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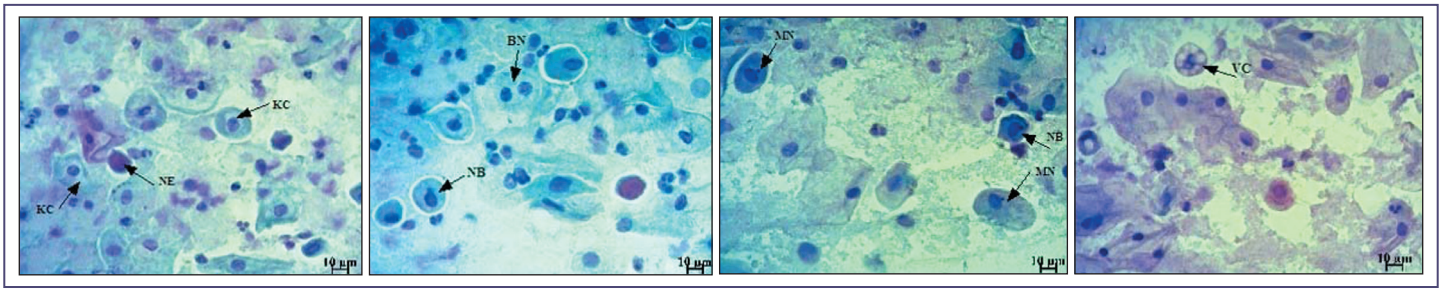

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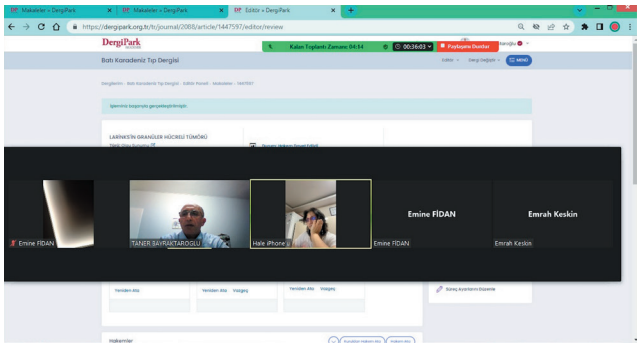
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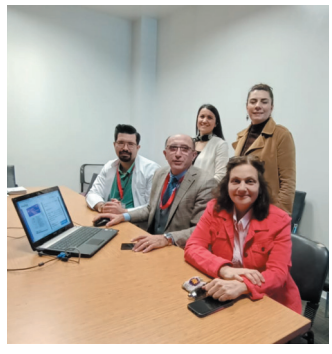

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YAZARLAR İÇİN BİLGİLER

"Batı Karadeniz Tıp Dergisi", Zonguldak Bülent Ecevit Üniversitesi Tıp Fakültesi'nin bilimsel yayım organıdır. Dergimiz 2017 yılında yayına başlamıştır, 2019 yılından itibaren TR Dizin ve Türk Atıf Dizini içinde yer alan hakemli bir dergidir. Dergi yılda üç kez olmak üzere Nisan-Ağustos ve Aralık aylarında yayımlanır. Derginin yayım dili Türkçe ve İngilizcedir.

Derginin amacı Türkiye'de ve yurtdışında ilgili alanlarda yapılan nitelikli araştırma çalışmalarını ulusal ve uluslararası bilim ortamına sunarak duyurmak, paylaşmak ve sürekli bir eğitim platformu oluşturarak bilimsel ve sosyal iletişimin sağlanmasına katkıda bulunmaktır. Dergide bu amaçlar doğrultusunda Temel, Dahili ve Cerrahi Tıp Bilimleri alanında özgün araştırmalar, olgu sunumları, derlemeler, kısa bilgi makalesi, editöre mektup, biyografi yazıları ve makale biçimine getirilen toplantı bildirileri yayımlanır. Kongre, sempozyum, elektronik ortamda sunulmuş bildiriler veya ön çalışmalar, bu durumun belirtilmesi koşuluyla yayımlanabilir. Bu dergiye gönderilen yazılar, daha önce herhangi bir yerde yayımlanmamış ve yayımlanmak üzere başka bir dergiye gönderilmemiş olması şartı ile kabul edilir.

Yazıların tüm bilimsel sorumluluğu yazarlara aittir. Yazarlar, yazar sıralamasını yayın hakkı devir formunda imzalı olarak belirtmek zorundadır. Yazarların tümünün ismi, yazının başlığının altındaki bölümde yer almalıdır. Yazarlık için yeterli ölçütleri karşılamayan ancak çalışmaya katkısı olan tüm bireyler "Teşekkür" kısmında sıralanabilir. Bu amaçla "**Yayın hakkı devir sözleşmesi formu**" sorumlu tüm yazarlar tarafından imzalanarak sisteme yüklenmelidir. Makaleler "**https://dergipark.org.tr/tr/pub/mjwbs"**adresinden sisteme yüklenmesi gerekmektedir. Sisteme kapak sayfasının, tablo ve grafiklerin de ayrı ayrı yüklenmelidir. Kapak sayfasının tüm yazarların ad, soyad, çalıştıkları kurum, 40 karakteri geçmeyen kısa başlık, e-posta adresleri ve ORCID ID bilgilerini içermelidir.

Tüm yazılar önce editör ve yardımcı editörler tarafından ön değerlendirmeye alınır. Daha sonra değerlendirilmesi için alanında uzman hakemlere gönderilir. Editör, yazıları düzeltme, değiştirme, reddetme veya yeniden düzenlenmesi için geri gönderme hakkına sahiptir. Dergide yayımlanmasına karar verilen yazılar sayfa düzenlenmesi sürecine alınır. Yazılar yayım öncesi son şekline getirilerek yazarların kontrolüne ve onayına sunulur. Tüm yazılar, uluslararası etik kurallara uygun olmalı ve s etik kurul izninin alındığına dair belge sisteme yüklenmelidir.

MAKALENİN HAZIRLANMASI

Kapak Sayfası

Yazının Türkçe ve İngilizce başlığı, yazarların ad ve soyadları belirtilir. Aynı kurumdan yazarlar, aynı numarayı almak üzere klinik, bölüm, enstitü veya kuruluşun ismi ve adresleri yazar sırasına göre numaralandırılarak yazılır. Yazının kısa başlığı da verilmelidir. Yazışmaların yapılacağı yazarın adı, tam posta adresi, telefon, faks numarası ve elektronik posta adresleri yazılmalıdır. Çalışma bir kongre ya da bir toplantıda bildiri olarak sunulmuşsa, yazarlar bu durumu sayfanın sonunda, yapılan toplantının adını, yerini ve tarihini veya destek alan kurum ile proje numarasını vererek belirtmelidir.

Öz

İki yüz elli sözcükten fazla olmayan Türkçe öz yazılmalıdır. Öz kısmı amaç, gereç ve yöntemler, bulgular ve sonuç bölümlerini içermelidir. Kısaltmalar ve kaynaklar kullanılmamalıdır. Özün sonunda yer alacak anahtar sözcükler, üç ile yedi sözcük arasında, Index Medicus Tıbbi Başlıklar (MeSH) listesine uygun olarak alfabetik sırada verilmelidir. Bir başka sayfaya, Türkçe öz ve anahtar sözcüklerin birebir tercümesi olacak biçimde İngilizce öz (abstract) yazılmalıdır.

Olgu sunumlarında ise; amaç, olgu (lar), sonuç (lar) bölümlerini içeren yapılandırılmış öz bulunmalıdır.

Metin Sayfaları

Makalenin ana metni giriş, gereç ve yöntemler, bulgular ve tartışma başlıkları altında verilmelidir. Bütün ölçümler metrik sistemde verilmelidir. Simge ve kısaltmalar uluslararası standartlarda olmalıdır. Kısaltmalar metinde ilk görüldüğünde açıklanmalı ve genel kabul görmüş olanlarla sınırlandırılmalıdır. İstatistiksel analiz için kullanılan testler metinde ve tablolarda belirtilmelidir. Yazarlar, metnin sonunda teşekkür başlığı altında, çalışmanın gerçekleşmesi için katkıda bulunan kişi, kurum ve kuruluşlar varsa bildirebilirler. Makalenin sonunda çıkar çatışması, yazar katkı beyanı, finansal destek ve etik kurul onay başlıkları doldurulmalıdır.

