda tüm derecelerdeki varikozellere tedavi uygulanırken bazı çalışmalarda yalnızca klinik varikozellere tedavi uygulanmıştır; bazı çalışmalarda mikroskopik varikosektomi uygulanırken bazı yayınlarda mikroskop kullanılmamıştır. Yapılan bazı randomize kontrollü çalışmalarda infertilite hastalarında varikosektominin fertiliteye katkısı gösterilememişken bazı çalışmalarda ise varikosektominin infertilitenin önemli bir tedavisi olduğu ve tedavi sonrası hastaların çoğunun çocuk sahibi olabildiği belirtilmiştir (10-15).

Biz de bu çalışma ile varikosektominin semen parametrelerinde iyileşmeye katkısı olup olmadığını belirlemek istiyoruz.

GEREÇ VE YÖNTEMLER

Yozgat Bozok Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan (Tarih:30.05.2025 Karar No: 2025-GOKAEK-258_30.04.2025_483) onay alındıktan sonra Ocak 2018-Nisan 2025 tarihleri arasında primer infertilite nedeniyle üroloji polikliniğine başvuran varikozel tespit edilip subinguinal varikosektomi yapılmış olan 18-40 yaşları arasında hastaların sistemde kayıtlı olan verileri retrospektif olarak değerlendirildi. Primer infertilite dışındaki varikosektomi hastaları, sekonder vakalar, azospermik hastalar, genital sistem enfeksiyonu (orşit, epididimit, üretrit vb.), kemoterapötik ilaç kullanımı olan hastalar ve hormon profilinde patoloji saptanan hastalar çalışmaya dahil edilmedi. Çalışmamızda varikozele bağlı infertil hastalarda varikozelin infertiliteye olan etkisi incelendiğinden tütün ve tütün ürünleri kullananlar, obez ve morbid obez hastalar, partnerinde açıklanabilen kadın infertilitesi olan hastalar da çalışma dışı bırakıldı. Tüm hastaların ayakta ve Valsalva manevrası ile yapılmış olan varikozel muayene kayıtları ve muayene sonrasında çekilen renkli skrotal doppler ultrasonografi (RDUS) kayıtları incelendi. Tüm hastaların Dubin ve Amelar sistemine göre evreleri kayıt altına alındı. Evreleme sisteminde

Grade 0 (inspeksiyon ve palpasyonla tespit edilemeyen sadece RDUS ile tespit edilebilen (subklinik); Grade 1 (sadece valsalva manevrası ile tespit edilebilen); Grade 2 (palpasyonla hissedilebilen fakat inspeksiyon ile tespit edilemeyen) ve Grade 3 (inspeksiyon ile net olarak görülebilen) varikozel olarak kabul edildi. Hastaların varikosektomi öncesi ve varikosektomiden 6 ay sonra alınmış olan semen analizleri değerlendirildi. Semen analizleri alınmadan önce Dünya Sağlık Örgütü kriterleri kullanılarak, 3-7 günlük cinsel perhiz uygulanmıştı. Taranan semen analizlerinde semen hacmi, total sperm sayısı, sperm konsantrasyonu, ileri hareketli sperm yüzdeleri ve toplam hareketli sperm oranları semen parametreleri olarak kayıt altına alındı. Hastaların preoperatif ve operasyondan sonra 6. ayda alınan semen analizi değerleri karşılaştırıldı. İstatistiksel analizler IBM SPSS statistics version 26.0 kullanılarak yapıldı. Verilerin normal dağılımının değerlendirilmesi için Kolmogorov– Smirnov testi kullanıldı. Parametrik verilerin karşılaştırılmasında Paired-sample T-test, non-parametrik verilerin karşılaştırılmasında Wilcoxon Signed Ranks Test kullanıldı. $p < 0,05$ istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Ocak 2018-Nisan 2025 tarihleri arasında primer infertilite nedeniyle başvuru varikosektomi tespit edilen ve subinguinal varikosektomi uygulanan hastalardan toplam 148 hastanın kayıtlarına ulaşılabildi. Dışlama kriterleri sonrası verileri tam olan 110 hasta çalışmaya dahil edildi. Hastaların tamamı primer infertil, tamamında en az grade 2 varikozel olup hepsi primer varikosektomi uygulanan hastalardı. Tanımlayıcı istatistikler de hastaların yaş aralığı 20-40 olarak belirlendi (ortalama:30,5). Hastaların operasyon öncesi ve sonrası bakılan semen analizlerinde toplam

sperm sayısı, sperm konsantrasyonu, ileri hareketli sperm oranları ve total hareketli sperm oranlarında postoperatif anlamlı artış vardı. Semen volümlerinde anlamlı değişiklik yoktu. Preoperatif toplam sperm sayısı ortancası 27 (1,4-148) milyon iken post-operatif toplam sperm sayısı ortancası 38 (1-168) milyon olarak tespit edildi. Preoperatif sperm konsantrasyonu ortancası 8 (0,35-52) milyon/ml iken post-operatif sperm konsantrasyonu ortancası 11 (0,2-61) milyon/ml olarak tespit edildi. İleri hareketlilik (a+b) ortancası preoperatif %25 (0-86) iken postoperatif %30 (0-73)'a yükseldi. Toplam hareketli sperm yüzdesi (a+b+c) ortancası ise preoperatif %45 (0-86) iken postoperatif %50 (0-85)'ye yükseldi (Tablo 1).

TARTIŞMA

Çalışmamızda, primer infertil ve en az grade 2 varikozeli olan hastalara uygulanan varikosektomi sonrası 6 aylık dönemde sperm konsantrasyonu, total sperm sayısı, progresif ve total motilite açısından anlamlı iyileşmeler gözlenmiştir; semen hacminde ise değişiklik olmamıştır. Bu veriler, literatürdeki sistematik inceleme ve meta-analizlerle uyum içindedir. Pek çok çalışmada varikosektomi sonrası sperm konsantrasyonu, motilite, morfoloji ve total sperm sayısında belirgin artışlar olduğu ve semen hacminde anlamlı değişiklik olmadığı bildirilmiştir (16-21). Yapılan bir meta-analizde varikosektomi sonrası sperm konsantrasyonunda 7,23 milyon/ml, total hareketli sperm sayısında %6,31'lik bir artış olduğu raporlanmıştır. Bizim çalışmamızda da 3 milyon/ml konsantrasyon artışı, %5 toplam hareketlilik artışı belirlenmiştir (20).

Yapılan çalışmaların çoğu varikosektominin olumlu sonuçlarından bahsederken varikozelin infertilite üzerine etkisi ve tedavisinin fertiliteye katkısı olmadığını savunanlar da vardır (10-12). Yapılan bir reviewda spontan gebelik oranlarında varikosektomi ile kontrol

Tablo 1. Hastaların pre-operatif ve post-operatif semen parametreleri

	Preoperatif	Postoperatif	P value ^a
Semen volumü, ml (median,min-max)	3 (0,4-8)	3 (0,4-7)	0,150
Sperm konsantrasyonu mil/ml (median,min-max)	8 (0,35-52)	11 (0,2-61)	<0,001
Total sperm sayısı, mil (median,min-max)	27 (1,4-148)	38 (1-168)	<0,001
Progresif motilite oranı (tip a+b) % (median,min-max)	25 (0-86)	30 (0-73)	0,007
Total motilite oranı (tip a+b+c) % (median,min-max)	45 (0-86)	50 (0-85)	0,044

a. Wilcoxon Signed Ranks Test

grubu arasında anlamlı fark bulunmamıştır (22). European Association of Urology (EAU) kılavuzlarının aksine National Institute for Health and Clinical Excellence (NICE) kılavuzlarında varikosektomi, doğurganlık üzerine faydası olmadığı belirtilerek infertilite tedavisinde önerilmemektedir (23).

Yapılan çalışmalarda varikosektomiden üç ay sonra 6. aya kadar semen parametrelerinde en optimal iyileşme süresi olduğu belirtilmiştir. Bizim çalışmamızda da kontrol semen analizi 6. ayda bakılmış ve anlamlı artışlar gözlenmiştir. Literatürde semen parametrelerinde maksimum iyileşme 3.–6. aylar arasında tespit edilmiş olmakla beraber bu konuda daha fazla sayıda randomize kontrollü çalışmalara ihtiyaç bulunmaktadır (20). Böylece gebelik planlaması için en optimum süre tespit edilip daha olumlu klinik sonuçlar alınabilir.

Literatürde varikosektomi sonrası semen parametrelerindeki düzelmede varikozel derecesi önemli bir parametre olarak gösterilmiştir. Bir çalışmada subklinik varikozeli olan hastalarda yapılan operasyonun sperm konsantrasyonu ve hareketliliğinde anlamlı artış yapmadığı belirtilmiştir (24). Bir meta-analizde subklinik varikozel hastalarının operasyondan çok az klinik fayda gördükleri belirtilmiştir (25). Bizim çalışmamızda en az grade 2 varikozeli olan hastalara operasyon yapılmış olup post-op analizlerde anlamlı fayda sağlandığı görülmüştür.

Çalışmamızda retrospektif doğası nedeniyle olası kayıt eksiklikleri; varikozel derecesi ile operasyon sonrası semen parametrelerindeki değişim oranının incelenmemesi; gebelik oranlarına ulaşamamış olması ve subklinik ve grade 1 varikozel hastalarının çalışmaya dahil edilmemesi çalışmamızın kısıtlılıkları arasında yer almaktadır.

Pek çok çalışmada seminal oksidatif stres ve DNA hasarının varikosektomi sonrası azaldığı bildirilmiştir (26). Ancak çalışmamızda oksidatif stres ve DNA hasarı değerlendirilemediğinden bu çalışmamızın bir limitasyonu sayılabilir. Yapılan çalışmalarda infertil varikozel hastalarında spontan babalık oranları varikosektomi yapılmayanlara göre yaklaşık 2 kat daha fazladır (15, 27, 28). Ancak çalışmamızın en büyük limitasyonlarından birisi babalık oranlarına ulaşamamış olmamızdır. Bu nedenle çalışmamızda sadece semen parametrelerindeki düzelme değerlendirilmiştir.

SONUÇ

Çalışmamız varikosektominin primer infertil hastalarda semen parametreleri ve sperm kalitesi üzerinde anlamlı ve klinik açıdan değerli etkileri olduğunu desteklemektedir. Bu veriler, hem IVF gibi yardımcı üreme tekniklerine hazırlık hem de doğal yolla gebe kalma şansının artırılması bağlamında klinik kararları desteklemektedir. Ancak heterojen çalışma dizaynları ve teknik farklılıklar araştırmaların genellenabilirliğini sınırlamaktadır. Daha güçlü kanıtlar için büyük ölçekli, tasarlanmış randomize kontrollü çalışmalara gereksinim vardır.

Tasdik ve Teşekkür

Yazarlar arasında herhangi bir çıkar çatışması yoktur.

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ADANA'DA 80 YAŞ VE ÜZERİ BİREYLERDE TOPLUM TEMELLİ GERİATRİK DEĞERLENDİRME: TANIMLAYICI KESİTSEL BİR ÇALIŞMA

Community-Based Geriatric Assessment in Individuals Aged 80 and Over in Adana: A Descriptive Cross-Sectional Study

Zeynep KAHYAOĞLU¹, Esmâ DAĞDELEN¹, Melih Gaffar GÖZÜKARA²

ÖZET

Amaç: İleri yaşlarda malnütrisyon, depresyon, bilişsel bozukluk, kırılabilirlik ve fonksiyonel yetersizlikler sık görülen geriatric sendromlardır. Bu sendromlar genellikle bir arada bulunur ve yaşlı bireylerin morbidite, mortalite ve yaşam kalitesini olumsuz etkiler. Bu çalışmada, Adana'da toplum temelli 80 yaş ve üzeri bireylerde geriatric sendromların sıklığı ve aralarındaki ilişkiler değerlendirildi.

Gereç ve Yöntemler: Tek merkezli, kesitsel ve tanımlayıcı bu çalışmada Adana'da yaşayan 80 yaş ve üzeri bireyler ev ziyaretleri kapsamında değerlendirildi (n=86). Katılımcılara Mini Nutrisyonel Test–Kısa Form (MNA-SF), Geriatric Depresyon Ölçeği–15 (GDS-15), Mini Mental Test (MMT), Klinik Kırılabilirlik Ölçeği (CFS), Günlük Yaşam Aktiviteleri (GYA), Enstrümantal Günlük Yaşam Aktiviteleri (EGYA), Zamanlı Kalk ve Yürü Testi (TUG) ve 5 Tekrar Otur-Kalk Testi (5xSST) uygulandı. Veriler tanımlayıcı istatistiklerle sunuldu; değişkenler arası ilişkiler Pearson korelasyon testiyle değerlendirildi.

Bulgular: Katılımcıların yaş ortalaması $85,8 \pm 3,0$ yıl, %57'si kadındı. Ortalama skorlar: MNA-SF $11,6 \pm 1,7$, GDS-15 $4,1 \pm 3,0$, MMT $24,6 \pm 2,6$, CFS $3,6 \pm 0,6$ idi. MNA-SF ile GDS-15 arasında negatif ($r = -0,39$, $p = 0,001$), MNA-SF ile MMT arasında pozitif korelasyon ($r = 0,47$, $p < 0,001$) saptandı. CFS, GYA ($r = -0,57$, $p < 0,001$) ve EGYA ($r = -0,63$, $p < 0,001$) ile güçlü ilişkilidi.

Sonuç: Çok ileri yaş bireylerde malnütrisyon, depresyon, bilişsel bozulma ve kırılabilirlik sık görülmekte olup birbirleriyle ilişkilidir. Bulgular, toplum temelli yaşlı bireylerde çok boyutlu geriatric değerlendirmenin önemi vurgulamaktadır.

Anahtar Kelimeler: Geriatri; Malnütrisyon; Depresyon; Geriatric Sendromlar

ABSTRACT

Objective: Malnutrition, depression, cognitive impairment, frailty, and functional decline are common geriatric syndromes in advanced age. These conditions frequently coexist and adversely affect morbidity, mortality, and quality of life in older adults. This study aimed to evaluate the prevalence and interrelationships of geriatric syndromes among community-dwelling adults aged 80 years and older in Adana, Türkiye.

Material and Methods: This single-center, cross-sectional, and descriptive study included 86 participants aged ≥ 80 years who were evaluated during home visits. Each participant underwent the Mini Nutritional Assessment–Short Form (MNA-SF), Geriatric Depression Scale–15 (GDS-15), Mini-Mental Test (MMT), Clinical Frailty Scale (CFS), Basic Activities of Daily Living (BADL), Instrumental Activities of Daily Living (IADL), Timed Up and Go (TUG), and Five Times Sit-to-Stand Test (5xSST). Data were analyzed using descriptive statistics, Pearson's correlation.

Results: The mean age was 85.8 ± 3.0 years, and 57% were female. Mean scores were MNA-SF 11.6 ± 1.7 , GDS-15 4.1 ± 3.0 , MMT 24.6 ± 2.6 , and CFS 3.6 ± 0.6 . A negative correlation was found between MNA-SF and GDS-15 ($r = -0.39$, $p = 0.001$) and a positive correlation between MNA-SF and MMT ($r = 0.47$, $p < 0.001$). CFS was strongly correlated with BADL ($r = -0.57$, $p < 0.001$) and IADL ($r = -0.63$, $p < 0.001$).

Conclusion: Malnutrition, depression, cognitive decline, and frailty were common and interrelated among very old, community-dwelling adults. The findings highlight the importance of comprehensive geriatric assessment in this population.

Keywords: Geriatrics; Malnutrition; Depression; Geriatric Syndromes

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GİRİŞ

İleri yaşlı bireylerde malnütrisyon, depresyon, bilişsel bozukluk, kırılabilirlik ve fonksiyonel yetersizlikler en sık karşılaşılan geriatrik sendromlar arasında yer almaktadır. Bu sendromlar yalnızca yaşam kalitesini düşürmekle kalmaz, aynı zamanda mortalite, hastane yatışlarında, bağımlılık riskinde ve bakım yükünde artış ile ilişkilidir. Literatürde, bu sendromların sıklıkla bir arada bulunduğu ve birbirleri üzerinde karşılıklı etkilerinin olduğu belirtilmektedir (1).

Malnütrisyonun taranmasında kullanılan Mini Nutrisyonel Test-Kısa Form (MNA-SF) geriatride en yaygın kullanılan geçerli ve pratik araçlardan biridir (2). Depresyon taraması için Geriatrik Depresyon Ölçeği Kısa Formu (GDS-15/Yesavage) yaşlı popülasyonda güvenilirliği kanıtlanmış bir ölçektir (3). Ayrıca bilişsel durumun değerlendirilmesinde Mini Mental Test (MMT) kırılabilirlik ölçümünde Klinik Kırılabilirlik Ölçeği (CFS) günlük yaşam bağımsızlığını ölçmede Katz Günlük Yaşam Aktiviteleri (GYA) ve Enstrümental Günlük Yaşam Aktiviteleri Ölçeği (EGYA) fiziksel performansta ise Zamanlı Kalk ve Yürü Testi (TUG) ve 5 Kez Otur Kalk Testi (5xSST) sık kullanılan araçlardır (4-9).