Tablo, Şekil ve Resimler

Tablolar ana metin içinde kaynaklardan sonra gelmeli, her tablo ayrı bir sayfada olacak şekilde ve çift aralıklı olarak yazılmalıdır. Makale içindeki geçiş sırasına göre numaralandırılmalı ve kısa başlık içermelidir. Metin içerisinde de yerleri belirtilmelidir. Tablo başlığı tablonun üstünde, tablo açıklamaları ve kısaltmalar altta yer almalıdır.

Resim ve şekiller ".jpeg" ya da ".tiff" formatında verilmelidir. En az 800x600 piksel boyutunda ve 300 dpi çözünürlükte sisteme yüklenmelidir. Histolojik kesit ve sitoloji fotoğraflarında büyütme ve boyama tekniği belirtilmelidir. Resim ve şekil alt yazıları makalenin sonunda ayrı bir sayfada verilmelidir. Şekil altyazıları kısa ve açıklayıcı olmalıdır. Aynı sütun içinde yer alan ve birlikte görünen şekiller aynı numarayı, farklı harflerle alabilirler (1A,1B gibi). Eğer mümkünse fotoğraf üzerine ölçek eklenmelidir.

Kaynaklar

Kaynaklar makalede geçiş sırasına göre numaralandırılmalı, numaraları metinde cümlenin sonunda parantez içinde belirtilmelidir ve metin içerisinde aldığı numaraya göre kaynak listesinde gösterilmelidir. Kaynak listesi ayrı bir sayfada olmalıdır. Kaynak listesinde "ve ark." (et al.) kısaltması kullanılmamalı, bütün yazarlar eklenmelidir.

Makale

Yazar ad(lar)ı, makale adı, dergi adı ("lndexMedicus" ta verilen listeye göre kısaltılmalıdır), yılı, cilt numarası, ilk ve son sayfa numarası.

Eser T, Ünver B, Alarçin G, Bayraktaroğlu T. Yetişkinlerde Bel/Boy Oranı ile Ayak Postürü Arasındaki İlişkinin İncelenmesi. Turk J Diab Obes. 2020;4:30–35.

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Kitaplar

Bölümün yazarlarının ad(lar)ı, kitabın adı, kaçıncı baskı olduğu, yayımlandığı yer, yayınevi, yıl.

Graber TM, Rakosi T, Petrovic AG. Dentofacial orthopedics with functio nal appliances. 2nd ed., St. Louis, Mosby; 1997.

Kitap bölümü

İlgili bölüm yazar ad(lar)ı, ilgili bölüm adı, editör(ler), kitabın adı, yayım landığı yer, yayınevi, yıl, ilk ve son sayfa numarası.

Marsh PD, Nyvad B. The oral microflora and biofilms on teeth. In: Fejerskov O, Kidd E, editors. Dental caries the disease and its clinical management. 2nd ed. Blackwell Munksgaard; 2004. 29-48.

Çevrimiçi makaleler

Abood S: Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet yayını]. 2002 Jun;102(6) (Erişim Tarihi:… Adres:http://www.nursingworld.org/AJN/2002/june/ Wawatch.htm).

Tez örneği

Sağlam C. Cerrahi menopoz modeli oluşturulan genç dişi sıçanlarda glp-1 agonistinin depresyon benzeri davranışlara etkisi (Yüksek Lisans Tezi), Zonguldak, Zonguldak Bülent Ecevit Üniversitesi, 2022, 1-106. (Erişim Tarihi:01.12.2023, Adres: http…).

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The aim of the journal is to report and share qualified research studies conducted in relevant fields in Tükiye and abroad by presenting them to the national and international scientific community, and to contribute to scientific and social communication by creating a continuous education platform. In accordance with these aims, the journal publishes original research in the field of Basic, Internal and Surgical Medical Sciences, including case reports, review articles, short communications, letters to the editor, biography articles and conference proceedings written in article format. Papers or preliminary studies presented in congresses, symposiums, or online can be published in the journal, provided that this situation is stated. Manuscripts sent to this journal are accepted on the condition that they have not been published anywhere before and have not been sent to another journal for publication.

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The abstract, not exceeding 250 words, needs to be written in Turkish and English. It should include aim, materials and methods, results and conclusion sections. Abbreviations and references should not be used. Turkish keywords provided at the end of the abstract should be between three and seven words and given in alphabetical order in accordance with the Index Medicus Medical Titles (MeSH) list. An English abstract should be written on another page, with a one-to-one translation of the Turkish abstract and keywords. In case reports, there should be a structured abstract that includes objective, case(s), and conclusion(s).

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The main text of the article should be given under the headings of introduction, materials and methods, results and discussion. All measurements must be given in the metric system. Symbols and abbreviations must comply with international standards. Abbreviations should be explained when first seen in the text and should be limited to those that are generally accepted. Tests used for statistical analysis should be stated in the text and tables. Authors can state, under the acknowledgment heading at the end of the text, any individuals, institutions and organizations that contributed to the realization of the study. Conflict of interest, author contribution declaration, financial support and ethics committee approval headings must be filled in at the end of the article.

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Tables should come after the references in the main text and each table should be on a separate page and double-spaced. It should be numbered according to the order of occurrence in the article and contain a short caption. Their locations should also be specified in the text. The table caption should be at the top of the table, and table descriptions and abbreviations should be at the bottom.

Images and figures must be uploaded to the system in ".jpeg" or ".tiff" format with a pixel size of at least 800x600 and a resolution of 1000 dpi. Magnification and staining techniques should be indicated in histological section and cytology photographs. Image and figure captions should be given on a separate page at the end of the article. Figure captions should be short and descriptive. Figures that appear together in the same column may have the same number with different letters (such as 1A, 1B). If possible, a scale should be added to the photograph.

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Author name(s), title of the article, journal name (must be abbreviated according to the list given in "IndexMedicus"), year, volume number, first and last page number.

Eser T, Ünver B, Alarçin G, Bayraktaroğlu T. Examining the Relationship Between Waist/Height Ratio and Foot Posture in Adults. Turk J Diab Obes. 2020;4: 30–35.

Book

Name(s) of the authors of the chapter, title of the book, edition, place of publication, publisher, year.

Graber TM, Rakosi T, Petrovic AG. Dentofacial orthopedics with functio nal appliances. 2nd ed., St. Louis, Mosby; 1997.

Book Chapter

Author name(s) for the chapter, chapter title, editor(s), title of the book, place of publication, publisher, year, first and last page numbers.

Marsh PD, Nyvad B. The oral microflora and biofilms on teeth. In: Fejerskov O, Kidd E, editors. Dental caries the disease and its clinical management. 2nd ed. Blackwell Munksgaard; 2004. 29-48.

Online articles

Abood S: Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet publication]. 2002 Jun 102(6) (Access Date: … Link:http://www.nursingworld.org/AJN/2002/june/ Wawatch.htm).

Thesis

Sağlam C. Effect of glp-1 agonist on depression-like behaviors in young female rats created as a surgical menopause model. (Master's Thesis), Zonguldak, Zonguldak Bülent Ecevit University, 2022, 1-106 (Access Date:01.12.2024, Link:http…).

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EDİTÖRDEN

Değerli Okuyucular,

Zonguldak Bülent Ecevit Üniversitesi Tıp Fakültesi (https://tip.beun.edu.tr/) tarafından yayınlanan Batı Karadeniz Tıp Dergisi'nin (https://dergipark.org.tr/tr/pub/mjwbs) (https://dergipark.org.tr/en/pub/mjwbs) 2025 Nisan Sayısını (2025 yılı, Cilt 9, Sayı 1) okumaktasınız.

Dergimiz tıbbi bilginin geniş yelpazesinde güncel araştırmaları ve pratik uygulamaları sizlere sunmayı hedefliyor. Bilim insanlarının ve sağlık profesyonellerinin özverili çalışmalarının bir yansımasıdır. Dergimizdeki yer alan makaleler, yalnızca mesleki bilgi birikiminizi artırmakla kalmayacak; aynı zamanda geleceğin sağlık hizmetlerini şekillendirecek yenilikçi yaklaşımları da keşfetmenize olanak tanıyacaktır. Bu sayımızda derginin hazırlanmasında emeği geçen tüm yazarlara, hakemlere ve editörlere teşekkürlerimizi sunuyoruz. Umuyoruz ki bu sayıda aşağıda özetle belirttiğimiz makaleler hem bilgi hem de ilham kaynağı olarak sizlere katkı sağlar.

- Human Papilloma Virüsünün Servikal Epitel Hücrelerinin Çekirdekleri ve Hücresel Yapısı Üzerindeki Etkisi; Işık Mikroskobu ve Sitomorfolojik Analiz
- Sağlık Hizmetlerinde Yapay Zekânın Tamamlayıcı Kullanımı
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- Tümör Lateralitesi, HER2-pozitif Meme Kanserinde Neoadjuvan Kemoterapiye Yanıtı Etkiler mi?
- Akut İskemik İnme Tedavisinde Sadece İntra-Arteriyel tPA ile Sadece İntravenöz tPA'nın Karşılaştırılması
- Fazio Lateralite Envanteri'nin Türkçe Geçerlilik ve Güvenilirlik Analizi
- Postmenopozal Kanama İle Başvuran Kadınların Endometrial Biyopsi Sonuçları ve Risk Faktörleri İlişkisi
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Dergipark ve Tubitak ULAKBİM TR Dizin koordinasyonunda uluslararası nitelikte yayın dinamizmi için Üniversiteler Yayın koordinatörü görevlendirmeleri yaptı. Bu bağlamda Üniversitemiz ve dergimiz de yayın koordinatörlüğü yapılanmasını tamamladı. Bu süreçte Yayın Kurulumuz, Editörler Kurulumuzu da güncelleyerek daha güçlü ve kaliteli bir yayın hayatına doğru ilerledik.

Yayınlanmaya 2017 yılında başlayan dergimiz, TUBİTAK ULAKBİM TR Dizin, Indeks Copernicus, Türkiye Atıf Dizini tarafından indekslenerek güncel ve bilimsel yayınlarıyla literatüre katkı sağlamaya devam etmektedir.

Dergimizin ulusal ve uluslararası görünürlüğü arttıkça değerli bilim insanlarının dergimize göndermiş olduğu yayın akışı da artmaktadır. Dergimizin yayınlanmasında; Rektör Prof. Dr. İsmail Hakkı ÖZÖLÇER'e, Tıp Fakültesi Dekanı Sayın Prof. Dr. Hande AYDEMİR'e, yazarlara, yazıları titizlikle değerlendiren hakemlerimize, Danışma Kurulumuza, Türkçe ve İngilizce Dil Redaksiyon Kurulumuza, Alan Editörlerine, Editör yardımcılarına, Yayın Kurulumuza, teknik görevlilerimize ve yayınevimize teşekkür ederiz.

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EDITORIAL

Dear Readers,

You are reading the December 2025 April issue (2025 year, Volume 9, Issue 1) of the Western Black Sea Medical Journal (https://dergipark.org.tr/tr/pub/mjwbs) (https://dergipark.org.tr/en/pub/mjwbs) published by the Zonguldak Bülent Ecevit University Faculty of Medicine (https://tip.beun.edu.tr/).

Our journal aims to provide you with up-to-date research and practical applications in a wide range of medical knowledge. It is a reflection of the devoted work of scientists and health professionals. The articles in our journal will not only increase your professional knowledge; they will also allow you to discover innovative approaches that will shape the future of health care. We would like to thank all the authors, referees and editors who contributed to the preparation of this issue. We hope that the articles summarized below in this issue will contribute to you as both a source of information and inspiration.

- The Effect of the Human Papilloma Virus on the Nuclei and Cellular Structure of Cervical Epithelial Cells; Light Microscopy and Cytomorphological Analysis
- Complementary Use of Artificial Intelligence in Healthcare
- Ergonomics and the Importance of Ergonomic Education
- Vaccination Indecision in Mothers with Children Aged 0-5 Years
- The Effect of Thyroid Hormones on the Postnatal Growth of the Premature Infant
- Factors Affecting Internet Addiction and Health-Promoting Behaviors in Adolescents: A Cross-Sectional Study
- Examining the Effect of Different Exercise Capacity Tests on Intercostal Muscle Oxygenation
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- Evaluation of Earthquake Victims Admitted to an Emergency Department in Izmir Following a Major Earthquake Occurring More Than 1000 Kilometers Away
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- Validity and Reliability Analysis of the Turkish Version of the Fazio Laterality Inventory
- Relationship Between Endometrial Biopsy Results and Risk Factors in Women with Postmenopausal Bleeding
- A Rare Clinic Related to Paclitaxel Use: Type 2 Kounis Syndrome
- Type II Mirizzi Syndrome: A Case Report

Under the coordination of Dergipark and TUBITAK ULAKBIM TR Index, Universities have appointed Publication Coordinators for international publication dynamism. In this context, our University and our journal have completed the publication coordination structure. In this process, we have updated our Section Editors and Editorial Board and moved towards a stronger and higher quality publication life. Our journal, which started publication in 2017, continues to contribute to the literature with its current and scientific publications by being indexed by TUBITAK ULAKBIM TR Index, Index Copernicus, and Turkey Citation Index.

In the publication of our journal; I would like to thank to Rector, Prof. Dr. İsmail Hakkı ÖZÖLÇER, to Dean Prof. Dr. Hande AYDEMİR, the authors, our referees who carefully evaluated the articles, our Advisory Board, our Turkish and English Language Editorial Board, Field Editors and Assistant Editors, our Editorial Board, our technical staff and our publishing house.

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Chief Editor
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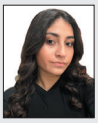




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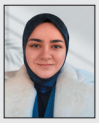

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REVIEW

Medical Journal of Western Black Sea
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Med J West Black Sea 2025;9 (1): 1-6
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The Effect of the Human Papilloma Virus on the Nuclei and Cellular Structure of Cervical Epithelial Cells; Light Microscopic and Cytomorphometric Analysis

Human Papilloma Virüsünün Servikal Epitel Hücrelerinin Çekirdekleri ve Hücresel Yapısı Üzerindeki Etkisi; Işık Mikroskobik ve Sitomorfometrik Analiz

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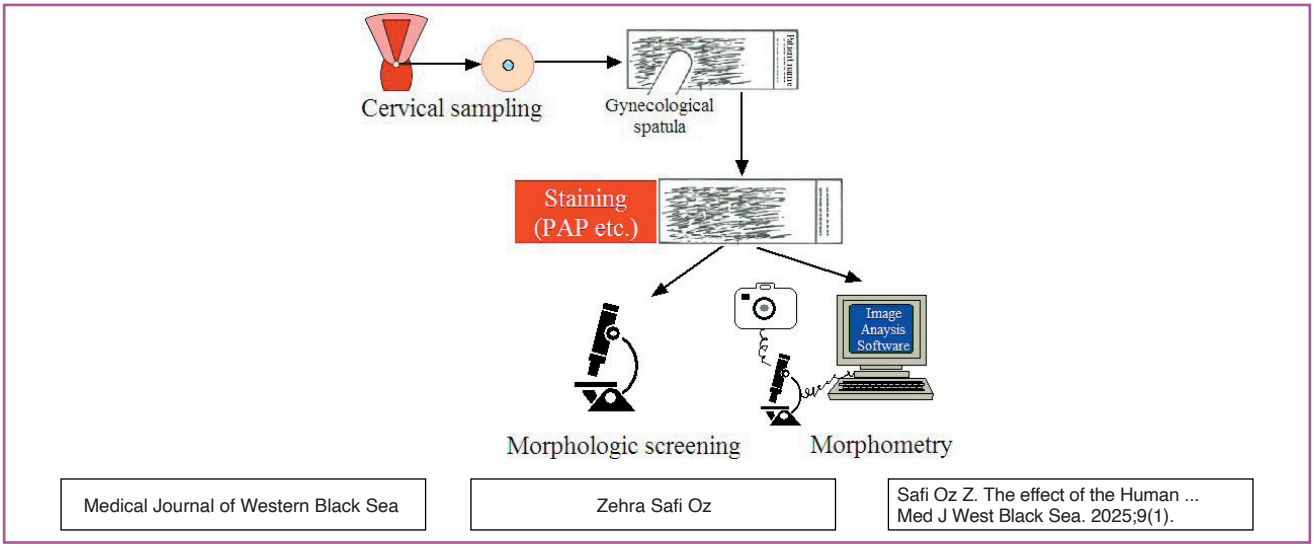
GRAPHICAL ABSTRACT



ABSTRACT

The most common sexually transmitted virus is Human papillomavirus (HPV), which comes in more than 280 types. The basal cells of epithelial tissues are responsible for taking up the HPV virus in cases of infection and malignancy caused by the virus. HPV, especially through the E6 and E7 proteins of high-risk HPV types, can cause benign infections or malignancies by inactivating tumor suppressor genes, disrupting cell cycle control, activating telomerase, preventing cell adhesion, polarity and differentiation, suppressing the immune system, and preventing apoptosis by inactivating tumor suppressor genes (especially p53, pRb).