Bu çalışma, Adana'da toplum temelli 80 yaş ve üzeri bireylerde geriatrik sendromların dağılımını ve bu parametreler arasındaki ilişkileri ortaya koymayı amaçlamaktadır.

GEREÇ VE YÖNTEMLER

Bu çalışma, tek merkezli ve kesitsel tasarımı bir araştırma olup, 80 yaş ve üzerindeki bireylerden oluşan bir örneklem üzerinde gerçekleştirilmiştir (n = 86). Katılımcılar Adana ili sınırlarında, sağlık bakanlığı koordinasyonunda yürütülen yaşlı izlem programı kapsamındaki ev ziyaretleri sırasında değerlendirilmiştir. Bu bireyler, Evde Sağlık Hizmetleri birimi tarafından izlenen ya da bakım ihtiyacı nedeniyle sürekli sağlık desteği alan hastalar değil, toplum içinde yaşayan, kendi evlerinde bağımsız veya yarı bağımsız yaşam sürdüren bireylerdir. Hastaların sosyodemografik özellikleri (yaş, cinsiyet, eğitim düzeyi) kaydedilmiştir. Çalışmaya dahil edilme kriterleri, en az 80 yaşında olmak, bilişsel olarak temel iletişimi sürdürebilmek ve çalışmaya gönüllü olarak katılmayı kabul etmek şeklinde belirlenmiştir.

Bu örneklem, Adana'daki ileri yaş nüfusun

sosyodemografik dağılımını yansıtan toplum temelli bir grup olup, elde edilen bulgular yaşlı popülasyonun genel özelliklerini temsil etmektedir.

Katılımcıların değerlendirilmesinde çok boyutlu bir yaklaşım benimsenmiştir. Kullanılan testler ve ölçekler aşağıda özetlenmiştir:

Mini Nutrisyonel Test-Kısa Form (MNA-SF): Yaşlı bireylerde beslenme durumunu değerlendirmek için kullanılan geçerli ve güvenilir bir tarama aracıdır (2). Toplam altı sorudan oluşur ve maksimum puan 14'tür. Puanlamaya göre ≥ 12 puan normal beslenme, 8–11 arası malnütrisyon riski, ≤ 7 puan ise malnütrisyon varlığı olarak kabul edilir.

Geriatrik Depresyon Ölçeği – 15 Madde Kısa Formu (GDS-15/Yesavage): Yaşlı bireylerde depresif belirtileri taramak için geliştirilmiştir. Evet/hayır yanıtı 15 sorudan oluşur. Yüksek puanlar depresif belirti düzeyinin arttığını göstermektedir. Klinikte ve saha araştırmalarında yaygın kullanılan geçerli bir ölçektir (3).

Mini Mental Test (MMT): Bilişsel fonksiyonları değerlendirmek amacıyla kullanılmıştır. Test 30 puan üzerinden değerlendirilir. 24 ve üzeri puanlar normal kabul edilirken, 18–23 puan arası kognitif bozulma riski, 17 ve altı ise demans göstergesi olarak kabul edilir (4). Klinik Kırılabilirlik Ölçeği (CFS): Bireylerin kırılabilirlik düzeyini ölçmek için kullanılan, 1'den 9'a kadar derecelendirilmiş görsel bir skala olup, 1 puan çok sağlıklı, 9 puan terminal derecede kırılabilir bireyi temsil etmektedir. Geriatri pratiğinde kırılabilirliğin hızlı taraması için yaygın kullanılan bir ölçektir (5).

Günlük Yaşam Aktiviteleri (GYA): Bireylerin bağımsız yaşama kapasitesini ölçen bu test, temel aktiviteleri (giyinme, banyo yapma, kontinans, mobilite, beslenme) değerlendirir. GYA puanı düştükçe bireyin bağımsızlık düzeyi azalmakta, bakıma ihtiyaç artmaktadır (6).

Enstrümental Günlük Yaşam Aktiviteleri (EGYA): Temel aktivitelerin ötesinde, bireyin toplumsal yaşamda bağımsız kalabilmesini sağlayan daha karmaşık görevleri (alışveriş yapma, telefon kullanma, ilaç yönetimi, ev işleri, finansal işler vb.) değerlendirir. EGYA, bireyin fonksiyonel kapasitesini GYA'ya göre daha ayrıntılı olarak yansıtır (7).

Zamanlı Kalk ve Yürü Testi (TUG): Katılımcının oturduğu sandalyeden kalkıp 3 metre yürüyerek geri dönüp oturma süresini ölçen basit ve pratik bir testtir.

Normalde 20 saniyenin altında tamamlanması beklenir. 20 saniyenin üzerindeki süreler düşme riski açısından uyarıcıdır (8). Çalışmamızda TUG skorları saniye cinsinden kaydedilmiştir.

5 Tekrar Otur-Kalk Testi (5xSST): Alt ekstremite kas gücü ve fonksiyonel mobiliteyi değerlendiren bir testtir. Katılımcıdan ardışık olarak 5 kez oturup kalkması istenir ve geçen süre saniye cinsinden kaydedilir. 15 saniyenin üzerindeki değerler sarkopeni riskine işaret eder (9).

Bu çalışma, Adana Şehir Eğitim ve Araştırma Hastanesi Bilimsel Araştırmalar Etik Kurulu tarafından onaylanmıştır (Toplantı Sayısı: 17, Karar Tarihi: 25.09.2025, Karar No: 759). Çalışmaya dahil edilen tüm katılımcılardan veya yasal temsilcilerinden yazılı bilgilendirilmiş onam alınmıştır. Katılımcı bilgilerinin gizliliği, Helsinki Bildirgesi ilkelerine uygun şekilde korunmuştur.

İstatistiksel Analiz

Verilerin analizinde IBM SPSS Statistics for Windows, Sürüm 26.0 (IBM Corp., Armonk, NY, ABD) programı kullanılmıştır. Tanımlayıcı istatistikler ortalama \pm standart sapma veya yüzde (%) olarak sunulmuştur. Değişkenler arasındaki doğrusal ilişkiler Pearson korelasyon analizi ile değerlendirilmiştir. $p < 0,05$ değeri istatistiksel anlamlılık sınırı olarak kabul edilmiştir.

BULGULAR

Çalışmaya toplam 86 birey dahil edilmiştir. Katılımcıların yaş ortalaması $85,83 \pm 3,04$ yıl olup, tüm bireyler 80 yaş ve üzerindedir. Örneklem, Adana'daki toplum temelli ileri yaş nüfusun karakteristiğini yansıtmaktadır.

Katılımcıların %57'si kadın ($n=49$), %43'ü erkek ($n=37$) idi. Eğitim düzeyi dağılımı incelendiğinde %27,2'si okur-yazar değil, %8,6'sı yalnızca okur-yazar, %33,3'ü ilkökul, %3,7'si ortaokul, %17,3'ü lise ve %9,9'u üniversite mezunu olarak kaydedilmiştir (Tablo 1).

Çalışma grubunun genel sağlık durumu, fiziksel performans ve psikososyal göstergeler açısından dengeli bir profil sergilediği görülmektedir. Beslenme durumunu gösteren MNA-SF ortalaması $11,58 \pm 1,71$ olup, katılımcıların %63,9'u normal beslenme durumunda ($n=55$), %32,9'u malnütrisyon riski altında ($n=28$) ve %2,3'ü malnütrisyon grubunda ($n=2$) olarak sınıflandırılmıştır.

GDS-15 ortalaması $4,11 \pm 3,04$ olup, katılımcıların

%52,3'ü normal ruhsal durumdadır ($n=45$). %37,2'sinde hafif depresif belirtiler ($n=32$) ve %10,5'inde belirgin depresyon riski ($n=9$) saptanmıştır.

MMT ortalaması $24,63 \pm 2,58$ olarak bulunmuştur. Katılımcıların MMT sonuçlarına göre %75,9'u normal bilişsel düzeyde ($n=60$), %22,8'inde hafif bilişsel bozukluk ($n=18$) ve %1,3'ünde orta-ileri düzey bilişsel bozukluk ($n=1$) saptanmıştır.

CFS ortalaması $3,64 \pm 0,65$ ile katılımcıların çoğunun "hafif kırılğan" kategorisinde yer aldığını göstermektedir.

Fonksiyonel bağımsızlık düzeyleri değerlendirildiğinde, GYA ortalaması $5,53 \pm 0,90$ ve EGYA ortalaması $6,76 \pm 1,81$ olarak hesaplanmış; bu da bireylerin kişisel bakım aktivitelerinde genellikle bağımsız olduklarını, ancak karmaşık işlevlerde (alışveriş, ulaşım, ilaç yönetimi gibi) zaman zaman desteğe gereksinim duyduklarını göstermektedir.

Fiziksel performans testlerinden TUG ortalaması $10,51 \pm 3,14$ sn olup, katılımcıların büyük bölümünün düşme riski açısından normal mobilite sınırlarında olduğu saptanmıştır. 5xSST ortalaması $14,30 \pm 4,64$ sn olup, alt ekstremite kas gücü ve fonksiyonel kapasitenin yaşa göre korunmuş, ancak bazı bireylerde sarkopeni eşliğine yaklaşan değerler gösterdiği belirlenmiştir.

Genel olarak örneklem, ileri yaşta olmasına karşın göreceli olarak iyi beslenme, hafif düzeyde kırılğanlık, bağımsız yaşam yetisi ve düşük düşme riski profili ile tanımlanabilir (Tablo 2).

Çalışmada, yaşlı bireylerde kullanılan temel geriatrik değerlendirme ölçekleri arasında anlamlı korelasyonlar saptanmıştır. Kırılğanlık ile fonksiyonel bağımsızlık göstergeleri olan GYA ve EGYA arasında güçlü negatif korelasyon bulunmuştur. Kırılğanlık arttıkça günlük yaşam aktivitelerinde bağımsızlığın azaldığı görülmektedir. Beslenme durumu ile bilişsel işlevler arasında pozitif, depresyon ile ise negatif ilişki saptanmıştır. Bu bulgular, yetersiz beslenmenin hem bilişsel hem de ruhsal sağlıkla yakından ilişkili olduğunu göstermektedir. GDS-15 puanı, GYA, EGYA ve CFS ile anlamlı şekilde ilişkili bulunmuş, depresyon arttıkça fiziksel ve işlevsel kapasitenin azaldığı belirlenmiştir. En güçlü korelasyonlar CFS-EGYA ($r=-0,63$) ve GYA-EGYA ($r=0,59$) arasında saptanmıştır. Bu bulgu, literatürle uyumlu olarak, kırılğanlık düzeyinin artışıyla fonksiyonel kapasitede belirgin bir azalma görüldüğünü ve yaşlı

bireylerde bu iki parametrenin klinik olarak birbirine sıkı biçimde bağlı olduğunu göstermektedir (Tablo 3).

TARTIŞMA

Bu çalışma, Adana'da toplum temelli olarak değerlendirilen 80 yaş ve üzeri bireylerde çok boyutlu

geriyatrik değerlendirme sonuçlarını ortaya koymuş ve geriyatrik sendromlar arasındaki etkileşimleri incelemiştir. Çalışmanın uygulandığı populasyon ülkemizdeki ileri yaşlı nüfusun demografik profilini temsil eden tipik bir tablo çizmiştir (10) Bulgular, ileri yaşlı bireylerde beslenme durumu, bilişsel performans,

Tablo 1. Katılımcıların Sosyodemografik Özellikleri

Değişken	n	%
Kadın	49	57,0
Erkek	37	43,0
Okur-yazar değil	22	27,2
Okur-yazar	7	8,6
İlkokul	27	33,3
Ortaokul	3	3,7
Lise	14	17,3
Üniversite	8	9,9

Tablo 2. Kapsamlı Geriyatrik Değerlendirme Testleri

Ölçek	Ortalama ± SS
MNA-SF	11,58 ± 1,71
Yesavage (GDS-15)	4,11 ± 3,04
MMT	24,63 ± 2,58
CFS	3,64 ± 0,65
GYA	5,53 ± 0,90
EGYA	6,76 ± 1,81
TUG (sn)	10,51 ± 3,14
5xSST (sn)	14,0 ± 4,64

MNA-SF: Mini Nutritional Test- Kısa Form; GDS-15: Geriyatrik Depresyon Ölçeği-15 Madde Kısa Formu; MMT: Mini Mental Test; CFS: Klinik Kırılabilirlik Ölçeği; GYA: Günlük Yaşam Aktiviteleri; EGYA: Enstrümantal Günlük Yaşam Aktiviteleri; TUG: Zamanlı Kalk ve Yürü Testi; 5xSST: Beş Tekrar Otur-Kalk Testi.

Tablo 3. Ölçekler ve Korelasyonlar (Pearson r, p < 0,05)

Değişken 1	Değişken 2	r	p
CFS	EGYA	-0,63	<0,001
GYA	EGYA	+0,59	<0,001
CFS	GYA	-0,57	<0,001
GDS-15 (Yesavage)	CFS	+0,48	<0,001
MNA-SF	MMT	+0,47	<0,001
GDS-15	EGYA	-0,41	<0,001
MNA-SF	GDS-15	-0,39	0,001
MNA-SF	EGYA	+0,34	0,002
GDS-15	GYA	-0,30	0,007
MNA-SF	CFS	-0,30	0,008
MMT	CFS	-0,28	0,016

MNA-SF: Mini Nutrisyonel Test-Kısa Form; GDS-15: Geriyatrik Depresyon Ölçeği-15 Madde Kısa Formu; MMT: Mini Mental Test; CFS: Klinik Kırılabilirlik Ölçeği; GYA: Günlük Yaşam Aktiviteleri; EGYA: Enstrümantal Günlük Yaşam Aktiviteleri; TUG: Zamanlı Kalk ve Yürü Testi; 5xSST: Beş Tekrar Otur-Kalk Testi.

depresyon, kırılabilirlik ve fonksiyonel bağımsızlık arasında güçlü ilişkiler bulunduğunu göstermektedir. Çalışmamızda MNA-SF ile GDS-15 skorları arasında orta düzeyde negatif bir korelasyon saptanmıştır. Bu bulgu, yetersiz beslenme durumunun depresif belirtilerle yakından ilişkili olduğunu bildiren önceki araştırmalarla paralellik göstermektedir. Literatürde, yaşlı bireylerde malnütrisyon riskinin depresyon olasılığını yaklaşık iki kat artırdığı bildirilmektedir (11). Bangladeş'te yapılan bir çalışmada yaşlı popülasyonda beslenme durumu ile depresyon skorları arasında benzer biçimde güçlü bir negatif ilişki ($r = -0,44$, $p < 0,001$) saptanmış; bu sonuç, beslenme yetersizliğinin ruhsal sağlık üzerindeki etkisini desteklemektedir (12). Bu ilişki iki yönlü değerlendirilebilir. Malnütrisyon nörotransmitter sentezinde azalma, triptofan metabolizmasında bozulma ve inflamasyon aracılığıyla duyu durumunu etkilerken; depresyon da iştah azalması, anhedoni ve özbakım bozukluğu yoluyla beslenmeyi olumsuz etkileyebilir (13, 14).

MNA-SF ile MMT arasındaki pozitif korelasyon beslenme durumunun bilişsel performansla yakından ilişkili olduğunu göstermektedir. Bu bulgu, mevcut literatürde bildirilen sonuçlarla da uyumludur. Yapılan çalışmalarda, toplumda yaşayan yaşlı bireylerde malnütrisyon ve bilişsel bozulma arasında anlamlı bir ilişki olduğu bildirilmiştir (15). Benzer biçimde 2021 yılında yayımlanan prospektif bir araştırmada, ileri yaşlı bireylerde beslenme durumundaki bozulmanın bilişsel işlevlerde azalma ile paralel seyrettiği gösterilmiştir (16). Bu durum, özellikle ileri yaşta enerji, protein ve mikrobeyin yetersizliklerinin nörolojik rezerv üzerinde olumsuz etki yarattığını düşündürmektedir.

Çalışmamızda GDS-15 skorları, CFS ve fonksiyonel kapasite ile anlamlı korelasyon göstermiştir. Bu ilişki, fiziksel ve zihinsel işlev bozukluklarının kırılabilirlik gelişimiyle örtüşüğünü ileri süren literatürle de uyumludur. Örneğin Park ve arkadaşlarının çalışmasında, fiziksel fonksiyon testleri, bilişsel performans ve depresyon düzeyleri ile kırılabilirlik durumu arasında güçlü bağlantılar saptanmıştır (17). Ayrıca Almeida ve arkadaşlarının prospektif çalışmasında, depresyonu olan yaşlı erkeklerin ileride fonksiyonel kapasite kaybı yaşama olasılığının daha yüksek olduğuna dikkat çekmiştir (18). Bu veriler, depresif belirtilerin yalnızca ruhsal değil, fiziksel ve fonksiyonel düzeylerde de

olumsuz etkileri olabileceğini desteklemektedir. Bu veriler, çalışmamızdaki ilişkilerin hem biyopsikososyal açıdan tutarlı olduğunu hem de ileri yaşta müdahale odaklı bakış açısının önemini vurgulamaktadır.