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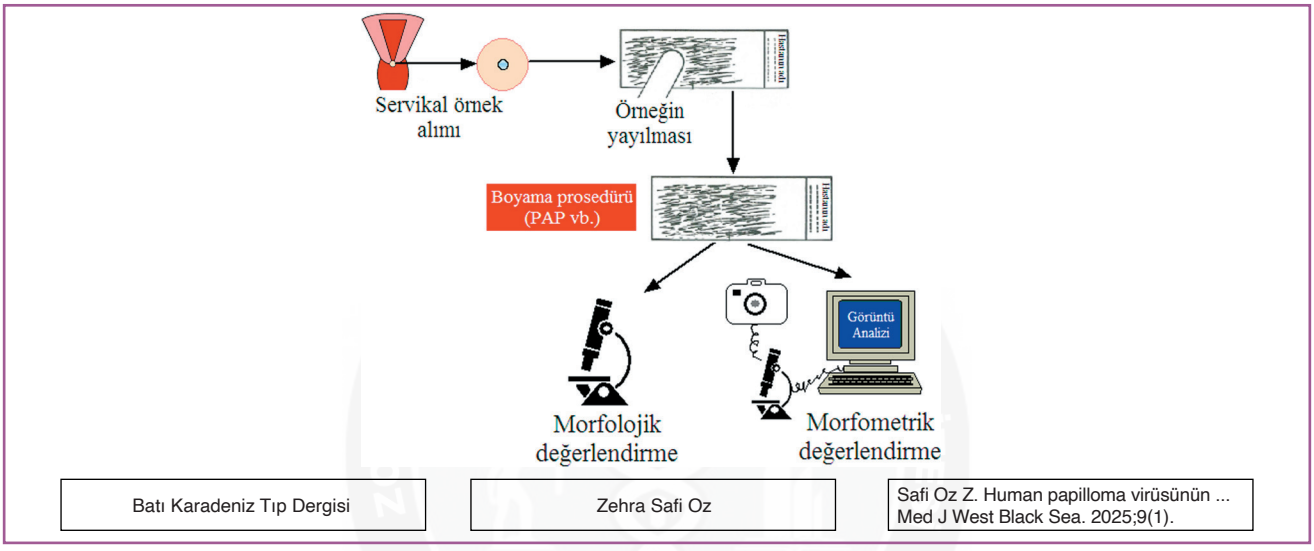
In this review, the effects of Human papillomavirus on epithelial cells were evaluated in terms of morphological changes and the nucleus-cytoplasm ratio mediated by specific proteins of the virus. Morphological changes are discussed under the headings of koilocytosis, cytoplasmic vacuolization, nuclear enlargement, nuclear membrane irregularities, hyperchromasia, abnormal chromatin distribution, micronucleation, binucleation, karyorrhexis, karyolysis karyopyknosis and nuclear budding. Nuclear architecture changes, which play a crucial role in gene regulation, are particularly prominent.

Finally, it is believed that knowledge of the changes that HPV causes in cell nuclear and cytoplasmic texture will facilitate the development of a cost-effective and appropriate approach to explaining cervical cancer pathophysiology, the development of specific biomarkers, and the development of new perspectives in understanding HPV's impact on cancer.

Keywords: Human Papilloma virus, HPV, cervical cancer, cytology, Squamous epithelial cell, PAP smear

GRAFİKSEL ÖZET



ÖZ

İnsan Papilloma Virüs (HPV), cinsel yolla bulaşan en yaygın viral enfeksiyon etkenidir ve 280'den fazla tipi bulunmaktadır. HPV'nin neden olduğu enfeksiyon ve malignitede virüsün epitel dokunun bazal hücrelerince alınması gerekmektedir. HPV özelllikle de yüksek riskli HPV tiplerinin E6 ve E7 proteinleri aracılığıyla, tümör baskılayıcı genlerin (özellikle p53, pRb) inaktivasyonu, hücre döngüsü kontrolünün bozulması, telomerazın aktivasyonu, hücre adezyonu, polarite ve epitel hücre farklılaşmasının bozulması, immün sistemin baskılanması ve apoptozun engellenmesi ile benign enfeksiyonlara ya da maligniteye neden olabilir.

Bu derlemede, Human papillomavirüsün epitel hücre üzerindeki etkileri virüsün özel proteinleri aracılığıyla gerçekleşen morfolojik değişiklikler ve nükleus-sitoplazma oranı açısından değerlendirilmiştir. Morfolojik değişiklikler, koilositozis, sitoplazmik vakuolizasyon, nükleer genişleme, nükleer membran düzensizlikleri, hiperkromazi, anormal kromatin dağılımı, mikronükleasyon, binükleasyon, karyoreksis, karyoliz karyopiknozis ve nükleer tomurcuklanma başlıkları altında ele alınmıştır. Gen regülasyonunda önemli rol oynayan nükleer mimarideki değişiklikler özelllikle öne çıkmaktadır. Sonuç olarak, HPV'nin hücrenin nükleer ve sitoplazmik tekstüründeki değişikliklerinin bilinmesinin, servikal karsinogenez patofizyolojisini açıklamak için uygun ve maliyet-etkin bir yaklaşımın önerilmesine, HPV kanserleri için spesifik biyobelirteçlerin geliştirilmesine ve HPV'nin karsinogenezdeki etkilerini anlamada yeni bakış açılarının geliştirilmesine katkıda bulunacağı düşünülmektedir

Anahtar Sözcükler: İnsan papilloma virus, İPV, serviks kanseri, sitoloji, skuamöz epithel hücre, PAP simir

INTRODUCTION

Human papilloma virus (HPV) consists of circular, covalently closed double-stranded DNA and a non-enveloped icosahedral capsid. To date, over 280 HPV genotypes have been identified based on differences in the HPV DNA sequence. Viral particles consist of eight open reading frames. The HPV genome is divided into three sections: the early (E) gene region (E1, E2, E4, E5, E6 and E7), the late gene region (L1, L2) and the long control region (LCR). LCR regulates the origin of replication (1). This virus infects basal cells and its active cycle is associated with cellular differentiation. Through its structural proteins, HPV causes various alterations. These cellular effects are presented under the headings of morphology and morphometry below (2-11).

EFFECTS OF HPV ON MORPHOLOGY

In HPV infection, koilocytosis is the most prominent cellular change in differentiated squamous epithelial strata. This is formed as a result of the interaction of cytoskeletal elements especially actin and microtubules and viral proteins such as E6 (HPV16, 18), E7 (HPV16, 18, 38), E5 (high and low-risk HPV types), E1^E4 (HPV16), E4 (HPV 16) (3). Cytoplasmic vacuolization is a morphological change observed in the epithelial cell cytoplasm due to various pathogens, including HPV (12).

Many significant degenerative nuclear alterations such as membrane irregularities, nuclear enlargement, hyperchromasia, abnormal chromatin distribution, micronucleation (MN) binucleation (BN), karyorrhexis (KR), karyolysis (KL), karyopyknosis (KP) and nuclear budding (NB) induced by HPV are detectable by light microscopy in Papanicolaou Smear (Figure 1). HPV leads to disarrangement of the nuclear lamina. This is responsible for maintaining nucleus morphology and is also an attachment point for chromosomes. Disruption of the lamina causes chromatin organization, gene expression and chromosomal instability irregularities. It can also cause nuclear membrane irregularities (4,13). Micronuclei (MN) indicate chromosomal instability (14-17). It is often a broken chromosome fragment (16). Previous studies have shown that micronuclei were significantly higher in the HPV 16/18 group. (10, 18, 19). However, it is still unclear how HPV affects micronucleus formation. HPV proteins support malignant cell proliferation by disrupting p53 of E6 and pRb of E7. Evaluation of MN is valuable for monitoring HPV-induced chromosomal instability. In carcinogenesis, HPV affects many significant mechanisms such as cell cycle, apoptosis, and tumor growth suppression (10). As a result of this interaction, karyorhexis, karyolysis, and karyopyknosis occur in cells. Karyorhexis is a nuclear membrane fragmentation. Chromatin breaks into small basophilic granules and spreads into the cytoplasm in this process. Karyolysis is a cell nucleus dissolution. Karyopyknosis involves shrinkage or condensation of the cell due to increased nucleus compactness. Although these changes are specific to infection, it remains unknown at what level these degenerative changes occur in that infection (20). Exfoliated epithelial cells undergo binucleation as a reactive cellular change (21). Although the mechanism of binucleation formation in HPV infections has not been explained in detail yet, it is thought that HPV structural proteins interact with cytoskeletal elements and affect cytokinesis, so cytoplasm division does not occur following nuclear division. Nuclear budding (NB) is commonly seen in cancer and is associated with chromosomal instability. NBs are connected to the nucleus by stalks of nucleoplasmic material depending on the stage of the budding process (13, 22). In addition to these changes, HPV causes nuclear enlargement and chromatin texture changes. Nuclear enlargement is one of the characteristic alterations in malignant cells. In these cells, nuclear enlargement is thought to produce abnormal nuclear shapes to maintain the ratio of nucleus to cytoplasm. Normal cells tend to maintain the ratio of the nucleus volume to cell volume. Along with the HPV-induced change in gene expression, the change in chromatin organization may also lead to nuclear architecture change (10, 23, 24). Alterations in nuclear architecture and chromatin organization during carcinogenesis and tumor progression can also lead to nuclear shape changes in the nucleus (24). Epigenetic modulations in chromatin and the nuclear membrane are related to gene expression and carcinogenesis (23, 25).