Bu çalışmada en güçlü korelasyon CFS ile EGYA arasında saptanmıştır. Bu sonuç, kırılabilirliğin özellikle enstrümantal günlük yaşam aktiviteleri üzerindeki etkisini açıkça göstermektedir. Bulgular, kırılabilirliğin yalnızca fiziksel kapasitedeki azalmayı değil, aynı zamanda karmaşık günlük işlevlerde (örneğin alışveriş, ilaç yönetimi, finansal işlemler gibi) bağımsızlığın kaybını da öngördüğünü desteklemektedir. Bu sonuçlar, Newman ve arkadaşlarının çalışmasında öne sürdükleri model ile uyumludur. Söz konusu çalışmada kırılabilirliğin bir spektrum boyunca ilerleyen dinamik bir süreç olduğu ve fonksiyonel kapasite ile güçlü şekilde ilişkili bulunduğu bildirilmiştir (19). Bu ilişkiye destek veren çalışmalardan biri de Chang ve arkadaşlarının prospektif gözlemsel çalışmasıdır. Bu çalışmada Geriatrik Akut Bakım Ünitesinde izlenen yaşlı hastalarda kırılabilirlik statüsü ile GYA arasında anlamlı bir ilişki bulunmuş; kırılabilir gruplar, fonksiyonel olarak bağımsız gruba kıyasla işlevsel iyileşme oranları farklı olarak saptanmıştır (20). Bu tür bulgular, kırılabilirlik durumunun yalnızca fonksiyonel düşüşle değil, aynı zamanda iyileşme potansiyeliyle de bağlantılı olduğunu göstermektedir. Bizim çalışmamızda da kırılabilirlik düzeyinin artışı, hem GYA hem EGYA skorlarındaki düşüşle birlikte seyretmiştir. Bu durum, ileri yaşlı bireylerde fonksiyonel bağımsızlığın korunması için kırılabilirliğin erken dönemde tanınması ve multidisipliner yaklaşımla yönetilmesinin klinik önemini vurgulamaktadır.

Bu çalışmanın güçlü yönü, 80 yaş ve üzeri ileri yaşlı bireylerde toplum temelli veri toplanmış olmasıdır. Evde sağlık hizmeti alan bireyler dahil edilmediğinden, örneklem aktif toplum yaşlılarını temsil etmektedir. Ayrıca çok boyutlu geriatrik değerlendirme yaklaşımıyla biyopsikososyal dengenin tüm bileşenleri analiz edilmiştir. Bu çalışmanın sınırlılıkları arasında örneklemin bölgesel (Adana) ve tek merkezli olması ve kesitsel tasarım nedeniyle nedensel ilişki kurulamayışı yer almaktadır.

SONUÇ

Adana'da toplum temelli 80 yaş ve üzeri bireylerde malnütrisyon riski, depresyon, bilişsel zayıflama ve kırılabilirlik sık görülmekte; bu durumlar birbirleriyle anlamlı biçimde ilişkili bulunmaktadır. Bulgular, çok ileri yaşlı bireylerde multidisipliner geriatrik değerlendirmenin zorunluluğunu vurgulamaktadır.

Klinik açıdan, yaşlı bireylerin izlemlerinde beslenme, bilişsel işlev, ruhsal durum ve fonksiyonel kapasitenin eşzamanlı değerlendirilmesi önerilmektedir. Bu sayede erken tanı ve müdahale olanağı sağlanarak yaşam kalitesi korunabilir. İleriye dönük olarak, prospektif ve girişimsel çalışmalar bu ilişkilerin nedensel yönünü ve olası müdahale hedeflerini netleştirecektir.

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IN VITRO EVALUATION OF THE EFFECTS OF IODINATED CONTRAST AGENTS ON GUT MICROBIOTA

İn Vitro İyotlu Kontrast Maddelerin Bağırsak Mikroorganizmaları Üzerindeki Etkilerinin Değerlendirilmesi

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ABSTRACT

Objective: The aim of this study was to investigate whether commonly used iodinated contrast agents exert bacteriostatic or bactericidal effects on selected commensal and opportunistic microorganisms that constitute the gut microbiota. Given the widespread use of these agents in diagnostic imaging, understanding their potential impact on microbial viability is of clinical importance.

Material and Methods: Strains of *Candida* spp., *Lactobacillus* spp., *Staphylococcus epidermidis*, *Enterococcus* spp., and *Escherichia coli* were cultured under standard laboratory conditions. Each strain was exposed to five different iodinated contrast agents at five dilution levels (1/1, 1/2, 1/4, 1/8, and 1/16). Antimicrobial activity was assessed using the disk diffusion method, a widely accepted in vitro technique for evaluating the inhibitory effects of chemical agents on microbial growth. All cultures were incubated aerobically at 37°C for periods ranging from 18 to 48 hours, depending on the growth characteristics of each microorganism.

Results: None of the tested contrast agents showed detectable bacteriostatic or bactericidal effects against any of the microorganisms at any dilution level. Growth patterns of all strains were consistent across different agent types and concentrations, indicating no inhibition of microbial proliferation.

Conclusion: Under controlled in vitro conditions, the iodinated contrast agents tested—including Ultravist 370, Omnipaque 350, Biemexol 350, Kopaç 300, and Omnipol 350—did not demonstrate any antimicrobial activity against selected gut microorganisms. These findings suggest that these agents are unlikely to directly affect gut microbial viability in the short term, supporting their safety in terms of maintaining normal intestinal microbial populations during routine diagnostic procedures.

Keywords: Iodinated Contrast Agents; Gut Microbiota; Antimicrobial Effects; Disk Diffusion

ÖZET

Amaç: Bu çalışmanın amacı, yaygın olarak kullanılan iyotlu kontrast ajanlarının, bağırsak mikrobiyotasını oluşturan seçilmiş kommensal ve fırsatçı mikroorganizmalar üzerinde bakteriyostatik veya bakterisidal etkiler gösterip göstermediğini araştırmaktır. Bu ajanların tanısal görüntüleme de yaygın olarak kullanılması göz önüne alındığında, mikroorganizma canlılığı üzerindeki olası etkilerini anlamak klinik açıdan önem taşımaktadır.

Gereç ve Yöntemler: *Candida* spp., *Lactobacillus* spp., *Staphylococcus epidermidis*, *Enterococcus* spp. ve *Escherichia coli* suşları standart laboratuvar koşullarında kültüre edildi. Her suş, beş farklı iyotlu kontrast ajana beş farklı seyreltme düzeyinde (1/1, 1/2, 1/4, 1/8 ve 1/16) maruz bırakıldı. Antimikrobiyal etkinlik, kimyasal ajanların mikroorganizma büyümesini inhibe etme etkilerini değerlendirmek için yaygın olarak kullanılan in vitro bir yöntem olan disk difüzyon yöntemi ile değerlendirildi. Tüm kültürler, mikroorganizmaların büyüme özelliklerine bağlı olarak 18–48 saat süreyle 37°C’de aerobik koşullarda inkübe edildi.

Bulgular: Test edilen kontrast ajanlarının hiçbiri, herhangi bir mikroorganizma üzerinde herhangi bir seyreltme düzeyinde bakteriyostatik veya bakterisidal etki göstermedi. Tüm suşların büyüme paternleri, ajan türü ve konsantrasyonundan bağımsız olarak tutarlıydı ve mikroorganizma çoğalmasının engellenmediğini gösterdi.

Sonuç: Kontrollü in vitro koşullarda, Ultravist 370, Omnipaque 350, Biemexol 350, Kopaç 300 ve Omnipol 350 dahil olmak üzere test edilen iyotlu kontrast ajanlar, seçilmiş bağırsak mikroorganizmaları üzerinde antimikrobiyal aktivite göstermedi. Bu bulgular, bu ajanların kısa vadede bağırsak mikrobiyal canlılığını doğrudan etkilemesinin olası olmadığını ve rutin tanısal işlemler sırasında normal bağırsak mikrobiyal popülasyonlarının korunması açısından güvenli olduklarını düşündürmektedir.

Anahtar Kelimeler: İyotlu Kontrast Ajanlar; Bağırsak Mikrobiyotası; Antimikrobiyal Etkiler; Disk Difüzyon

INTRODUCTION

In modern medicine, medical imaging is indispensable for diagnosing and monitoring diseases (1). Imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography facilitate non-invasive evaluation of internal organs and early detection of pathological changes. To enhance the effectiveness of these techniques, contrast agents are frequently used to more clearly visualize tissue density differences, and therefore, lesions (2). These agents are critical for comprehensively evaluating vascular structures, the gastrointestinal system, and hollow organs (2, 3). Contrast agents can be administered through various routes, such as oral, rectal, and intravenous, depending on the clinical indication (3). Oral or rectal contrast agents are preferred for gastrointestinal imaging, while intravenous agents are used for detailed evaluations of the circulatory system and internal organs (3). The route of administration directly affects both image quality and systemic absorption, potentially influencing biological effects.

Iodinated contrast agents are the most frequently used in radiological imaging, especially CT. Iodine, with its high atomic number, strongly absorbs X-rays, creating contrast. Non-ionic, low-osmolar formulations are preferred in clinical practice because of their good biological tolerance and low toxicity (3). While these agents are primarily excreted renally, a portion of them can be eliminated through the gastrointestinal system. This raises concerns about their potential impact on a person's gut microbiota, which refers to the community of microorganisms living symbiotically within their body.

The compositions of a person's microbiotas are influenced by numerous factors such as genetics, birth method, diet, environmental exposures, and medication use. These microbiotas densely populate different regions of the body, including the gastrointestinal tract, skin, respiratory tract, oral cavity, and urogenital system, and they play vital roles in maintaining the host's health (4, 5).

The gut microbiota is the most densely populated microbial ecosystem in the human body, consisting of trillions of microorganisms—mainly Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria—

that contribute to fermentation, short-chain fatty acid production, immune regulation, and maintenance of intestinal barrier integrity (6–8).

Disruptions in this ecosystem, known as dysbiosis, are linked to several conditions including, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), obesity, diabetes, neuropsychiatric disorders, and cancer, largely through impaired immunity and chronic inflammation (6,9). The microbiota is highly sensitive to external factors such as antibiotics, diet, medications, and chemical exposures (10).

In this context, the impact of iodinated contrast agents on gut microorganisms remains poorly understood (11,12). Although early ionic agents containing free iodine exhibited antimicrobial activity, evidence regarding modern non-ionic agents is limited. Mosler et al. suggested that residual free iodine may provide minimal antimicrobial effects (13). These findings highlight the need to investigate the potential direct or indirect influence of iodinated contrast agents on gut microbiota.

MATERIALS AND METHODS

This study was approved by the Sivas Cumhuriyet University Ethics Committee (Decision No: 2025/07-07). Five different microorganisms were included in the study: *Candida* spp., *Lactobacillus* spp., coagulase-negative *Staphylococcus epidermidis*, *Enterococcus* spp., and *Escherichia coli*. All strains were American Type Culture Collection standard strains and were stored in milk at -20°C until the study day. One day before the study, they were subcultured onto appropriate media and revitalized.

The contrast agents tested were Ultravist 370 mg/ml, Omnipaque 350 mg/ml, Biemexol 350 mg/ml, Kopaq 300 mg/ml, and Omnipol 350 mg/ml. For each contrast agent, solutions were prepared immediately before use with distilled water at dilution ratios of 1/1 (undiluted), 1/2, 1/4, 1/8, and 1/16.

The disk diffusion method was used to detect and measure the antimicrobial activities of radioopaque substances. Whatman paper (Whatman No.4) was punched with a hole punch, and the obtained paper disks were placed in glass petri dishes and sterilized in an autoclave at 121°C for 15 minutes. Each disk was impregnated with 20 µl of contrast agent solution.

Following EUCAST (The European Committee on Antimicrobial Susceptibility Testing) recommendations, coagulase-negative *Staphylococcus epidermidis*, *Enterococcus* spp., *Lactobacillus*, and *Escherichia coli* strains were prepared to 0.5 McFarland, and *Candida* spp. to 1 McFarland in IDBroth. From the prepared solutions, *Staphylococcus epidermidis*, *Escherichia coli*, and *Candida* spp. were inoculated onto Mueller-Hinton agar (MHA) using swab sticks for lawn plating. *Enterococcus* spp. and *Lactobacillus* were lawn-plated onto blood agar media. Within five minutes, contrast agent-impregnated Whatman papers were placed onto the media using forceps.

Plates with disks were placed in an incubator at 35±1°C and incubated for 18±2 hours. Evaluations were performed by measuring with a ruler from the back of the plate against a dark background for MHA, and from the front with the plate lid open for disks placed on blood agar media. Due to the qualitative nature of growth observations (presence or absence of growth) and the lack of quantitative measurements, formal statistical analysis was not performed. All disk diffusion assays were performed in triplicate to ensure

reproducibility.

RESULTS

All tested microorganisms showed visible growth at all dilution levels of each contrast agent (Table 1, Figure 1 a-b). No bacteriostatic (growth inhibition) or bactericidal (growth cessation) effects were observed in any group. All microorganisms *Lactobacillus* spp., *Enterococcus* spp., *Staphylococcus epidermidis*, *Escherichia coli*, and *Candida* spp. successfully grew in the presence of Ultravist 370, Omnipaque 350, Biemexol 350, Kopaq 300, and Omnipol 350 at 1/1, 1/2, 1/4, 1/8, and 1/16 dilutions.

No observable differences in growth patterns were detected between different contrast agents or between various dilution levels (Table 2). No inhibition zone formation was detected in any contrast agent in the disk diffusion test (Figure 1 a-b). All microorganisms showed normal growth patterns around contrast agent disks, and no growth restriction was observed. The diameter of inhibition zones remained the same as the disk diameter in all cases (6 mm), indicating no antimicrobial activity.

Table 1. Results of antimicrobial activity of iodinated contrast agents against tested microorganisms by disk diffusion method.

Microorganism	Ultravist 370	Omnipaque 350	Biemexol 350	Kopaq 300	Omnipol 350
	Dilution Levels (1/1, 1/2, 1/4, 1/8, 1/16)				
<i>Candida</i> spp.	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)
<i>Lactobacillus</i> spp.	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)
<i>S. epidermidis</i>	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)
<i>Enterococcus</i> spp.	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)
<i>E. coli</i>	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)	(-), (-), (-), (-), (-)

(-) No inhibition zone/bacterial growth present. No antimicrobial effect was detected for any microorganism at all contrast agents and dilution levels.

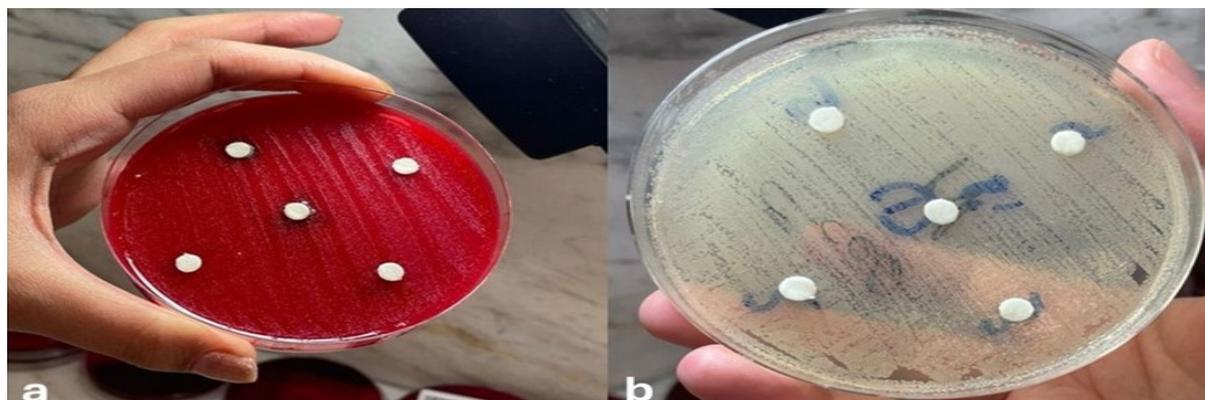


Figure 1. a. Application of disk diffusion method for measuring antibiotic resistance on blood agar medium. **b.** Application of disk diffusion method for measuring antibiotic resistance on Mueller-Hinton agar medium.

Table 2. Microbial growth evaluation according to incubation periods.