In the literature, Guillaud et al. indicate that a correlation between HPV and chromatin condensation and measuring E2 and E6/E7 expression will effectively reveal this relationship (26). In addition, Gautam and Moody indicated that DNA damage response (DDR) facilitates HPV replication (27). Understanding how DDR alters viral chromatin modifications in HPV infection is a crucial question to clarify in the future.

EFFECTS OF HPV ON MORPHOMETRY

Computerized image analysis is one of the methods used to eliminate diagnostic variability in cytological and histopathological samples, with high sensitivity and reproducibility. Digital morphometry allows observers to create a database of various parameters to characterize cells as normal, preneoplastic, or neoplastic (28,29). Digital morphometry also has reproducibility, save digital records, and reuse them when necessary. Morphometry also characterizes cells of size, area, and shape (10, 23, 30). This method can provide two-dimensional measurements of parameters such as cellular area (CA) and nuclear area (NA), perimeter, and diameter, and can additionally be used to evaluate the staining

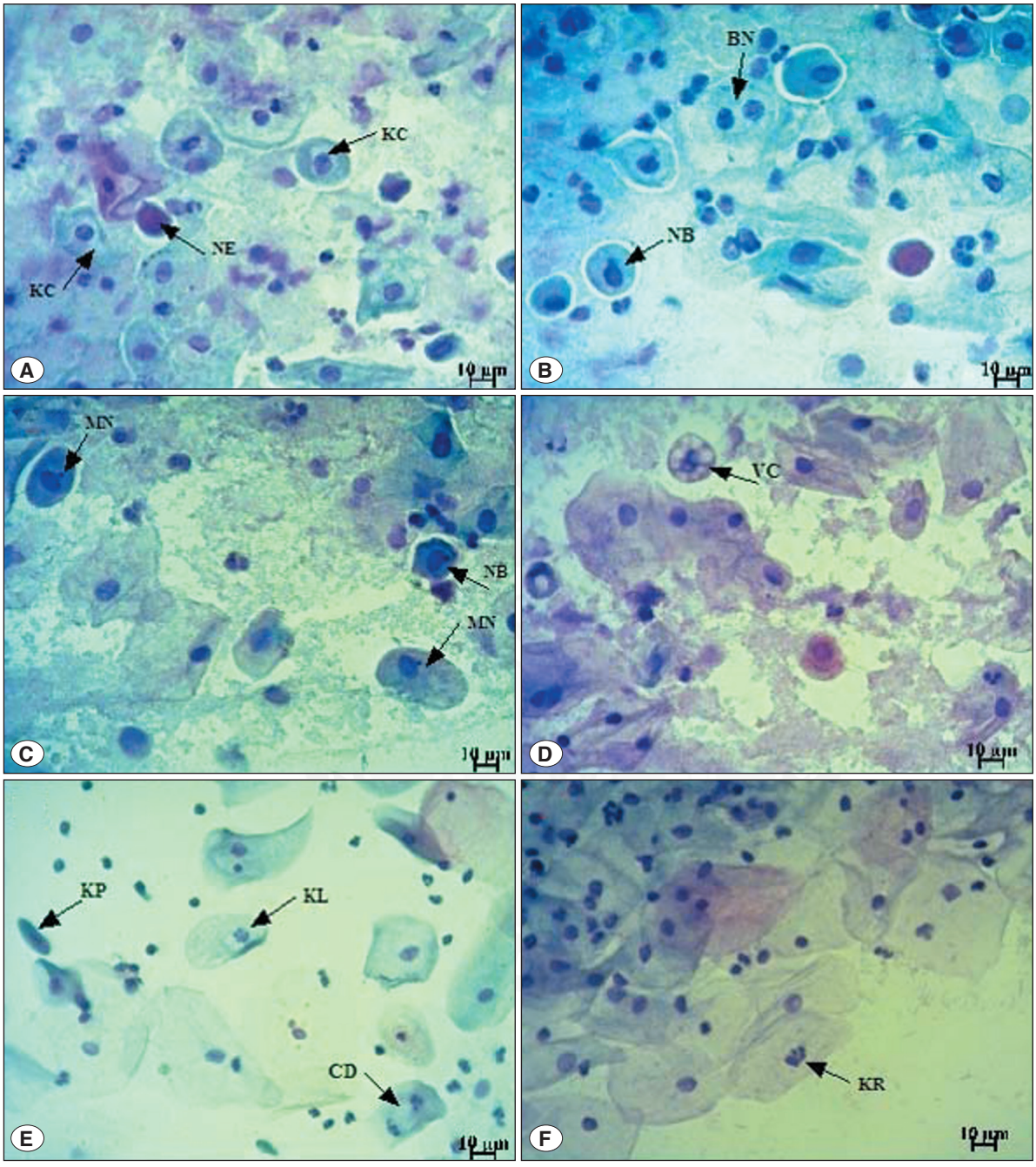


Figure 1. General appearance of cervical epithelial cells in HPV infection (Papanicoaou X 40). **A)** Exfoliated cervicovaginal epithelial cells with koilocytosis (KC) and nuclear enlargement (NE). **B)** Binucleated epithelial cell (BN) and nuclear budding (NB). **C)** Micronucleated (MN) cells and nuclear budding (NB). **D)** Vacuolization in cervical epithelial cell (VC). **E)** Karyolytic (KL) and karyopynotic (KP) cells and cellular division (CD). **F)** Karyorhectic epithelial cell (KR)

intensity of the cell and nucleus. Furthermore, it can detect subtle changes in cell shape, size, and/or texture, which can't be seen with light microscopy or even electron microscopy (28-31).

HPV causes various changes in the cell nucleus and cytoplasm, and these changes can be observed microscopically in cytological smears (Figure 1). These changes are detailed under the title "Effects of HPV on morphology". Cellular changes in HPV are also reflected in the morphometry of the cells (Figure 2). Evaluation of NA, CA and NA/CA provides non-classical HPV cytological data. These non-classical criteria can be evaluated by morphometric methods. Morphometry can provide information not detected by tradi-

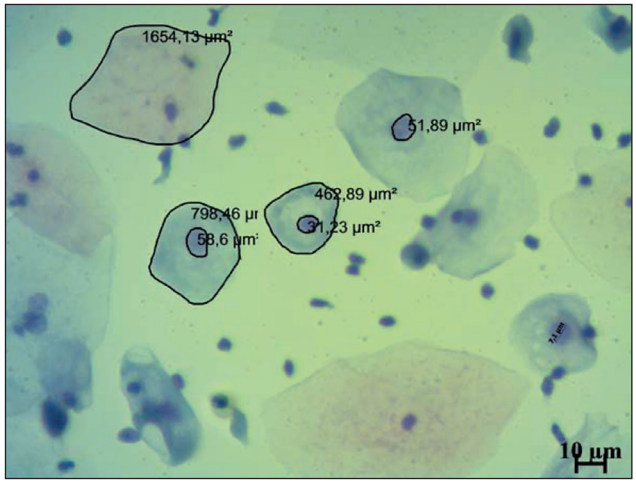


Figure 2. Measuring cellular diameter of Papanicolaou stained cervical epithelial cells in HPV infection.

tional cytology. It can explain the incompatibilities between molecular methods and morphological approaches.