Contrast Agent	Incubation Period	Microbial Growth Status
Ultravist 370	18 hours	Positive growth in all microorganisms
	24 hours	Positive growth in all microorganisms
	48 hours	Positive growth in all microorganisms
Omnipaque 350	18 hours	Positive growth in all microorganisms
	24 hours	Positive growth in all microorganisms
	48 hours	Positive growth in all microorganisms
Biemexol 350	18 hours	Positive growth in all microorganisms
	24 hours	Positive growth in all microorganisms
	48 hours	Positive growth in all microorganisms
Kopaq 300	18 hours	Positive growth in all microorganisms
	24 hours	Positive growth in all microorganisms
	48 hours	Positive growth in all microorganisms
Omnipol 350	18 hours	Positive growth in all microorganisms
	24 hours	Positive growth in all microorganisms
	48 hours	Positive growth in all microorganisms

DISCUSSION

In this in vitro study, none of the five iodinated contrast agents—Ultravist 370, Omnipaque 350, Biemexol 350, Kopaq 300, and Omnipol 350—demonstrated bactericidal or bacteriostatic activity against *Candida* spp., *Lactobacillus* spp., *Staphylococcus epidermidis*, *Enterococcus* spp., or *Escherichia coli*. These findings indicate that, under standard laboratory conditions, iodinated contrast agents do not directly inhibit microbial growth.

This study contributes to the limited literature evaluating the direct effects of modern non-ionic iodinated contrast agents on microorganisms relevant to the gut microbiota. Given their widespread use in diagnostic imaging, particularly during gastrointestinal examinations, understanding their microbiological safety is clinically important. Oral contrast agents are frequently used to improve visualization of bowel pathology, and therefore clarifying their interaction with gut microorganisms holds clinical relevance.

Although CT enterography (CTE) is now a key modality for small bowel imaging, especially in inflammatory bowel disease, the detailed technical aspects of contrast administration vary across clinical settings. Neutral oral contrast agents are preferred because they enhance assessment of bowel wall enhancement without obscuring mucosal detail. As patients typically

ingest relatively large volumes of oral contrast during CTE, evaluating whether these agents affect gut microbiota is of practical importance. Our findings provide reassurance that commonly used iodinated contrast agents do not exert direct antimicrobial effects on representative commensal or opportunistic microorganisms (14,15).

Previous studies have reported inconsistent antimicrobial properties among contrast agents. Brönnimann et al. found minimal inhibition at pH 7.4 and more notable suppression at acidic pH, suggesting that pH may modulate antimicrobial effects. However, no inhibition was observed against *S. aureus* or *P. aeruginosa*, consistent with our findings (16). Older ionic agents were known to possess antimicrobial effects due to free iodine content, whereas modern non-ionic formulations appear to have minimal or no direct activity (12,13). Our results further support the view that current iodinated contrast agents have limited antimicrobial potential.

The clinical implications of these findings are noteworthy. Since contrast-enhanced imaging is widely used across diverse patient populations, including those with inflammatory bowel disease or chronic conditions requiring repeated examinations, the absence of direct antimicrobial effects reduces concern about potential acute disruption of gut microbial populations.

This study has several limitations. The *in vitro* design does not reflect the complexity of the human gastrointestinal environment, where factors such as pH fluctuations, osmolarity, host immunity, microbial interactions, and metabolic activity all contribute to microbial dynamics (5,6). Our experiments were conducted under standard laboratory pH (7.0–7.4), and therefore do not account for potential pH-dependent effects described in previous literature. Additionally, anaerobic gut conditions could not be simulated, and many dominant gut microorganisms were not represented in our model.

While no direct antimicrobial activity was observed, indirect effects of contrast agents—such as alterations in intestinal permeability, osmotic balance, or metabolic signaling—cannot be excluded (8). Future studies using fecal microbiota cultures, gut-on-a-chip models, animal experiments, and metagenomic approaches are required to better elucidate contrast agent–microbiota interactions and to assess long-term or cumulative exposure effects.

CONCLUSION

In conclusion, this study demonstrated that iodinated contrast agents do not possess bactericidal or bacteriostatic effects under *in vitro* conditions. While these findings provide preliminary evidence suggesting that contrast-enhanced imaging procedures are safe in terms of microbial viability in the short term, they do not exclude the possibility of indirect or long-term effects on the gut microbiota. Advanced studies incorporating more comprehensive, physiologically realistic, and *in vivo* models are urgently needed to fully elucidate this topic.

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YOZGAT BOZOK ÜNİVERSİTESİ ARAŞTIRMA VE UYGULAMA HASTANESİ CERRAHİ KLİNİKLERİNDE YATIŞI YAPILAN HASTALARDA OBSTRÜKTİF UYKU APNE SENDROMU PREVELANSI VE FARKINDALIĞININ DEĞERLENDİRİLMESİ

Evaluation of the Prevalence and Awareness of Obstructive Sleep Apnea Syndrome in Hospitalized Patients in the Surgical Clinics of Yozgat Bozok University Research and Training Hospital

Ümmühan Tuğba TUMÜKLÜ¹, Vugar Ali TÜRKSOY², Zehra SEYFİKLİ¹

ÖZET

Amaç: Bu çalışmanın amacı, Yozgat Bozok Üniversitesi Araştırma ve Uygulama Hastanesi cerrahi kliniklerinde hospitalize edilen hastalarda Obstrüktif Uyku Apne Sendromu (OUAS) prevalansını belirlemek ve bireylerin hastalık farkındalık düzeylerini değerlendirmektir. Elde edilen bulguların, preoperatif dönemde uygulanacak sistematik tarama protokollerinin hasta güvenliği ve cerrahi sonuçlara etkisini ortaya koyması hedeflenmiştir.

Gereç ve Yöntemler: Bu kesitsel, tanımlayıcı ve analitik araştırma, 2024 yılı boyunca cerrahi kliniklerde yatarak tedavi edilen 18 yaş üzeri erişkin bireylerde yürütülmüştür. Bilgilendirilmiş onamı bulunan ve iletişim kurabilen hastalar çalışmaya dahil edilmiş; OUAS tanısı ile izlenenler ile bilişsel bozukluğu veya akut psikiyatrik hastalığı olanlar dışlanmıştır. Veriler yüz yüze görüşmelerle yapılandırılmış anket formu ve Epworth Uykululuk Ölçeği ile toplanmış, yüksek riskli olgular polisomnografi için aday kabul edilmiştir. Etik kurul onayı alınan çalışma Helsinki Deklarasyonu'na uygun yürütülmüş, veriler SPSS 20.0 programında analiz edilmiştir.

Bulgular: Çalışmaya dahil edilen 250 hastanın yaş ortalaması 60,1±9,2 yıl olup %68'i erkekti. En sık OUAS ilişkili semptom horlama (%57,2), ardından gündüz uykululuk hali (%31,6) ve tanıklı apne (%8,4) geldi. Ortalama Epworth skoru 5,13±3,89 olup olguların %89,2'si normal düzeydeydi. BMI ortalaması 29,21±4,80 kg/m² olup erkeklerde anlamlı olarak yüksekti (p<0,001). Sigara kullanım oranı %19,6 olup erkeklerde daha fazlaydı. PFÖ Ayırimsama Alt Ölçeği puanı kadınlarda anlamlı düzeyde yüksekti (p<0,001).

Sonuç: Bulgular, preoperatif dönemde farkındalık temelli tarama yaklaşımlarının önemini vurgulamakta; yalnızca semptom sorgulamasının yetersiz kalabileceğini göstermektedir. OUAS'nın multidisipliner yönetimi cerrahi güvenliği ve hasta sonuçlarını olumlu yönde etkileyebilir.

Anahtar Kelimeler: *Obstrüktif Uyku Apne Sendromu; Cerrahi Hastalar; Farkındalık*

ABSTRACT

Objective: This study aimed to determine the prevalence of Obstructive Sleep Apnea Syndrome (OSAS) among patients hospitalized in the surgical clinics of Yozgat Bozok University Research and Training Hospital and to assess their level of disease awareness. The findings are intended to highlight the potential impact of systematic preoperative screening protocols on patient safety and surgical outcomes.

Material and Methods: This cross-sectional, descriptive, and analytical study was conducted throughout 2024 among adult patients hospitalized in the surgical clinics. Individuals aged 18 years and older who were able to communicate and provided informed consent were included. Patients with a prior diagnosis of OSAS or those with cognitive impairment or acute psychiatric illness were excluded. Data were collected through face-to-face interviews using structured questionnaires and the Epworth Sleepiness Scale, with positive screening results considered indicative of a need for polysomnographic evaluation. Ethical approval was obtained, and the study was carried out in accordance with the Declaration of Helsinki. Data were analyzed using SPSS 20.0 with appropriate parametric and non-parametric tests.

Results: The study included 250 patients with a mean age of 60.1±9.2 years, 68% of whom were male. The most frequent OSAS-related symptom was snoring (57.2%), followed by daytime sleepiness (31.6%) and witnessed apnea (8.4%). The mean Epworth score was 5.13±3.89, with 89.2% of participants within normal limits. The mean BMI was 29.21±4.80 kg/m² and significantly higher in men (p<0.001). Smoking prevalence was 19.6% and markedly higher among men. The PFÖ Differentiation Subscale score—reflecting awareness—was significantly higher in women (p<0.001).

Conclusion: The findings underscore the importance of incorporating awareness-based assessments into preoperative screening. Relying solely on symptom inquiry may be insufficient; integrating patients' awareness, lifestyle, and psychosocial characteristics into diagnostic and management strategies may yield more effective outcomes. A multidisciplinary approach to OSAS has the potential to enhance surgical safety and improve overall patient care.

Keywords: *Obstructive Sleep Apnea Syndrome; Surgical Patients; Awareness*

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Giriş

Obstrüktif Uyku Apne Sendromu (OUAS), uyku sırasında farengel kas tonusunun azalması sonucu üst solunum yolunun tekrarlayıcı şekilde daralması veya tamamen kapanmasıyla karakterize edilen hem bireysel yaşam kalitesini hem de toplum sağlığını tehdit eden ciddi bir uyku bozukluğudur (1). Apne ve hipopne epizodlarının tekrarı, bireyde uyku bölünmelerine, hipoksemiye ve nihayetinde kardiyovasküler, nörolojik ve metabolik sistemlerde önemli komplikasyonlara yol açmaktadır (2). OUAS; hipertansiyon, aritmi, inme, insülin direnci, obezite ve depresyon gibi birçok hastalıkla doğrudan ilişkilendirilmiştir (3).

Son yıllarda yapılan araştırmalar, bu sendromun toplumda beklenenden çok daha yaygın olduğunu ortaya koymaktadır. Özellikle gelişmekte olan ülkelerde, tanı konmamış OUAS prevalansı yüksektir ve çoğu birey sendromun farkında bile değildir (4). Yapılan epidemiyolojik çalışmalar, OUAS'nin yalnızca yaşam kalitesini değil, aynı zamanda bireyin sosyal ve mesleki fonksiyonlarını da olumsuz etkileyebileceğini göstermektedir (5). Öte yandan bu sendrom, yalnızca kronik bir sağlık sorunu olmakla kalmamakta; aynı zamanda cerrahi süreçlerde ciddi riskler doğuran bir faktör olarak karşımıza çıkmaktadır (6).

Cerrahi girişim planlanan hastalarda OUAS varlığı, anestezi yönetimini, intraoperatif stabiliteyi ve postoperatif iyileşme sürecini doğrudan etkileyebilecek düzeydedir (7). Özellikle tanı almamış vakalarda, solunum depresyonu, kardiyak aritmiler, uzamış entübasyon süresi ve hatta yoğun bakım ihtiyacı gibi komplikasyonlarla karşılaşabilmektedir (8). Buna karşın, pek çok sağlık kurumunda OUAS riski yeterince değerlendirilmemekte, hasta öyküsü ve fizik muayene sırasında bu potansiyel risk göz ardı edilebilmektedir (9).

Nitekim literatürde yer alan sistematik derlemeler, cerrahiye aday hastaların büyük bir kısmında OUAS taramasının rutin olarak yapılmadığını göstermektedir (10). Bu da komplikasyonlara zemin hazırlayan bir boşluk oluşturmakta ve sağlık hizmeti maliyetlerini artırmaktadır. Özellikle pozisyonel OUAS gibi alt grupların tanı koyma süreçlerinde yeterince dikkate alınmaması, tanısal süreci daha da karmaşıklştırmaktadır (11). Türkiye'de yapılan çalışmalar ise, genel toplumun OUAS hakkında bilgi

sahibi olma düzeyinin oldukça düşük olduğunu ortaya koymuş ve bu durumun tanı gecikmelerine neden olabileceğine dikkat çekmiştir (12).

Güncel klinik uygulama kılavuzları, ameliyat öncesi dönemde OUAS yönünden riskli hastaların uygun tanı yöntemleriyle değerlendirilmesini önermektedir. Bu kapsamda; polisomnografi, kardiyopulmoner eşleştirme gibi ileri tekniklerin, özellikle yüksek riskli gruplarda tanı koyma sürecine dahil edilmesi önerilmektedir (4,6). Ancak ülkemizde bu kılavuzların rutin uygulamalara entegrasyonu konusunda belirgin eksiklikler mevcuttur ve klinik farkındalık henüz istenilen düzeyde önerilmektedir (4,9).

Bu bağlamda, çalışmamızın temel amacı; Yozgat Bozok Üniversitesi Araştırma ve Uygulama Hastanesi cerrahi kliniklerinde yatışı yapılan hastalarda OUAS'nin prevalansını değerlendirmek ve bu hastaların sendrom hakkında sahip oldukları farkındalık düzeyini belirlemektir. Elde edilecek bulgular sayesinde, preoperatif dönemde uygulanacak sistematik bir tarama protokolünün hasta güvenliği ve cerrahi başarıya katkısı hakkında somut veriler elde edilmesi hedeflenmektedir (12).

GEREÇ VE YÖNTEMLER

Bu çalışma, kesitsel, tanımlayıcı ve analitik bir araştırma olarak planlandı. Araştırma, Yozgat Bozok Üniversitesi Araştırma ve Uygulama Hastanesi'nin genel cerrahi, üroloji, kadın doğum ve ortopedi kliniklerinde 2024 yılı içerisinde hastaneye yatırılan erişkin hastalar üzerinde yürütülerek çalışmaya 18 yaş ve üzerindeki, bilgilendirilmiş onam vermiş ve iletişim kurma becerisi olan bireyler dahil edildi. Daha önce OUAS tanısı almış ancak aktif tedavi görmekte olan hastalar ile bilişsel bozukluk, akut psikiyatrik hastalık veya yoğun bakım gereksinimi bulunan bireyler çalışma dışında bırakıldı. Örneklem büyüklüğü, benzer epidemiyolojik çalışmaların sonuçları ve tahmini prevalans oranları göz önünde bulundurularak güç analizi ile belirlendi. Araştırmada veriler, yüz yüze görüşme tekniği ile yapılandırılmış anket formu aracılığıyla toplandı. Anket formu; demografik bilgiler, medikal öykü, OUAS semptomlarına ilişkin subjektif değerlendirmeler ve Epworth Uykululuk Ölçeği (Epworth Sleepiness Scale - ESS) gibi tarama araçlarını içermekle birlikte ek olarak hastaların horlama, gündüz uykululuk hali, gece

uyanmaları ve sabah yorgunluğu gibi OUAS ile ilişkili semptomları sorgulandı. Pozitif tarama sonuçları OUAS açısından riskli kabul edilerek kayıt altına alınarak polisomnografik değerlendirme planlandı. Verilerin toplanması, eğitilmiş araştırmacılar tarafından hasta mahremiyeti gözetilerek gerçekleştirildi.

Bu araştırma için gerekli etik onay, Yozgat Bozok Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından verilmiş olup, kurulun 2024-GOKAEK-2415_2024.12.18_210 sayılı kararı ile uygun bulunmuştur. Katılımcılara araştırmanın amacı açıklanmış, gönüllü katılım ilkesi doğrultusunda yazılı aydınlatılmış onam alınmıştır. Çalışma süresince Helsinki Deklarasyonu ilkelerine tam uyum gösterilmiştir.

İstatistiksel Analiz

Çalışmadan elde edilen veriler, IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA) programı kullanılarak analiz edildi. Sürekli değişkenlerin dağılım özellikleri, Kolmogorov-Smirnov testi ile değerlendirildi. Normal dağılım gösteren verilerde iki grup arasındaki fark Bağımsız Örneklem t Testi ile, birden fazla grubun karşılaştırılması ise Tek Yönlü Varyans Analizi (ANOVA) ile analiz edildi. Normal dağılım göstermeyen verilerde ise iki grup karşılaştırmaları için Mann-Whitney U testi, üç ve daha fazla grup karşılaştırmaları için Kruskal-Wallis testi kullanıldı. Değişkenler arasındaki korelasyonel ilişkileri incelemek amacıyla, parametrik varsayımlar sağlandığında Pearson korelasyon analizi, parametrik olmayan durumlarda ise Spearman korelasyon analizi tercih edildi. Tüm analizlerde istatistiksel anlamlılık düzeyleri $p < 0,05$ ve $p < 0,01$ olarak kabul edildi.

BULGULAR

Çalışmaya, Yozgat Bozok Üniversitesi Araştırma ve Uygulama Hastanesi'nin cerrahi kliniklerinde yatan ve 18-70 yaş aralığında olan toplam 250 hasta dâhil edildi. Katılımcıların 80'i kadın (%32,0) ve 170'i erkek (%68,0) idi. Tüm grubun yaş ortalaması $60,1 \pm 9,2$

yıl olarak hesaplandı. Cinsiyetlere göre ayrı ayrı değerlendirildiğinde, kadın hastaların yaş ortalaması $59,3 \pm 9,0$ yıl, erkek hastaların yaş ortalaması ise $60,6 \pm 9,4$ yıl olarak bulundu. Yapılan istatistiksel analizde, iki grup arasındaki yaş ortalamaları farkı anlamlı bulunmadı (Mann-Whitney U testi, $p = 0,155$). (Tablo1).

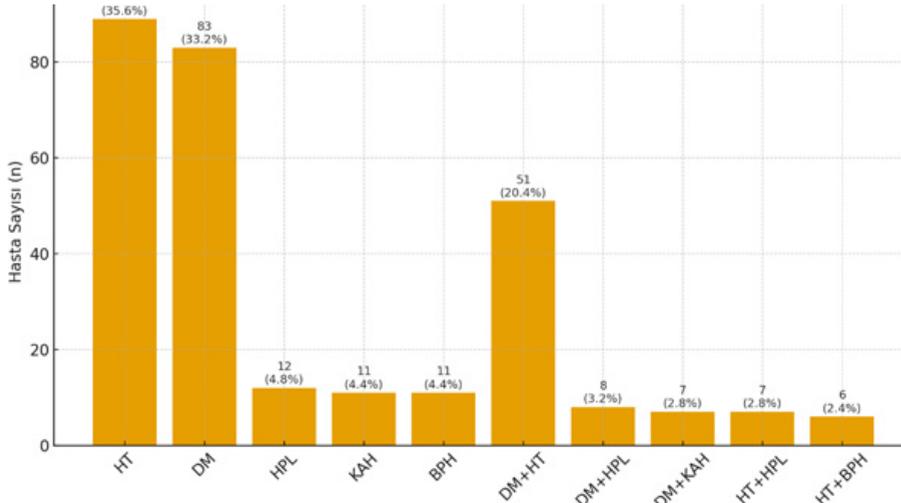
Çalışmaya dâhil edilen 250 hastanın meslek gruplarına göre dağılımı; ev hanımı ($n = 114$; %45,6), emekli ($n = 69$; %27,6), çiftçi ($n = 17$; %6,8) ve diğer ($n = 50$; %20,0) şeklinde idi. Cinsiyet bazında değerlendirildiğinde, kadın hastaların büyük çoğunluğu ev hanımı ($n = 113$; %91,9) olup bunu emekli ($n = 9$; %7,3) ve diğer ($n = 1$; %0,8) grupları izlerken, çiftçi grubunda kadın hasta yoktu (%0,0). Erkek hastalarda ise dağılım emekli ($n = 60$; %47,2), diğer ($n = 49$; %38,6), çiftçi ($n = 17$; %13,4) ve ev hanımı ($n = 1$; %0,8) şeklinde olup, meslek profilinin cinsiyetlere göre belirgin farklılık gösterdiği, tarımsal faaliyetlerin (çiftçi) erkeklerde anlamlı oranda temsil edildiği görüldü.

Ek hastalık durumları incelendiğinde, 87 hastada (%34,8) herhangi bir ek hastalık bildirilmediği görülürken 163 hasta (%65,2) en az bir ek hastalığa sahip olduğunu belirtti. En sık görülen ek hastalıklar arasında hipertansiyon (HT) ($n = 89$; %35,6) ve diabetes mellitus (DM) ($n = 83$; %33,2) ön plana çıkarken, daha düşük sıklıklarda hiperlipidemi (HPL) ($n = 12$; %4,8), koroner arter hastalığı (KAH) ($n = 11$; %4,4) ve benign prostat hiperplazisi (BPH) ($n = 11$; %4,4) tespit edildi. Ek hastalık birliktelikleri değerlendirildiğinde, en sık rastlanan kombinasyonun DM + HT olduğu ve toplam 51 hastada (%20,4 tüm örneklemde; %31,3 ek hastalığı olanlarda) bu birlikteliğin bulunduğu saptandı. Daha nadir birliktelikler arasında DM + HPL ($n = 8$; %3,2), DM + KAH ($n = 7$; %2,8), HT + HPL ($n = 7$; %2,8) ve HT + BPH ($n = 1$; %0,4) yer aldı (Şekil 1).

Çalışmaya katılan hastaların sigara kullanım durumları incelendiğinde, toplam 48 hastanın (%19,6) sigara kullandığı, 202 hastanın (%80,4) ise sigara kullanmadığı belirlendi. Cinsiyet bazlı dağılımlara bakıldığında, kadınların 13'ü (%10,6) sigara kullanırken 110'u (%89,4)

Tablo 1. Kadın ve Erkek Hastaların Yaş Karşılaştırması

Grup	N	Ortalama±SS	Medyan [CAA]
Kadın	123	67,76±11,40	69,00 [61,00-75,00]
Erkek	127	67,94±25,88	68,00 [61,00-73,00]
p değeri		Mann-Whitney U testi	0,155



Şekil 1. Çalışmaya dahil edilen hastalarda en sık görülen ek hastalıklar ve birliktelikleri. HT: Hipertansiyon, DM: Diabetes Mellitus, HPL: Hiperlipidemi, KAH: Koroner Arter Hastalığı, BPH: Benign Prostat Hiperplazisi.

kullanmadığı tespit edildi. Erkeklerde ise 35 erkek hasta (%27,6) sigara kullandığı, 91'i (%71,7) kullanmadığı tespit edildi. Bu bulgular, erkek hastalarda sigara kullanım sıklığının kadınlara göre yaklaşık üç kat daha yüksek olduğunu gösterdi. Sigara kullanan hastalarda paket-yıl değerleri hesaplandığında önemli farklılıklar gözlenmiştir. Toplamda sigara kullanan 48 hastanın (13 kadın, 35 erkek) verileri incelenmiş olup, tüm grubun ortalama paket-yıl değeri $31,36 \pm 29,74$ olarak bulundu. Cinsiyetlere göre değerlendirildiğinde, erkek hastalarda ortalama $36,18 \pm 33,32$ paket-yıl saptanırken, kadınlarda bu değer belirgin şekilde daha düşük olup $18,38 \pm 8,36$ paket-yıl olarak hesaplandı.

250 hastanın yalnızca 6'sı (%2,4) alkol kullandığını belirtirken, geri kalan 244'ü (%97,6) alkol kullanmadığını belirtti. Alkol kullandığı tespit edilen hastaların hepsi erkek idi.

Tüm grubun genel ortalama Vücut Kitle İndeksi (VKİ) değeri $29,21 \pm 4,80$ kg/m^2 olarak bulundu. Bu değer, hastaların büyük kısmının fazla kilolu veya obez sınırında olduğunu gösterdi. Cinsiyetlere göre ayrı değerlendirildiğinde, erkek hastalarda ($n=123$) ortalama VKİ $30,51 \pm 4,90$ kg/m^2 olarak hesaplanırken,

kadın hastalarda ($n=127$) ortalama VKİ $27,95 \pm 4,37$ kg/m^2 bulundu. Yapılan bağımsız örneklem t-testi sonucunda bu farkın istatistiksel olarak anlamlı olduğu ($p < 0,001$) saptandı (Tablo2).

Çalışmaya katılan tüm grubun boyun çevresi ortalaması $37,18 \pm 4,83$ cm olarak saptandı. Cinsiyetlere göre ayrı değerlendirildiğinde, kadın hastalarda ($n=123$) ortalama boyun çevresi $35,93 \pm 4,32$ cm iken, erkek hastalarda ($n=127$) bu değer $38,39 \pm 5,00$ cm olarak bulundu. Bu bulgu, erkeklerde boyun çevresinin kadınlara kıyasla daha geniş olduğunu gösterdi. Ayrıca yapılan korelasyon analizlerinde, boyun çevresi ile VKİ arasında zayıf ancak istatistiksel olarak anlamlı bir pozitif ilişki tespit edildi (Spearman $r=0,13$; $p=0,044$). Bu sonuç, boyun çevresi arttıkça VKİ değerinin de artma eğiliminde olduğunu gösterdi.

Çalışmaya katılan 250 hastanın uyku alışkanlıkları değerlendirildiğinde, tüm grubun ortalama uyku süresi $8,58 \pm 2,01$ saat olarak hesaplandı. Cinsiyetlere göre incelendiğinde, kadın hastaların ($n=127$) ortalama uyku süresinin $8,37 \pm 1,98$ saat, erkek hastaların ($n=123$) ise $8,80 \pm 2,03$ saat olduğu belirlendi. Erkeklerdeki bu hafif üstünlük, istatistiksel olarak anlamlı bir farklılık

Tablo 2. Cinsiyetlere Göre Boy, Kilo ve Vücut Kitle İndeksi (BMI) Dağılımı ve İstatistiksel Karşılaştırma

Grup	n	Boy (m)	Kilo (kg)	Vücut Kitle İndeksi (BMI, kg/m^2)	p-değeri
Genel	250	$1,65 \pm 0,09$	$79,55 \pm 13,22$	$29,21 \pm 4,80$	-
Kadın	123	$1,59 \pm 0,06$	$76,76 \pm 12,62$	$30,51 \pm 4,90$	$p < 0,001$
Erkek	127	$1,72 \pm 0,07$	$82,25 \pm 13,27$	$27,95 \pm 4,37$	$p < 0,001$

oluşturmamakla birlikte, erkeklerin daha uzun süre uyuma eğiliminde olabileceğine dikkati çekti. Bununla birlikte her iki cinsiyet grubunda da ortalama uyku süresinin 8 saatin üzerinde olması, çalışmaya dahil edilen hasta grubunun uyku süreleri açısından görece dengeli olduğunu gösterdi. Buna karşılık, uykuya dalma süresi yani uyku latansı incelendiğinde farklı bir tablo ortaya çıktı. Tüm grubun ortalama uykuya dalma süresi $29,36 \pm 29,66$ dakika olarak hesaplandı. Ancak cinsiyet bazlı değerlendirmede, kadın hastalarda bu sürenin $23,74 \pm 25,29$ dakika ile daha kısa olduğu, erkeklerde ise $35,16 \pm 32,67$ dakikaya çıktığı görüldü.

Çalışmaya katılan 250 hastanın uyku ile ilişkili semptomları düzenlenen anket soruları ile değerlendirildiğinde, bildirilen yakınmalar arasında horlama ön plana çıkmıştır. Hastaların %60'ı "horladığınızı söylerler mi?" sorusuna olumlu yanıt verdi, %39,6'sı ise kendi horlamalarının farkında olduklarını belirtti. Horlamanın yatış pozisyonu ile ilişkili olduğu ise %15,2 oranında saptandı. Bunun yanı sıra, hastaların %12,4'ü horlarken nefesinin durduğunun kendisine söylendiğini ve %8–10 civarında bir grup da uykuda boğulma hissi ile uyandığını ifade etti.

Sabah yakınmalarına bakıldığında, ağız kuruluğu (%47,6) ve baş ağrısı (%36,4) gibi şikâyetlerin dikkate değer oranlarda görüldü. Aynı şekilde, unutkanlık (%41,2) ve dikkat toplama güçlüğü (%44,4) gibi bilişsel semptomlar da hastaların önemli bir kısmında mevcuttu. Ayrıca, hastaların yaklaşık yarısında gece terlemesi ve noktüri (gece tuvalete kalkma) şikâyetleri

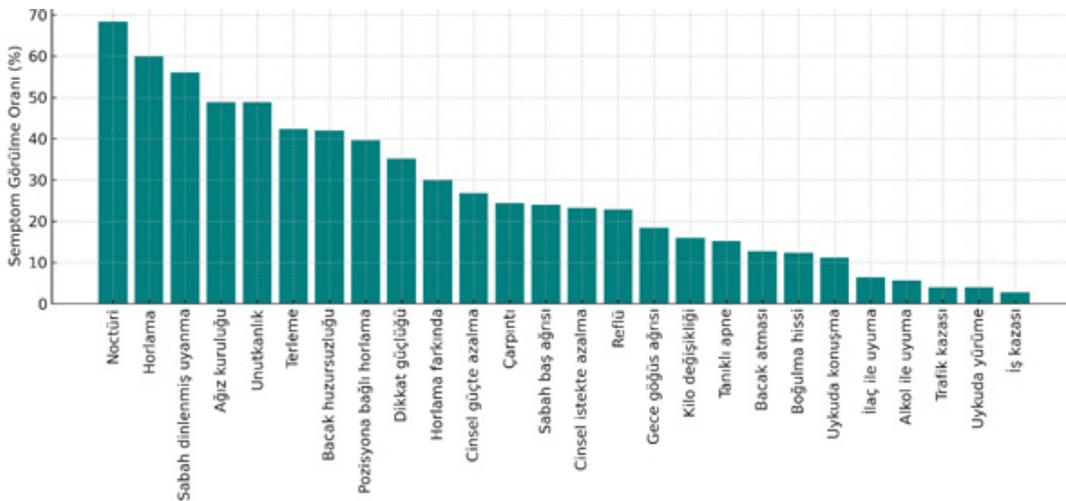
bulunması, uyku bölünmelerinin yaygın olduğunu gösterdi.

Daha nadir görülen belirtiler arasında, uykuda yürüme (%2,4), uykuda konuşma (%6,8) ve eşin bildirdiği bacak atması (%9,2) gibi parasomniler yer aldı. Dikkat çekici olarak, hastaların %5,6'sı uykulama nedeniyle iş kazası yaptığını, %6,4'ü ise trafik kazası geçirdiğini belirtti.

Son olarak, çalışmaya katılan bireylerde cinsel istekte azalma (%28,8) ve cinsel güçte azalma (%20,8) gibi şikâyetlerin de belirgin oranda rapor edildi. Bu bulgular, uyku bozukluklarının yalnızca fizyolojik değil, aynı zamanda psikososyal yaşam kalitesini de olumsuz yönde etkilediğini göstermektedir bilgisini destekleyen nitelikte idi (Şekil 2).

Çalışmaya dâhil edilen hastaların OUAS ile ilişkili olarak horlama, tanıklı apne ve gündüz uykululuk hali doğrudan sorgulandığında da en sık görülen bulgunun horlama olduğu belirlendi (kadınlarda $n=72$, %58,5; erkeklerde $n=71$, %55,9; toplam $n=143$, %57,2; $p=0,651$). Gündüz uykululuk hali kadınlarda $n=43$, %35,0, erkeklerde $n=36$, %28,3 oranında saptandı (toplam $n=79$, %31,6; $p=0,279$). Tanıklı apne semptomu ise kadınlarda $n=12$, %9,8, erkeklerde $n=9$, %7,1 oranında görüldü (toplam $n=21$, %8,4; $p=0,440$).

Semptom birliktelikleri incelendiğinde, en sık görülen ikili kombinasyonun horlama ve gündüz uykululuk hali olduğu tespit edildi (kadınlarda $n=24$, %19,5; erkeklerde $n=22$, %17,3; toplam $n=46$, %18,4; $p=0,689$). Bunu horlama + tanıklı apne ($n=15$, %6,0; $p=0,419$) ve tanıklı apne + gündüz uykululuk ($n=12$, %4,8; $p=0,695$)



Şekil 2. Çalışmaya Katılan Hastalarda Uykuya Bağlı Semptomların Dağılımı

birliktelikleri izledi. Üç semptomun bir arada bulunma sıklığı ise kadınlarda n=7, %5,7, erkeklerde n=4, %3,1 olup (toplam n=11, %4,4; p=0,329), cinsiyetler arasında anlamlı fark saptanmadı (Tablo3).

Çalışmaya katılan 250 hastada gündüz aşırı uykululuk hali Epworth Uykululuk Ölçeği (ESS) ile değerlendirildi. Tüm grubun ortalama ESS skoru $5,13 \pm 3,89$ olarak hesaplandı. Cinsiyetlere göre incelendiğinde, kadınlarda (n=127) ortalama skor $5,04 \pm 3,94$, erkeklerde (n=123) ise $5,22 \pm 3,86$ bulundu. Bu değerler, her iki cinsiyette de gündüz uykululuk düzeyinin genel olarak normal sınırlar içinde seyrettiğini gösterdi. Klinik sınıflandırmaya göre dağılım incelendiğinde, hastaların büyük çoğunluğunu (%89,2; n=223) normal uykululuk düzeyine sahip olanlar oluşturdu. Hafif derecede gündüz uykululuk saptanan 23 hasta (%9,2) bulunurken, 2 hasta (%0,8) orta düzeyde ve 2 hasta da (%0,8) ciddi düzeyde gündüz uykululuk bulundu. Bu sonuçlar, araştırmaya katılan hastaların önemli bir

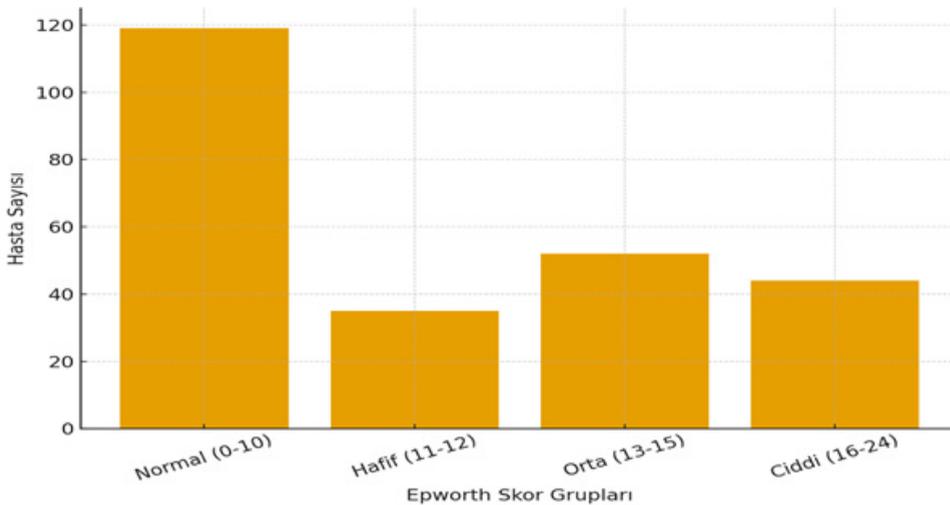
kısımında klinik olarak belirgin aşırı gündüz uykululuk olmadığını, yalnızca küçük bir grupta patolojik düzeyde uykululuk bulunduğunu ortaya koydu (Şekil 3).