There are limited studies in the literature on the morphometric changes of HPV. Safi Oz et al. measured cellular, nuclear, and cytoplasmic areas in their cytomorphometric study of patients infected with HPV 16. They calculated the nucleus/cytoplasmic ratio and compared it with the control group. Cellular, nuclear, and cytoplasmic areas were lower in the HPV 16 positive group than the control group. However, no statistically significant difference was found between the values (10).

Safi Oz et al., in their cytomorphometric study of HPV 18 infected patients, measured the cellular, nuclear and cytoplasmic area. They calculated the nucleus/cytoplasmic ratio, and measured the width, length and perimeter values of the cell and nucleus. They compared them with the control group. Cellular area, nuclear area, cytoplasmic area, nucleus/cytoplasm ratios, cell width, length and perimeter values and nucleus width, length and perimeter values were lower in the HPV 18 positive group than in the control group. The nucleus width and length values were also statistically significant between the HPV 18 and control groups (31). It ıs consıdered that morphologıcal and morphometrıc studİes related to HPV will contribute to the enlightenment of the mechanism of HPV infection.

CONCLUSION

This review evaluated HPV structural effects on cervical cell morphology and morphometry. Knowing the structural changes induced by HPV can help gain new perspectives on gene regulation architecture in the cell. This will enable us to understand HPV's effects on carcinogenesis. Micronucleus scoring may contribute to the evaluation of different HPV types in this respect, as it shows chromosomal instability in this infection. Since the texture of the nucleus shows the degree of chromatin condensation and integration of HPV, a detailed examination of the texture in the presence of different HPV types is thought to be a valuable and effective tool in cervical cell evaluation and is potentially useful for the development of specific drug targeting and biomarkers specific to HPV-induced cancer. Morphometry is thought to provide information that cannot be detected by traditional cytological methods. It is also thought to explain the incompatibilities between molecular methods and morphological approaches. I believe that morphometric evaluations need to be performed on different HPV types.

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None.

Author Contributions

The study conception and design, writing of the manuscript, and preparation of images were all made by the author.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Ethical Approval

Since it is not an experimental or human study and is a review, ethical approval is not required. In the preparation process of this study, scientific and ethical principles were followed and all studies used were indicated in the references. This article was scanned by iTenticate software. The plagiarism rate was detected as 14%.

Review Process

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REVIEW

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Complementary Use of Artificial Intelligence in Healthcare

Sağlık Hizmetlerinde Yapay Zekânın Tamamlayıcı Kullanımı

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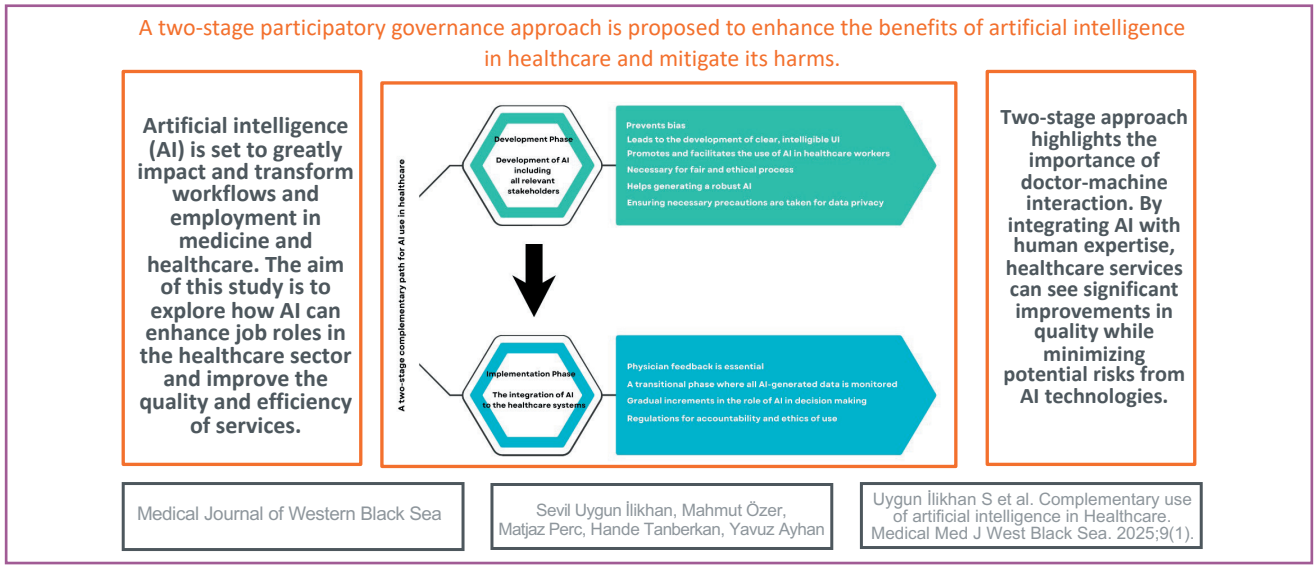
GRAPHICAL ABSTRACT



ABSTRACT

Artificial intelligence (AI) is set to greatly impact and transform workflows and employment in medicine and healthcare. This study explores how AI can enhance job roles in the healthcare sector and improve the quality and efficiency of services. A two-stage approach is proposed. In the first stage, doctors and healthcare workers are involved in developing AI systems. Their participation ensures ethical use, boosts effi-

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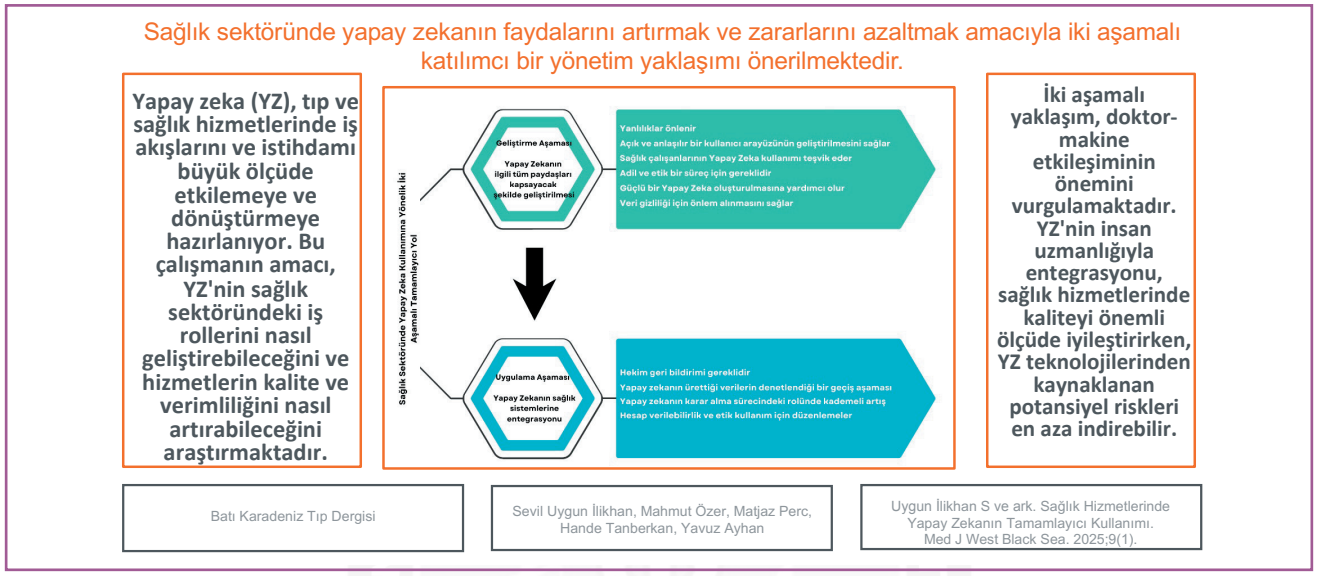
ciency, and prevents biases from the data or algorithms. In the second stage, continuous monitoring of AI systems by healthcare professionals is crucial. They act as filters for AI-generated results during decision-making processes. This ongoing oversight helps maintain accuracy and reliability. This two-stage approach highlights the importance of doctor-machine interaction. By integrating AI with human expertise, healthcare services can see significant improvements in quality while minimizing potential risks from AI technologies.

Keywords: Artificial intelligence, data bias, healthcare, human complementation, medicine

GRAFİKSEL ÖZET



ÖZ

Yapay zekâ (YZ), tıp ve sağlık hizmetlerinde iş akışlarını ve istihdamı büyük ölçüde etkilemeye ve dönüştürmeye hazırlanmaktadır. Bu çalışma, YZ'nin sağlık sektöründeki iş rollerini nasıl geliştirebileceğini ve hizmetlerin kalite ve verimliliğini nasıl artırabileceğini araştırmaktadır. Bu kapsamda iki aşamalı bir yaklaşım önerilmektedir. İlk aşamada, doktorlar ve sağlık çalışanları YZ sistemlerinin geliştirilmesine dahil edilmektedir. Doktorlar ve sağlık çalışanlarının katılımı, etik kullanımın sağlanmasını, verimliliğin artırılmasını ve verilerden veya algoritmalardan kaynaklanan önyargıların önlenmesini sağlamaktadır. İkinci aşamada ise, YZ sistemlerinin sağlık profesyonelleri tarafından sürekli izlenmesi kritik öneme sahiptir. Sağlık profesyonelleri, karar verme süreçlerinde YZ tarafından üretilen sonuçlar için bir filtre görevi görmektedir. Bu sürekli denetim, doğruluk ve güvenilirliği korumaya yardımcı olmaktadır. Bu iki aşamalı yaklaşım, doktor-makine etkileşiminin önemini vurgulamaktadır. YZ'nin insan uzmanlığıyla entegrasyonu, sağlık hizmetlerinde kaliteyi önemli ölçüde iyileştirirken, YZ teknolojilerinden kaynaklanan potansiyel riskleri azaltacaktır.

Anahtar Sözcükler: İnsanı tamamlama, sağlık hizmetleri, tıp, veri yanlılığı, yapay zekâ

INTRODUCTION

Artificial intelligence (AI) is rapidly spreading across all fields, from education to healthcare, economy to defense industry, with its significant advantages (1-6). The transformation brought about by AI technologies is occurring on a significantly different scale compared to previous major technologies, and an AI ecosystem is forming in a short period. Particularly, the widespread digitalization in all areas ensures the sustainability of AI systems.

Medicine is among the first application areas of AI technology. AI had already had its impact on different aspects of medicine, including the patient care (diagnostics and therapeutics), medical training and healthcare systems (7,8). Particularly, the prevalence of digitalization efforts, especially related to image processing, has accelerated the use of AI systems in diagnostics (9,10). As evidence of the benefits provided by AI systems, the advantages they offer, particularly in the healthcare sector, are highlighted (11-13). Beyond patient care, the incredible increase in the amount of digital data in healthcare and technological advancements, as well as significant investments by technology companies and governments in the application of AI, serves enormous potential to improving healthcare systems (14). Therefore, the spread of AI technologies in healthcare is expected to be much faster.

In this context, AI technologies particularly enhance efficiency and reduce costs in tasks related to clinical documentation, such as processing and recording requests by allied health personnel, or in support services like prescription renewal or appointment scheduling (14-16). On the other hand, it is also possible to identify and monitor patients in need of advanced healthcare services using big patient data (17). Thus, proper utilization of big data via AI may even have a significant impact on single individual level.

Concerns regarding AI technologies mainly revolve around how the transformations in the labor market will impact employment and how negatively they will affect professions (18-21). In other words, how AI systems will affect current employment, especially in the fields of health and medicine, is a major point of curiosity. In this context, it is expected that AI systems will transform existing skills and create new professions in the fields of medicine and healthcare (14,22). Similarly, the World Health Organization (23) also predicts that AI technologies will significantly change the workflows and jobs of health professionals such as doctors and nurses. Despite ongoing debates on this issue, findings regarding how AI technologies will affect employment often contradict each other (20). However, the most agreed-upon point is that the expected skill level will significantly increase with the use of AI technologies (24). Moreover, it is observed that even companies that do not directly use AI technologies now prefer individuals with AI skills in their employment (25).

AI systems are transforming processes in medicine and healthcare, taking over most tasks through automation (26). This shift has sparked discussions regarding the employment of healthcare workers. While AI can automate many routine tasks in healthcare, there are three main reasons it cannot replace doctors (27): First, there is still a need for doctors to give specific task instructions to AI systems and to evaluate their outputs. Second, the support provided by AI systems is extremely specific and limited according to the complexity of doctors' responsibilities. Third, while public data sets often contain biases, making the clinical applicability of algorithms trained on these data extremely limited, there is also a significant lack of accessible data formats needed by AI systems that require training data sets. Consequently, the alternative path that will be explained in the next section will not adversely affect employment and will increase efficiency in the field where it is used involves using AI to complement humans (28). We believe that the AI will not replace physicians but AI literacy will be a cardinal feature in medicine especially for healthcare workers in executive and administrative positions (27,29).

The discussion on how AI technologies will transform workflows in the healthcare sector, from education to diagnosis and treatment processes, and which skills will come to the forefront in this transformation is a hot topic. In this context, international initiatives to address the risks of artificial intelligence mentioned above have begun to increase, and steps towards multinational regulation, beyond national regulations, are also on the rise. For example, the European Union recently published the EU AI Act, which provides a framework for regulating artificial intelligence within the EU (30).

Therefore, this study explores how AI technologies can be used in a way that complements humans in the healthcare field. For this purpose, it is primarily recommended to increase AI literacy among all healthcare workers. Additionally, a two-stage solution is presented to complement human efforts. The first stage requires the active participation of healthcare professionals in the development process of AI technologies in the healthcare field, while the second stage necessitates these professionals to guide and filter the results produced during the implementation phase of AI technologies.

TWO PATHS FOR THE DEPLOYMENT OF AI: AUTOMATION AND COMPLEMENTARY PATHS

It is known that major technological transformations significantly reshape the skill sets of professions, forcing a restructuring of the labor market (31). In this process, while some professions disappear, the losses in the employment market are balanced by the new professions emerging from technological transformation. A similar expectation applies to AI technologies (18). However, recent studies indicate that this expectation may not be entirely accurate, suggesting that the number of new job positions created may not compensate for the ones eliminated (4-6,32,33). Therefore, there are warnings that if the automation trend enhanced by AI technologies is not addressed, significant waves of unemployment could occur. In this context, creating a sector that prioritizes employment for AI technologies is proposed as an alternative path that could increase efficiency by using AI technologies in a way that complements humans.

AI technologies are creating new opportunities in workplaces that support the alternative path. For instance, a study using GitHub Copilot at a workplace has shown that a test group with access to Copilot, a productive AI-powered programming assistant, completed programming tasks about 56% faster than the control group without access (34). Another study, using data from 5,179 customer support representatives, examined the effects of a productive AI-powered chat assistant on employee performance (35). It found that the AI-supported chat assistant increased productivity, measured by the number of problems solved per hour, by an average of 14%. However, the increase in productivity showed significant variations according to the skill levels of the employees. The study revealed that the AI-powered

chat assistant improved performance by 34% for newcomers and low-skilled workers, while it had a minimal impact on experienced and high-skilled workers.

Another study examining the impact of ChatGPT on writing tasks demonstrated that ChatGPT significantly improved the performance of the least skilled writers, leading to notable enhancements in writing speed and quality (36). In other words, the productivity gains caused by AI in workplaces predominantly benefit mid-skilled or novice low-skilled workers, significantly enhancing their productivity, with this contribution diminishing as the skill level increases. Similar findings from other studies show that the complementary contribution of AI technologies is realized by compressing the skill range among workers (37-40). Therefore, these findings suggest that the alternative path of using AI to complement humans could provide an opportunity to increase the overall productivity of the workplace by enhancing the efficiency of mid and low-skilled workers rather than displacing them from employment.

In fact, the alternative path for AI technologies is not entirely new. Particularly in Germany, during the period when the first wave of automation led to significant shifts in labor market dynamics, the initial steps of the alternative path were taken using two different approaches: inclusive education and the application of innovations in workplaces in a way that supports mid-skilled or unskilled workers (41). Thus, on one hand, inclusive education ensures that all individuals receive education of the same quality, preventing the clustering of new jobs within the elite class. On the other hand, it prevents new investments in workplaces from favoring highly skilled workers, thereby helping to avoid job losses among mid-skilled or unskilled workers. Consequently, Germany's previous stance on handling the challenges posed by automation, now intensified by AI technologies, supports the significance of the alternative path for AI technologies in preventing profound disruptions in employment (42).

CURRENT SHORTCOMINGS OF AI

With the current status of AI, a system needs to be established in the healthcare field in which the generation and the use of AI-produced data is regulated. To build up a framework for this reasoning, below, first we will discuss the shortcomings of AI and the risks it may pose. Secondly we will explain why human supervision is necessary in healthcare decisions. We will then propose a two stage model of a complementary path to utilize AI in healthcare.