Epworth Uykululuk Skoru (EPWORTH TOPLAM) ile yapılan istatistiksel analizlerde, çalışmaya katılan hastaların gündüz aşırı uyku hali düzeyleri ile temel klinik ve demografik değişkenler arasındaki ilişkiler incelenmiş ve anlamlı farklılık saptanmadı. VKİ ile Epworth skoru arasında çok zayıf pozitif korelasyon bulunmuş ($r = 0,08$; $p = 0,21$), ancak bu ilişki istatistiksel olarak anlamlı düzeye ulaşmadı. Benzer şekilde, yaş ile Epworth skoru arasında da düşük düzeyde pozitif bir ilişki tespit edilmiş ($r = 0,09$; $p = 0,14$), fakat anlamlılık saptanmadı. Boyun çevresi ile Epworth skoru arasındaki ilişki ise zayıf negatif yönde oldu ($r = -0,07$; $p = 0,25$) ve anlamlı bulunmadı. Ayrıca cinsiyet açısından yapılan karşılaştırmada erkeklerde ortalama Epworth skoru 5,22, kadınlarda ise 5,04 olarak hesaplanmış olup, bu fark istatistiksel olarak anlamlı değildir ($p = 0,55$).

Tablo 3. Cinsiyete Göre OUAS Semptomlarının Dağılımı

Semptomlar	Kadın n (%)	Erkek n (%)	Toplam n (%)	p değeri
Horlama	72 (58,5)	71 (55,9)	143 (57,2)	0,770
Tanımlı Apne	12 (9,8)	9 (7,1)	21 (8,4)	0,594
Gündüz Uykululuk	43 (35,0)	36 (28,3)	79 (31,6)	0,323
Horlama + Tanımlı Apne	9 (7,3)	6 (4,7)	15 (6,0)	0,551
Horlama + Gündüz Uykululuk	28 (22,8)	18 (14,2)	46 (18,4)	0,112
Tanımlı Apne + Gündüz Uykululuk	7 (5,7)	5 (3,9)	12 (4,8)	0,724
Üç Semptom Birlikte	7 (5,7)	4 (3,1)	11 (4,4)	0,502

OUAS: Obstrüktif Uyku Apne Sendromu



Şekil 3. Çalışma grubunda Epworth Uykululuk Skoru dağılımı

Çalışmaya katılan tüm grup değerlendirildiğinde, Philadelphia Farkındalık Ölçeği (PFÖ) toplam puan ortalaması $32,13 \pm 7,19$ olarak hesaplandı. Bu sonuç, katılımcıların genel olarak düşüncelerini, duygularını ve bedensel duyularını ayırt edebilme kapasitelerinin orta düzeyde olduğunu gösterdi. Alt gruplar incelendiğinde ise kadın hastalarda ortalama puan $33,45 \pm 7,21$, erkek hastalarda ise $30,78 \pm 6,94$ olarak bulundu. Yapılan istatistiksel analiz, bu farklılığın tesadüfi olmadığını ortaya koydu ve kadınların erkeklere kıyasla anlamlı derecede daha yüksek farkındalık düzeyine sahip olduğunu gösterdi. (Mann-Whitney U = 9815,5; p <0,001).

Çalışmamızda uykuya ilişkin semptomların, Epworth Uykululuk Skoru ve PFÖ Ayrımsama Alt Ölçeği ile ilişkisi incelendi. Bulgular, "horlamanın yatış pozisyonu ile ilişkili olduğunun söylenmesi" ile "uykuda boğulma hissi ile uyanma" yakınmalarının gündüz aşırı uyku hali ile anlamlı olarak ilişkili olduğunu göstermiştir (p=0,049 ve p=0,031). Diğer taraftan, PFÖ Ayrımsama Alt Ölçeği açısından değerlendirildiğinde, "uykuda nefesin durduğunun söylenmesi" yakınması bulunan bireylerde farkındalık düzeyinin anlamlı biçimde düşük olduğu saptanmıştır (p=0,019). Ayrıca, "uykuda boğulma hissi ile uyanma" bildirenlerde bu düşünüş çok daha belirgin olup, istatistiksel olarak güçlü anlamlılık göstermiştir (p<0,001).

TARTIŞMA

Çalışmamızda cerrahi kliniklerde yatan 18–70 yaş aralığındaki hastaların demografik özellikleri incelendiğinde, kadın ve erkek grupları arasında yaş ortalamaları açısından anlamlı bir fark bulunmamıştır. Bu bulgu, obstrüktif uyku apnesi (OUA) açısından yaşın önemli bir risk faktörü olarak tanımlanmasına rağmen, cinsiyetler arasında belirgin bir farklılığın her zaman ortaya çıkmayabileceğini düşündürmektedir. Literatürde, OUA'nın özellikle ileri yaşlarda ve erkek cinsiyette daha sık görüldüğü bildirilmiştir (16,17). Bununla birlikte, bazı araştırmalar cerrahi hastalar arasında yaş ve cinsiyet dağılımındaki farklılıkların OUA riskini tek başına belirlemediğini ortaya koymuştur (2,3). Ayrıca Mehra ve arkadaşlarının klinik kılavuzunda, hastanede yatan yetişkinlerde OUA değerlendirmesinde yaş ve cinsiyetin tek başına yeterli olmadığını, multifaktöriyel risklerin göz önünde

bulundurulması gerektiğini vurgulamaktadır (11). Bu nedenle, çalışmamızda cinsiyetler arasında yaş ortalamaları açısından anlamlı fark bulunmamış olması klinik olarak OUA riskinin daha çok multifaktöriyel bir temele dayandığını göstermektedir.

Hastaların meslek gruplarına göre dağılımları incelendiğinde, cinsiyetler arasında belirgin farklılıklar olduğu görülmüştür. Kadınların büyük çoğunluğunun ev hanımı olması, erkeklerde ise emeklilik, serbest meslek ve tarımsal faaliyetlerin daha yüksek oranda temsil edilmesi dikkat çekicidir. Bu bulgu, OUA ve benzeri uyku bozukluklarının toplum içindeki mesleki roller ve yaşam tarzı ile de ilişkili olabileceğini düşündürmektedir. Daha önce yapılan çalışmalarda, OUA'nın yalnızca biyolojik ve anatomik özelliklerle değil, aynı zamanda yaşam biçimi, mesleki alışkanlıklar ve sosyodemografik faktörlerle de etkileşim içinde olduğu vurgulanmıştır (15,23). Ayrıca, toplum temelli araştırmalarda da OUA prevalansının erkeklerde daha yüksek olduğu, bunun da hem hormonal hem de yaşam tarzı farklılıklarından kaynaklanabileceği bildirilmiştir (17,20). Bu bağlamda, Yıldız ve arkadaşlarının Türk toplumunda yaptığı çalışmada da OUA farkındalığının düşük olmasının mesleki ve sosyal rollerle ilişkili olabileceği bildirilmiştir (8). Çalışmamızda elde edilen mesleki dağılım sonuçları da bu literatür bilgisi ile uyumlu görünmektedir.

Çalışmamızda ek hastalık durumları değerlendirildiğinde, hastaların üçte ikisinden fazlasında en az bir komorbiditenin eşlik ettiği saptandı. En sık birlikte görülen komorbiditenin ise hipertansiyon ve diyabetes mellitusun olması dikkat çekici idi. OUAS farkındalığının değerlendirilmesi için taranan cerrahi planı yapılan hastalarda özellikle HT ve DM birlikteliğinin yüksek oranlarda görülmesi, OUA ile kardiyometabolik risk faktörleri arasındaki güçlü bir ilişki olması bakımından oldukça önemliydi. Nitekim literatürde, OUA'nın hem hipertansiyon hem de tip 2 diyabet gelişiminde bağımsız bir risk faktörü olduğuna dair güçlü kanıtlar bulunmaktadır. Bu durum, Punjabi ve McNicholas'ın yaptığı çalışmalarda da açıkça ortaya konmuştur (17,29). Ayrıca OUA varlığında sempatik aktivitenin artışı, oksidatif stres ve inflamatuvar yanıtların tetiklenmesi gibi mekanizmalar üzerinden kardiyometabolik bozuklukların daha da kötüleştiği bildirilmektedir (1,31). Bu bulgular, Hou ve arkadaşlarının cerrahi hastalar üzerinde yaptıkları

çalışmada da desteklenmiş olup, preoperatif dönemde kardiyopulmoner risk faktörlerinin titizlikle değerlendirilmesi gerektiği vurgulanmaktadır (4). Bizim çalışmamızda da hastaların önemli bir kısmında bu ek hastalıkların bulunması, OUA'nın çok boyutlu sistemik etkilerini ve multidisipliner yaklaşımla değerlendirilmesi önemini bir kez daha ortaya koymaktadır.

Çalışmamızda sigara kullanımının erkeklerde kadınlara kıyasla belirgin şekilde daha yüksek olduğu gösterilmiştir. Erkek hastalarda yalnızca sigara içme oranı daha fazla değil, aynı zamanda paket-yıl değerlerinin de anlamlı düzeyde yüksek bulunması, maruziyetin kümülatif etkisinin önemini vurgulamaktadır. Literatürde de benzer şekilde, Punjabi ve arkadaşlarının çalışmasında erkek cinsiyetin OUA hastalarında daha yüksek sigara prevalansı ile ilişkili olduğu bildirilmiştir (17). Ayrıca, sigara kullanımının OUA'nın patogenezinde rol oynayarak hastalığın klinik şiddetini artırabileceği farklı araştırmalarca da ortaya konmuştur (32). Nitekim Tracy ve arkadaşlarının güncel derlemesinde, sigaranın üst hava yolu inflamasyonu ve mukozal ödem üzerinden OUA'nın fizyopatolojisine katkıda bulunabileceği vurgulanmaktadır (1). Bunun yanı sıra, Ceban ve arkadaşlarının meta-analizinde, sigara kullanımının perioperatif komplikasyon riskini artırarak cerrahi hastalarda OUA ile ilişkili riskleri daha da ağırlaştırdığı ortaya konmuştur (7). Bu durum, çalışmamızdaki sonuçlarla da uyumludur.

Bu çalışmada hastaların büyük çoğunluğunun alkol kullanmadığı, yalnızca %2,4'ünün alkol kullanım öyküsü bulunduğu ve bu bireylerin tamamının erkeklerden oluştuğu saptanmıştır. Literatürde alkol tüketiminin, özellikle yatmadan önce alındığında, üst hava yolu kas tonusunu azaltarak obstrüktif olayların sıklığını ve süresini artırdığı, dolayısıyla OUA'nın klinik şiddetini kötüleştirebileceği belirtilmektedir (1,32). Nitekim, Hersch ve arkadaşlarının yaptığı çalışmada, alkol kullanımının postoperatif dönemde OUA hastalarında komplikasyon riskini artırdığına dikkat çekilmiştir (31). Bu bağlamda, çalışmamızda alkol kullanımının düşük sıklıkta saptanmış olması, klinik açıdan önemli bir risk faktörünün toplumumuzda görece sınırlı düzeyde bulunduğunu göstermektedir.

Çalışmamızda elde edilen bulgular, hasta grubunun ortalama VKİ değerinin fazla kilolu ile obezite sınırında yer aldığını ve bu durumun özellikle erkeklerde daha

belirgin olduğunu ortaya koymaktadır. Erkek hastalarda yalnızca VKİ değerleri daha yüksek bulunmakla kalmamış, aynı zamanda boyun çevresinin de anlamlı şekilde geniş olduğu gözlenmiştir. Bu iki parametre arasındaki pozitif korelasyon, vücut yağlanmasının boyun çevresine yansiyarak üst hava yolu darlığına katkıda bulunabileceğini düşündürmektedir. Literatürde de benzer şekilde, obezitenin OUA için en güçlü risk faktörlerinden biri olduğu, artmış boyun çevresinin ise üst hava yolu kollapsını kolaylaştırarak apne gelişimine zemin hazırladığı bildirilmiştir (5,14). Niu ve arkadaşlarının meta-analizinde, VKİ ve boyun çevresindeki artışların OUA prevalansında bölgesel ve demografik farklılıkları açıklayan en önemli değişkenlerden olduğu vurgulanmıştır (6). Ayrıca Liu ve arkadaşları da makine öğrenimi tabanlı modellerle yaptıkları çalışmada, VKİ ve boyun çevresi gibi antropometrik parametrelerin OUA için güçlü prediktörler olduğunu göstermiştir (22). Bu bulgular ışığında, çalışmamızdaki sonuçlar da tanısal süreçlerde bu ölçümlerin dikkate alınması gerektiğini ortaya koymaktadır.

Çalışmamızda uyku süresi açısından her iki cinsiyet grubunun da ortalama 8 saatin üzerinde uyuduğu belirlenmiştir. Ancak erkeklerde uyku latansının belirgin şekilde daha uzun olması dikkat çekmiştir. Literatürde, OUA hastalarında uzamış uyku latansının gündüz aşırı uyku hali, dikkat dağınıklığı ve bilişsel performans kaybı ile ilişkili olduğu ifade edilmektedir (14,26). Iber'in uyku skorlamasına ilişkin kılavuzunda da uyku latansının hem klinik tanı hem de şiddet tayini açısından kritik bir parametre olduğunun altı çizilmektedir (28). Bu bağlamda, Erbaş ve arkadaşlarının Türk anesteziistler üzerinde yaptıkları çalışmada da preoperatif değerlendirmelerde uyku latansının dikkate alınmamasının anestezi yönetiminde sorunlara yol açabileceği rapor edilmiştir (9).

Çalışmamızda uyku ile ilişkili semptomlar değerlendirildiğinde horlama, tanıklı apne ve gündüz uykululuğun öne çıktığı görülmüştür. Bu bulgular, Young ve arkadaşlarının klasik çalışması ve Schwab'ın tanımladığı semptom triadı ile de uyumludur (16,18). Ayrıca Udawadia ve arkadaşlarının Hindistan'da yaptığı çalışmada da orta yaş grubunda horlama ve tanıklı apnenin en sık bildirilen semptomlar olduğu ortaya konmuştur (19). Bunun yanı sıra, Akbay ve arkadaşlarının

Türk popülasyonunda yaptığı araştırmada, özellikle pozisyona bağlı horlamanın klinik değerlendirmelerde göz ardı edilmemesi gerektiği belirtilmiştir (12). Bu sonuçlar, semptom çeşitliliğinin ayrıntılı sorgulamanın önemini bir kez daha ortaya koyduğunu göstermektedir. Çalışmamızda elde edilen ESS sonuçları, gündüz uykululuk düzeylerinin büyük çoğunlukla normal sınırlar içinde seyrettiğini ortaya koymuştur. Literatürde de ESS'nin OUAS tanısında tek başına yeterli olmamakla birlikte, semptomların belirlenmesinde değerli bir yöntem olduğu vurgulanmıştır (21,27). Ayrıca Shaw ve arkadaşlarının İngiltere'de National Institute for Health and Care Excellence (NICE) kılavuzlarının uygulanması sonrası yaptıkları çalışmada, ESS'nin preoperatif taramalarda standartlaştırılmış bir ölçüm aracı olarak klinik kararlara doğrudan etki ettiği belirtilmiştir (33). Bu bulgular, ESS'nin klinik pratikteki önemini bir kez daha desteklemektedir.

Son olarak, çalışmamızda PFÖ Ayrımsama Alt Ölçeği sonuçları değerlendirildiğinde, kadınların erkeklere kıyasla daha yüksek farkındalık düzeyine sahip olduğu belirlenmiştir. Literatürde de uyku bozukluklarının yalnızca fizyolojik parametrelerle değil, aynı zamanda farkındalık, öz düzenleme ve emosyonel süreçlerle yakından ilişkili olduğu gösterilmiştir (23,28). Ayrıca Atahan ve arkadaşlarının yaptığı çalışmada, farkındalık düzeyinin tedaviye uyum ve basınç gereksinimi gibi parametreleri etkileyebileceği ortaya konmuştur (30). Bu açıdan, çalışmamızda PFÖ skorlarının değerlendirilmesi yalnızca semptom farkındalığı değil, aynı zamanda olası tedavi süreçleri açısından da önemli bilgiler sunmaktadır.

Bu çalışmanın bazı sınırlamaları mevcuttur. Öncelikle, kesitsel bir tasarım kullanılmış olup, neden-sonuç ilişkisi çıkarılamaz. Ayrıca, tek bir merkezde gerçekleştirilen bu araştırma, bulguların genellenebilirliğini sınırlayabilir. Çalışmaya katılan hastaların demografik özellikleri, farklı popülasyonlardaki prevalans ve farkındalık düzeylerini yansıtmayabilir. Semptomlar ve farkındalık, öznel raporlara dayalıdır ve bu durum sonuçların doğruluğunu etkileyebilir. Gelecekte, daha geniş ve farklı merkezlerde yapılacak prospektif çalışmalara ihtiyaç vardır.

SONUÇ

Obstrüktif Uyku Apne Sendromu (OUAS), cerrahi

süreçlerde klinik yönetimi doğrudan etkileyebilecek, sistemik komplikasyonlara neden olabilecek önemli bir sağlık sorunudur. Cerrahi hastalarda OUAS varlığının fark edilmemesi; anestezi yönetimi, intraoperatif stabilite ve postoperatif iyileşme süreci açısından ciddi riskler doğurabilmektedir. Bu çalışma, cerrahi kliniklerde yatan hastalarda OUAS ile ilişkili bireysel farkındalık düzeylerinin değerlendirilmesinin, sadece tanılabilirliği artırmakla kalmayıp, aynı zamanda olası komplikasyonların önlenmesinde de kritik bir rol oynayabileceğini ortaya koymaktadır.

Bulgular, yalnızca semptom sorgulamasına dayalı yaklaşımların yetersiz kalabileceğini ve bunun yerine farkındalık ile yaşam tarzı gibi özelliklerin tanı ve yönetime entegre edilmesi gerektiğini göstermektedir. Preoperatif dönemde, hastaların yalnızca semptomatik sorgulamalarla değil; aynı zamanda yaşam tarzı, psikososyal faktörler ve farkındalık düzeyleri gibi çok boyutlu değişkenlerle değerlendirilmesi, OUAS'nın kapsamlı bir şekilde ele alınmasını mümkün kılmaktadır. Bu çok boyutlu yaklaşım, hastaların sadece semptomatik değerlendirmesinin ötesine geçerek, tedavi sürecinin her aşamasında daha doğru ve etkili bir müdahale sağlayacaktır.

Tanı ve tarama süreçlerinde farkındalık odaklı yaklaşımlar ile klinik değerlendirme yöntemlerinin entegre edilmesi, cerrahi başarıyı ve hasta güvenliğini arttıracak stratejik bir adımdır. Bu bütünsel yaklaşım, cerrahi süreçlerde karşılaşılabilecek komplikasyonları en aza indirmek için kritik öneme sahiptir. Ayrıca, multidisipliner bir anlayışla OUAS'nın ele alınması, cerrahi güvenliği ve hasta sonuçlarını olumlu yönde etkileyebilir. Farkındalık düzeyinin, klinik karar süreçlerine dâhil edilmesi, hem bireysel hem de toplumsal sağlık çıktıları açısından önemli katkılar sağlayacaktır.

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GREATER OCCIPITAL NERVE BLOCK IN THE MANAGEMENT OF VESTIBULAR MIGRAINE: A CASE OF MISDIAGNOSIS AND RECOVERY

Vestibüler Migren Tedavisinde Büyük Oksipital Sinir Blokajı: Yanlış Tanıdan Etkili Tedaviye

Sadettin ERSOY¹, Sule AYDIN TURKOGLU²

ABSTRACT

Vestibular migraine (VM) is a challenging condition, characterized by episodic vertigo and migraine symptoms, often misdiagnosed as peripheral vertigo. This case report describes a 25-year-old female with refractory VM who was successfully treated with greater occipital nerve (GON) block. The GON block provided rapid and significant relief of both headache and vestibular symptoms, highlighting its potential as a cost-effective and underused intervention. This case emphasizes the importance of accurate diagnosis and a multimodal treatment approach in the management of refractory VM.

Keywords: *Greater Occipital Nerve Block; Vertigo; Vestibular Migraine*

ÖZET

Vestibüler migren (VM), genellikle periferik vertigo olarak yanlış teşhis edilen, epizodik vertigo ve migren semptomları ile karakterize, engelliliğe neden olan bir hastalıktır. Bu olgu sunumunda, dirençli VM'si olan 25 yaşındaki bir kadın hastanın, büyük oksipital sinir (GON) blokajı ile başarılı bir şekilde tedavi edilmesi anlatılmaktadır. GON blokajı, hem baş ağrısı hem de vestibüler semptomlarda hızlı ve belirgin bir rahatlama sağlamış olup, maliyet etkin ve az kullanılan bir müdahale olarak potansiyelini vurgulamaktadır. Bu olgu, dirençli VM yönetiminde doğru tanının ve multimodal tedavi yaklaşımlarının önemini vurgulamaktadır.

Anahtar Kelimeler: *Büyük Oksipital Sinir Blokajı; Vertigo; Vestibüler Migren*

INTRODUCTION

Vestibular migraine (VM) is a multifaceted neurological condition defined by the intersection of vestibular symptoms and migraine features. Despite its relatively high prevalence (estimated to affect up to 2.7% of the general population), it remains frequently misdiagnosed or overlooked in clinical practice, especially outside of specialized centers (1, 2). Patients typically present with episodic vertigo, lasting from minutes to days, often accompanied by migrainous symptoms such as throbbing headache, photophobia, phonophobia, or aura (1, 3). The variability in presentation, ranging from spontaneous to positional vertigo, contributes to diagnostic uncertainty, especially in the absence of concurrent headache (2, 4).

Differentiating VM from conditions such as Ménière's disease (MD) or benign paroxysmal positional vertigo (BPPV) poses a considerable challenge. Both VM and MD share overlapping cochlear and vestibular features (such as tinnitus, aural fullness, and fluctuating hearing loss) yet no single diagnostic test can reliably distinguish between them. As many as half of VM patients are initially misdiagnosed with MD, leading to inappropriate or delayed treatment (2).

Vestibular testing, including video head impulse test, caloric testing, vestibular-evoked myogenic potentials (VEMPs), and ictal video-oculography (VOG), can aid in identifying VM-specific patterns. For instance, ictal spontaneous nystagmus in VM often shows low velocity, may be horizontal, vertical, or torsional, and typically occurs with fixation denied (4). Still, interictal test results are frequently within normal limits, which further

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complicates diagnosis.

Management of VM is similarly complex. While various prophylactic treatments (such as β -blockers, tricyclic antidepressants, calcium channel blockers, and anticonvulsants) have shown potential benefit, the absence of standardized treatment protocols has limited clinical consensus (1, 3). Triptans and NSAIDs, commonly used for migraine, appear less effective in managing vertigo-specific symptoms (1).

Among the interventional strategies under exploration, greater occipital nerve (GON) block has emerged as a potentially effective yet underutilized option. In a recent randomized controlled trial, patients receiving bilateral GON blocks every four weeks with lidocaine showed a significantly greater reduction in headache days compared to placebo, with 40.9% achieving a $\geq 50\%$ reduction in frequency (5). Another prospective study focusing on menstrual migraine found that monthly GON blocks not only reduced headache intensity and frequency but also improved quality of life measures that persisted for up to three months post-treatment (6). The duration of benefit seems to range from days to several weeks depending on the protocol, and mild adverse effects such as transient local discomfort are the most commonly reported events (5). Interestingly, meta-analyses evaluating GON block in related headache syndromes such as postdural puncture headache support its analgesic efficacy within the first 24 hours, suggesting a potential for acute relief as well (7). The proposed mechanism involves modulation of nociceptive signaling within the trigeminocervical complex, where cervical and trigeminal afferents converge providing a plausible anatomical link between occipital nerve input and vestibular symptom modulation (8).

In this report, we present a case of a 25-year-old woman initially misdiagnosed with peripheral vertigo, who was subsequently identified as having VM. Her refractory symptoms improved markedly following a course of GON block, suggesting a possible role for this intervention in cases resistant to standard therapies.

CASE REPORT

A 25-year-old female presented with a three-year history of episodic vertigo. The vertigo episodes lasted 2–3 days, were exacerbated by head movements and

were associated with nausea. She had been treated with betahistine, dimenhydrinate and piracetam under the assumption of peripheral vertigo, with little to no symptom relief.

On further evaluation, the patient reported accompanying headaches during vertigo episodes. These headaches were moderate to severe, throbbing in quality, and localized bilaterally in the temporal region. Associated symptoms included photophobia and phonophobia. The patient also admitted to excessive analgesic use to manage her symptoms, which likely contributed to rebound headache episodes. The recurrent symptoms significantly disrupted her daily activities and work.

A thorough neurological examination and vestibular function tests were within normal limits. Imaging studies, including brain MRI, ruled out structural abnormalities. With these findings, the diagnosis of peripheral vertigo was deemed incorrect, and the clinical features strongly suggested VM.

Given the refractory nature of her symptoms, the significant impact on her quality of life, and her history of excessive analgesic use, a GON block was proposed as part of the treatment strategy for VM. The decision was made to address not only the migraine-related vertigo but also to reduce the need for analgesics and mitigate potential rebound headache episodes.

The initial procedure was performed bilaterally with 2 mL of 1% lidocaine injected at the GON injection site near occipital protuberance. The patient tolerated the procedure well, with no immediate adverse effects. Over the following month, weekly GON blocks were administered for a total of four sessions, which further contributed to the significant reduction in her symptoms.

One month after the initiation of GON block therapy, duloxetine was added to her treatment plan at a low dose. This aimed to provide additional preventive benefits for both migraine and associated symptoms, including chronic pain and emotional distress related to her condition.

Although the primary outcome was the reduction in vertigo and headache severity assessed by Visual Analog Scale (VAS), the patient's self-reported improvements extended beyond pain. During follow-up visits, she spontaneously reported better sleep

quality, reduced emotional distress, and increased daily functioning. Formal scales for mood, sleep, or quality of life were not administered in this case; however, the patient noted feeling "more balanced" and "less anxious," which coincided with the reduction in vertiginous episodes. These observations may suggest a broader effect of GON block beyond pain modulation, possibly through central mechanisms influencing affective and autonomic regulation. Over the next month she experienced only one mild vertigo episode with mild headache, compared to frequent and debilitating episodes prior to the intervention.

DISCUSSION

VM remains an underdiagnosed condition despite its prevalence and significant impact on quality of life. This case illustrates the clinical complexities of distinguishing VM from peripheral vestibular disorders, emphasizing the importance of a thorough evaluation, including detailed history-taking, neurological examination, and appropriate diagnostic imaging. The patient's initial misdiagnosis as peripheral vertigo, emphasizes the need for heightened awareness among clinicians regarding VM's diverse symptoms.

The delayed diagnosis of VM in this case reflects a common diagnostic pitfall. The patient was initially treated for peripheral vertigo over an extended period, largely because her episodic vertigo was not immediately accompanied by classic migrainous headache. This dissociation between vestibular and cephalic symptoms is a known barrier to timely diagnosis, as many patients with VM may present with isolated vertigo or non-specific dizziness, especially in early stages (2, 4).

Clinicians should maintain a high index of suspicion for VM in patients with recurrent vertigo episodes lasting from 5 minutes to 72 hours, particularly if there is a history of migraine or if attacks are accompanied by migrainous features such as photophobia, phonophobia, or visual aura. According to the Bárány Society and International Classification of Headache Disorders (ICHD-3) criteria, a diagnosis of VM requires at least five episodes of vestibular symptoms with moderate or severe intensity, a current or past history of migraine, and the presence of at least one migrainous symptom during at least 50% of vertigo

episodes (9).

Of particular note, the administration of GON block in this case was not only therapeutic but also indirectly diagnostic. The rapid and marked improvement following the block supported a migrainous etiology of symptoms, further distancing the clinical picture from peripheral causes. While GON block is not a formal diagnostic tool, its response profile may be viewed as supportive evidence in ambiguous presentations.

The resolution of vestibular symptoms following GON block therapy in this case is particularly intriguing. While GON block is primarily utilized for managing headache disorders, its impact on vestibular symptoms is less well-documented, making this observation noteworthy. The improvement in vertigo raises important questions about the underlying mechanisms linking vestibular dysfunction and migraine pathophysiology.

One possible explanation involves the shared neural pathways between the trigeminal and vestibular systems. The trigeminocervical complex, a key relay station in migraine pathophysiology, has connections with the vestibular nuclei via brainstem circuits. By modulating nociceptive input at the occipital nerve level, the GON block may influence this interconnected network, leading to concurrent improvement in both migraine and vestibular symptoms (10, 11).

This dual benefit of GON block aligns with findings from a limited number of studies that reported reductions in vestibular symptoms in patients treated for migraine with GON block. For instance, a recent preliminary study found significant decreases in both the frequency and severity of vertigo attacks in VM patients after GON block treatment. This effect was attributed to the modulation of trigeminovascular and vestibular pathways through shared brainstem connections (12). GON block therapy is an effective and cost-efficient option for managing conditions. However, despite its simplicity and efficacy, it remains under-researched in the literature and underutilized in clinical practice.

CONCLUSION

This case highlights the diagnostic challenge of VM and the therapeutic potential of GON block. Clinicians should maintain a high index of suspicion for VM in patients with vertigo that is refractory to conventional treatments for peripheral causes. Early and accurate diagnosis,

combined with appropriate interventions such as GON block, can dramatically improve patient outcomes.

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THE IMPACT OF HEMOGLOBIN J (HbJ) VARIANT ON HbA1c MEASUREMENT: A CASE REPORT

Hemoglobin J (HbJ) Varyantının HbA1c Ölçümü Üzerindeki Etkisi: Bir Olgu Sunumu

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ABSTRACT

In this case report, discrepancies in HbA1c measurements were observed in a 54-year-old female patient with Type 2 diabetes due to the presence of a haemoglobin (Hb) variant, most likely HbJ. HbA1c were measured as 10.5% using capillary electrophoresis(CE), 8.92% using ion-exchange high-performance liquid chromatography(HPLC), and 10.4% using immunoassay. The lower HbA1c value obtained with the HPLC method suggested interference from the Hb variant(most likely HbJ detected in the Z13 region). Hb variants can lead to inaccurate HbA1c results, which may influence clinical decisions, particularly in diabetes management. This case highlights that CE can be a reliable method even in the presence of Hb variants, but results from different methods should be interpreted with caution. Due to the poor glycemic control, the treatment plan was revised, and the patient was recommended for monitor the clinical implications of the Hb variant. In conclusion, considering Hb variants in the interpretation of HbA1c is critical to prevent misdiagnosis and inappropriate treatment.

Keywords: Hb J; High-Performance Liquid Chromatography; HbA1c; Capillary Electrophoresis; Immunoassay

ÖZET

Bu olgu sunumunda, Tip 2 diyabetli 54 yaşındaki kadın hastada hemoglobin (Hb) varyantı (muhtemel HbJ) nedeniyle HbA1c ölçümlerinde farklılıklar gözlemlenmiştir. HbA1c düzeyi kapiller elektroforez (CE) yöntemiyle %10,5, iyon değişimli yüksek performans sıvı kromatografisi(HPLC) yöntemiyle %8,92 ve immünoassay yöntemiyle %10,4 olarak ölçülmüştür. İyon değişimli HPLC yöntemiyle elde edilen daha düşük HbA1c değeri, Hb varyantının (Z13 bölgesinde tespit edilen muhtemel HbJ) interferans etkisini düşündürmektedir. Hb varyantları, özellikle diyabet yönetiminde klinik kararları etkileyebilecek hatalı HbA1c sonuçlarına yol açabilir. Bu olgu, Hb varyantlarının varlığında bile kapiller elektroforezin güvenilir bir yöntem olabileceğini, ancak farklı yöntemlerle elde edilen sonuçların dikkatle değerlendirilmesi gerektiğini göstermektedir. Hastanın glisemik kontrolünün yetersiz olması nedeniyle tedavi planı yeniden düzenlenmiş ve Hb varyantının klinik etkilerinin izlenmesi amacıyla takibe alınması önerilmiştir. Sonuç olarak, HbA1c sonuçlarının yorumlanmasında Hb varyantlarının dikkate alınması, yanlış tanı ve uygunsuz tedavilerin önlenmesi açısından büyük önem taşımaktadır.

Anahtar Kelimeler: Hb J; Yüksek Performanslı Sıvı Kromatografisi; HbA1c; Kapiller Elektroforez; İmmünoassay

INTRODUCTION

In cases of clinical discrepancy, it is appropriate to repeat the analysis using a sample collected and transferred under standard conditions (i.e., cold chain). Glycated hemoglobin (HbA1c), formed through non-enzymatic glycation of hemoglobin (Hb) molecules, quantitatively reflects mean plasma glucose levels over the erythrocyte lifespan (approximately 120 days), with the strongest correlation to the preceding 2-3 months, establishing its role as the gold standard for long-term diabetes management assessment. HbA1c is considered the gold standard for the diagnosis and evaluation of diabetes. Hemoglobinopathies are prevalent in numerous regions around the world. Over 900 variants of Hb have been identified, accounting for at least 43% of all possible single-point mutations. HbJ is a less common alpha-globin gene variant that can affect HbA1c results (1, 2).

Clinical laboratories can determine HbA1c levels using various principal methodologies, including enzymatic analysis, immunoturbidimetric analysis, boronate affinity chromatography, capillary electrophoresis (CE), and ion-exchange high-performance liquid chromatography (HPLC). Ion-exchange HPLC and CE are among the commonly used methods for HbA1c measurement. HbA1c measurement relies on

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methodologies that exploit differences in the affinity, charge, and immune response of glycosylated Hb molecules (3, 4). Both anion- and cation-exchange HPLC and CE methods can detect the presence of Hb variants. Hemoglobin J was first characterized in 1963 by Baglioni and Weatherall, who identified the variant in an African American family (5). Although HbJ carriers generally show no hematologic abnormalities, this variant causes significant analytical interference in HPLC-based HbA1c testing, potentially yielding unreliable glycemic monitoring results. Several studies have detailed the effects of silent hemoglobinopathy variants on HbA1c values; variants such as Hb Camden, Hb Austin, and Hb N-Baltimore have been reported to cause falsely elevated HbA1c results (6). If an HbA1c result does not correlate with a patient's clinical condition, hemoglobinopathies and conditions affecting red blood cell lifespan should be considered as potential causes.

In this case report, we characterize a suspected HbJ case detected via CE with an accompanying electropherogram and describe the implications of this Hb variant on the accurate interpretation of HbA1c results obtained using HPLC and immunoassay methods.

CASE REPORT

A 54-year-old female patient with a diagnosis of Type 2 diabetes was undergoing routine follow-up. During her routine check-up, her fasting blood glucose was found to be 192 mg/dL, Hb level was 14.1 g/dL, and TSH level was within normal limits at 1.33 µIU/mL. HbA1c was measured as 10.5% using the CE method (Sebia Capillarys 3, France), and an atypical Hb variant profile was observed on the CE electropherogram (Figure 1). To confirm the Hb variant and conduct a detailed analysis, repeat CE Hb variant analysis was performed (Figure 2). Further investigation revealed a variant in the Z13 region, suggesting a rare Hb variant, most likely HbJ. Genetic analysis to determine the specific HbJ variant type could not be performed. The patient's medications included Ryzodeg (insulin degludec + aspart), Galvus Met (vildagliptin + metformin), and Jardiance (empagliflozin). Written informed consent was obtained from the patient for publication of this case report.

The same blood sample was reanalysed for HbA1c using two different methods: ion-exchange HPLC (Lipotronic HPLC System GH900, China) and immunoassay (Cobas 8000, Roche Diagnostics, Germany). HbA1c values were 8.92% and 10.4%, respectively.

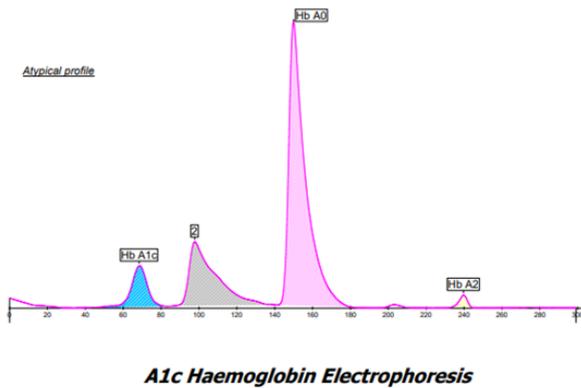
Laboratory Findings:

- HbA1c: 10.5% (92 mmol/mol) (capillary electrophoresis)
- HbA1c: 8.92% (74 mmol/mol) (ion-exchange HPLC)
- HbA1c: 10.4% (92 mmol/mol) (immunoassay)
- Fasting Blood Glucose: 192 mg/dL (10.71 mmol/L)
- Hb: 14.1 g/dL (previous result: 14.0 g/dL)
- TSH: 1.33 µIU/mL
- Hb Variant Analysis: Variant in Z13 region, most likely HbJ (Figure 2).

DISCUSSION

HbA1c is formed by the reaction between glucose and the NH₂-terminal valine of the Hb beta chain. It has been used as the gold standard in the clinical management of diabetes for approximately 30 years for routine monitoring of glycemic status. Hb variants can cause falsely elevated or decreased HbA1c results in some measurement methods. However, the CE method used in this case is considered reliable in the presence of hemoglobinopathies. The patient's high fasting blood glucose level was consistent with the HbA1c value, suggesting that the measurement was valid despite the variant.

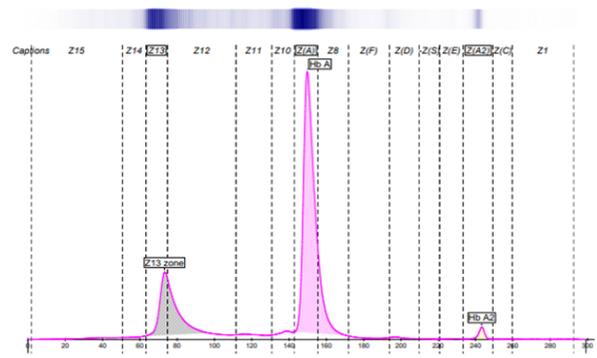
The National Glycohemoglobin Standardization Program (NGSP) considers HPLC the gold standard for HbA1c analysis, while the International Federation of Clinical Chemistry (IFCC) recommends CE (7, 8). Both CE and ion-exchange HPLC can incidentally detect Hb variants, which may interfere with HbA1c assays. Immunoassays, boronate affinity chromatography, and enzymatic methods are generally less likely to detect such variants. In this case, we measured HbA1c using ion-exchange HPLC, immunoassay, and CE. The results suggested that the HbJ variant negatively interfered with the HPLC method. Barakat et al. also reported a case where ion-exchange HPLC yielded a negatively biased result due to a variant (9). Clinical biochemists must recognize factors that may lead to spuriously high or low HbA1c measurements and should collaborate with clinical departments when an abnormal Hb



A1c Haemoglobin Electrophoresis

Fractions	%	mmol/mol	Cal. %
Hb A1c (*)	-	92	10.5
2	24.3		
Hb A0	65.2		
Hb A2	1.5		

Figure 1. Capillary electrophoresis performed for HbA1c measurement revealed an atypical hemoglobin variant detection in the electrophoretogram. An unknown peak was observed in region number two.



Haemoglobin Electrophoresis

Name	%	Normal Values %
Z13 zone	24.9	
Hb A	73.4	
Hb A2	1.7	

Figure 2. A high probability HbJ variant was detected in the Z13 region of the capillary electrophoresis for hemoglobin variant analysis.

variant is suspected.

The patient’s clinical course indicated poorly controlled Type 2 diabetes despite current treatment. The high HbA1c value and fasting blood glucose level of 192 mg/dL suggested inadequate glycemic control. HbA1c levels were 10.5% by CE, 8.92% by HPLC, and 10.4% by immunoassay, all indicating poor diabetes control. In this case, there was no significant clinical discrepancy between glucose levels and HbA1c values across methods, although the HPLC result was lower. However, such consistency may not occur in all cases, potentially leading to errors in diabetes management based on HbA1c. Therefore, both clinical biochemists and clinicians should exercise caution when encountering discrepancies between HbA1c and glucose levels or when different methods yield inconsistent results.

HbJ has various characteristics and functions, with variable effects on HbA1c levels. The most common HbJ variant, HbJ Capetown ($\alpha 2$ 92Gln $\beta 2$), causes falsely elevated HbA1c levels, as does HbJ Valencia, while HbJ Baltimore and HbJ Meerut cause falsely low HbA1c values. No Reports indicate that the HbJ variant can lead to either spuriously high or low HbA1c results, depending on the analytical method used (9- 11). In a recent study, Song et al. investigated the interference of Hb Q-Thailand, Hb G-Honolulu, Hb Ube-2, Hb New York, Hb J-Bangkok, Hb G-Coushatta, and Hb E variants

on HbA1c measurement using five different methods (Intelligene Biosystems QuanTOF, Sebia Capillarys 3 TERA, Premier Hb9210, Arkray HA-8190V, Tosoh G11, and Bio-Rad D-100). In the evaluation of Hb J-Bangkok, LC-MS/MS served as the reference method. Among six comparative methods, interference was observed in five—including CE, boronate affinity chromatography, and three HPLC techniques—highlighting method-dependent variability in HbA1c measurement. (12).

A limitation of our case was the inability to confirm the suspected HbJ variant (Z13 zone variants) through genetic testing. Variants in the Z13 zone detected by CE include Hb AJ-Ain Abu Dhabi, HbJ-Europa, HbJ-Baltimore, HbJ-Ravigo, HbJ-Lome, HbJ-Norfolk, HbJ-Nigeria, and HbJ-Kaohsiung.

As a result, this case highlights the utility of CE for HbA1c measurement in the presence of Hb variants (HbJ and Z13 zone) and underscores the importance of treatment optimization in poorly controlled diabetes management. The suspected HbJ variant in the Z13 region is a rare mutation, and its clinical significance should be evaluated through patient follow-up.

CONCLUSION

Rigorous interpretation of HbA1c results is crucial to avoid misleading clinical conclusions, particularly in certain populations with a relatively high prevalence

of Hb variants. Additionally, it necessitates method-specific validation of HbA1c measurements to ensure accuracy. Routine laboratory tests can be affected by various Hb variants, which is an important consideration. HbA1c results that do not correlate clinically or with blood glucose levels should raise suspicion of a Hb variant and should be confirmed using different methods. In patients with Hb variants, an appropriate HbA1c measurement method should be selected and consistently used for follow-up. This is critical to prevent misdiagnosis and mismanagement of patients. Interferences in HbA1c measurement can lead to incorrect diagnosis and treatment.

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EDİTÖRE MEKTUP

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Bozok Tıp Dergisi 2023;14(4):190-195 sayısında Arslan ve arkadaşlarının “İskemik Serebrovasküler Hastalık Nedeni ile Acile Başvuran Hastalarda Kan Gazı Parametreleri” başlıklı çalışması, inme nedeniyle acil servise başvuran hastalarda beyin dokusundaki metabolik değişimlerin periferik arteriyel kan gazı parametrelerine yansıyor yansımadığını incelemesi bakımından dikkat çekicidir. Araştırmacılar, beyin iskemisinin neden olduğu hipoksi, karbondioksit retansiyonu ve pH değişikliklerinin arteriyel kan gazı değerlerine etkisini araştırarak acil servislerde hızlı laboratuvar desteği sağlama potansiyelini değerlendirmeyi amaçlamışlardır. Ancak çalışmanın bazı sınırlılıkları göze çarpmaktadır. Öncelikle, çalışma tek merkezli olup hasta sayısı sınırlıdır (n=50+50). Kontrol grubu olarak acil servise baş ağrısı veya karın ağrısı gibi şikayetlerle başvuran kişiler seçilmiş, ancak bu bireylerde yapılan tetkiklerin kapsamı ve beyin görüntülemesi olup olmadığı belirtilmemiştir. “Sağlıklı” olarak tanımlanan kontrol grubunun acil serviste yatan heterojen bir hasta topluluğu içinden seçilmiş olması metodolojik olarak sorun yaratabilir. Ayrıca, hasta ve kontrol gruplarının demografik özellikleri arasında da farklar vardır. Örneğin, inme grubunda cinsiyet dağılımı eşitken (kadın/erkek %50), kontrol grubunda erkek oranı %32’dir(1). Yaş ortalamaları benzer olsa da, bu gibi farklılıklar metabolik parametreleri etkileyebilebilir.

Çalışmanın tasarımında ise arteriyel kan gazı örneğinin ne zaman alındığı net olarak belirtilmemiştir. Örnekler başvuru anında mı, yoksa semptom başlangıcından belli bir süre sonra mı alınmıştır, bu belirsizdir. Oysa inme sırasında beyin metabolizmasındaki değişiklikler zamana bağlı olarak dinamik biçimde ilerler. Oksijen tedavisi, sedasyon veya hiper/hipopnö gibi faktörler kan gazı sonuçlarını etkileyebilir. Ayrıca örneğin hangi arterden alındığı (radial, femoral vb.) veya örnekleme tekniğine dair bilgiler de eksiktir. Bu durum elde edilen değerlerin güvenilirliğini azaltmaktadır.

Çalışmanın bulguları arasında HCO_3^- ve baz fazlası (BE) düzeylerinde saptanan değişimler, yazarlar tarafından iskemiyeye bağlı metabolik asidozla ilişkilendirilmiştir. Ancak bu parametrelerin beyin dokusuna özgü değişimleri yansıttığını söylemek zordur. Küçük boyuttaki doku hipoksisinin sistemik kan gazlarına yansımaları sınırlı olabilir. Elde edilen farkların mutlak değerlerinin de düşük olması (örneğin bikarbonatta yaklaşık 1 mmol/l, BE’de yaklaşık 1,2 mmol/l fark) klinik olarak anlamlı olmayabilir. Bunun yanında inmenin şiddeti, eşlik eden sistemik hastalıklar veya ventilasyon durumu da bu değerleri etkileyebilir. Bu nedenle yazarların “kan gazı incelemeleri iskemik inme tanısını destekleyebilir” yorumu henüz spekülatif niteliktedir ve infarkt yeri veya büyüklüğüne dair belirleyici bilgi sağlamamaktadır. Literatür karşılaştırmasında da bazı tutarsızlıklar göze çarpmaktadır. Mevcut literatürde yapılan çalışmaların çoğu intrakraniyal örnekler kullanarak değerlendirme yapmaktadır. Örneğin Spears ve arkadaşlarının yaptığı çalışmada, mekanik trombektomi sırasında sistemik arteriyel kan ile intrakraniyal kan gazı değerleri karşılaştırılmış ve sistemik kandaki pO_2 , pCO_2 ve HCO_3^- düzeylerinin intrakraniyal değerlere göre anlamlı derecede yüksek olduğu gösterilmiştir(2). Bu bulgu, periferik arteriyel kan gazı ile beyin dokusu arasındaki farklılıkları ortaya koymaktadır. Arslan ve arkadaşlarının çalışmasında infarkt alt tiplerine göre anlamlı fark bulunmaması ise muhtemelen periferik ölçümlerin sınırlı duyarlılığından veya örneklem büyüklüğünün yetersizliğinden kaynaklanmaktadır. Kısacası, periferik arteriyel kan gazı analizlerinin infarkt yerini veya büyüklüğünü saptamada sınırlı olduğu sonucuna varılabilir. Bu çalışma, iskemik inme olgularında periferik arteriyel kan gazı analizlerinin tanısal değerini araştırma açısından önemli bir başlangıçtır. Ancak sınırlı örneklem, metodolojik belirsizlikler ve sistemik etkilerin dışlanamaması, bulguların yorumunu zorlaştırmaktadır. Literatür verileri de, periferik kan gazı değerlerinin beyin dokusundaki gerçek metabolik değişimleri yansıtmada yetersiz olabileceğini göstermektedir. Bu nedenle, bu yöntem klinik uygulamada ancak destekleyici bir araç olarak değerlendirilebilir; tanısal güvenilirliği arttırmak için daha kapsamlı çalışmalara ihtiyaç vardır.

KAYNAKLAR

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Verilerin elde edilmesi:	
Verilerin analizi ve yorumlanması:	
Yazının kaleme alınması:	
Eleştirel gözden geçirme:	
İstatistiksel değerlendirme:	

Makaledeki Sırasıyla Yazarın Adı Soyadı İmza Tarih

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BOZOK MEDICAL JOURNAL

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Acquisition of data:	
Analysis and interpretation of data:	
Drafting of manuscript:	
Critical revision:	
Statistical Analysis:	

Author Name Surname Sign Date

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Yazarlara Bilgi

Kapsam

Bozok Tıp Dergisi, Yozgat-Bozok Üniversitesi'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.

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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:

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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 cümlelerin 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 fotoğraflar 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 arasında 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 nerve 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, kaçınıcı 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 bildirimler:

-2000 sözcüğü aşmamalı, şekil ve tablo en fazla 2, kaynak sayısı en fazla 20 olmalıdır.

Olgu Sunumu:

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İçerik:

- Özet (ortalama 100-150 kelime; bölümsüz; Türkçe ve İngilizce)

- Giriş

- Olgu Sunumu

- Tartışma

- Kaynaklar

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Son bir yıl içinde dergide yayınlanmış makalelere yanıt olarak gönderilir. Yazı hakkında okuyucuların farklı görüş, deneyim ve sorularını içerir.

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- 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.

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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.

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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.

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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 abbreviations 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 acknowledgements section; conflict of interest, financial support, grants, and all other editorial (statistical analysis, language editing) and/or technical assistance 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; initials 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 than 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