One of the significant challenges encountered in the use of AI technologies is the production of biased results based on biases in training data sets or erroneous assumptions in algorithms (2,4,43). Health systems serve a heterogeneous population that varies according to different environments, socioeconomic status, gender, religion, and race. Therefore, the use of AI technologies in healthcare can only contribute to the improvement of healthcare services if it produces unbiased results. Consequently, biased data or assumptions used in algorithms compromise the impartiality of AI technologies in healthcare (2). For example, it has been observed that a machine learning algorithm trained at a university hospital using data from wealthy, young, white patients to create a clinical report produces biased results when used in hospitals serving minorities and patients with low socioeconomic status (44). Similarly, an algorithm developed to predict Acute Kidney Injury (AKI), which primarily comprised data from white, older male patients, when used to predict AKI in young and female patients exhibited gender-based biases (45,46). It has been identified that AI applications actively used in health systems disadvantage individuals with darker skin tones in determining SpO2, and in dermatological imaging systems (17,47). The cause of this bias lies not only in the underrepresentation of different skin colors in the training data set but also in the low sensitivity of the scales used to determine skin tone (48,49). In particular, The Monk Skin Tone Scale (MST) (50) is recommended in AI algorithms rather than the Fitzpatrick scale which is the widely accepted in clinical settings, to provide more sensitive results and helps combat algorithmic injustice (48). We would like to emphasize that this intervention (using appropriate measurement protocol) is a significant strategy and an essential step in machine learning, addressing biases linked to the data set. Moreover, the MST scale was originally developed for social sciences. Thus AI-based systems may encourage an interdisciplinary approach to provide generalizable results (50). This approach not only enhances the fairness of AI applications but also underscores the need for cross-disciplinary contributions to improve AI's accuracy and ethical application in healthcare.

On the other hand, the assumptions made during the development of AI algorithms can inherently include biases, and this directly affects the outcomes they produce. In this context, a recent study highlighted the biases in an AI system used to identify patients needing advanced healthcare, which considered the amount of healthcare expenditures (17). The study demonstrated that the results were biased according to race and socioeconomic status. The criterion used by the algorithm assumes that everyone, regardless of their socioeconomic background, has equal access to the healthcare system. In reality, wealthy families, who have easier access to healthcare systems and thus higher healthcare expenditures, benefit more from advanced healthcare services as a result of the AI system's decision-making process, compared to individuals who may need similar or more advanced care but have already less access to healthcare services. This situation showcases a critical flaw in how AI systems evaluate and provide healthcare services, emphasizing the need for algorithms that ac-

curately reflect the diverse conditions and barriers different populations face in accessing healthcare. By addressing these biases, AI can truly enhance the equity and effectiveness of healthcare delivery.

Similarly, the lack of transparency in AI systems complicates the recognition of biases embedded in algorithmic assumptions. For instance, an algorithm which is used in hospitals to recommend treatments for cancer patients is known to make inappropriate treatment recommendations, such as the use of an anticancer drug which is associated with an increased risk of bleeding in a patient with severe bleeding. The 'black box' nature of these algorithms makes it impossible to explain why a medication unsuitable for the patient's history was prescribed, contradicting the principle of transparency in healthcare (51,52). Consequently, a flawed algorithm has the potential to commit medical errors and cause serious harm to patients.

One of the second-tier risks associated with the use of AI, particularly generative AI technologies like ChatGPT, in healthcare—from writing academic articles to preparing patient reports and treatment processes—is the phenomenon of hallucinations (53). Recently, it has been suggested that using the term "confabulation" rather than "hallucination" to describe this behavior would be more accurate (54). This term describes the issue where AI systems do not consistently produce accurate answers and can frequently generate incorrect or non-existent content. For example, it has been shown that some references created in research proposals or articles entirely prepared by ChatGPT neither appear in Google searches nor have an existing Digital Object Identifier (DOI) (55). Thus, while the responses produced by generative AI can seem reasonable, they may actually be nonsensical.

It is suggested that these hallucinations occur when AI systems either lose connection with the dataset they were trained on (source amnesia) or face difficulty and tension due to contradictory data in their training set, which drives this behavior (56). Even worse, once AI systems begin hallucinating, they can continue this behavior in a consistent manner in subsequent responses, potentially causing a snowball effect of hallucinations (57). In the healthcare setting, hallucinations can misdirect diagnosis and treatment processes, thus posing a high cost to human health.

On the other hand, AI systems' ability to generate meaningful outcomes from complex and large datasets can undesirably boost confidence in their results, making automation of healthcare processes appear attractive (58). However, this approach often fails to achieve the superior performance that could be realized by combining the unique strengths of humans and AI. Furthermore, studies have shown that AI has the potential to err in disease diagnosis, leading to a decline in the quality of healthcare services (58-60). For example, while AI can interpret acute neurological scans much faster than radiologists in diagnosing head trauma, its diagnostic accuracy remains lower (61). Similarly AI misled radiologists for interpreting chest radiography (62,63). Therefore, relying solely on the automation capabilities of AI technologies carries significant risks.

As with all technological advancements, equitable use is a serious concern in AI. There is economical and geographical discrepancy for the development of technology and the data availability (9). A recent review of AI life science publications demonstrated that Northern America, Western Europe and Oceania countries produced the highest number of publications and also the highest number of high-quality and with clinical relevance (64). The lack of equitable and inclusive use of AI is not only a problem for the disadvantaged countries but also constitutes a major hurdle for generalizability of AI-generated data in HIC and HMIC with a heterogeous population structure. In the HIC and HMIC, the available health data may be biased for certain socioeconomic, racial or ethnic groups which results in flawed AI-generated predictions (65). The already evident disparities in healthcare may reflect itself onto AI -based diagnostic systems (66). However fair use of big data and AI may provide significant improvements in detecting and eliminating these disparities. In addition, there are numerous other opportunities that AI can provide to the healthcare systems of LICs. AI can support the use of telemedicine to reach out to rural disadvantaged populations, enhance healthcare supply systems and support management systems in the LIC (67). Thus, it is pivotal to include unbiased data preferably representing all strata of the target population to acheive the most accurate results from AI and capitalize its benefits on global health.

THE NECESSITY OF HUMAN INVOLVEMENT

The shortcomings of AI underscore the necessity for continuous monitoring of AI in autonomous systems that oversee patient health (68). Hence, the focus should not solely be on AI's capacity to fully automate medical processes but rather on the potential to enhance healthcare professionals' expertise concerning AI technologies (59). Emphasis should be placed on using AI to complement human capabilities, thereby improving the quality of healthcare services (9,69). In this manner, while AI technologies can analyze large datasets that humans may struggle to assess independently, the interpretation of these data should be performed in collaboration with healthcare personnel, leading to more accurate and reliable solutions.

Thus, a facilitator role for AI can be instituted. A study consulting experts on the use of AI in healthcare shows that all experts agree AI will take over time-consuming, repetitive routine activities not requiring completion by doctors, thus facilitating daily work in healthcare services and becoming

an indispensable part of clinical routine (27). In a study on how ChatGPT affects doctors' decision-making processes and biases in health systems, doctors were asked to assess chest pain in patients with different demographic features (gender, race), and then they used ChatGPT to question their own assessments (70). The study found that ChatGPT increased the accuracy of the doctors' decisions and reduced biases related to gender and race. Similarly, in studies examining ChatGPT's advice to doctors on cardiovascular diseases and hypertension, it was highlighted that ChatGPT could accelerate doctors' decision-making processes in diagnosing hypertension (71,72). However, viewing ChatGPT not as a replacement but as a complementary tool to decision-making processes enhanced accuracy (71).

The platforms developed with AI support and providing diagnostic assistance based on patients' complaints, enhances its diagnostic capability by allowing for online consultations with doctors. Consequently, to keep the platform up-to-date and ensure medical accuracy, doctors provide medical consultancy to this AI application (73). The interaction between robots and doctors in surgical areas is another example of how AI can enhance the complementary role of humans and ultimately provide healthcare services of higher quality (74).

A COMPLEMENTARY PATH FOR AI IN HEALTH CARE

The establishment of complementary path of AI use in healthcare systems consists of two stages as shown in Figure 1 (27, 75). The first stage is the development phase of AI systems, which involves the adoption of a society-in-loop approach. This approach not only includes AI experts but also involves doctors and health administrators, and all relevant healthcare stakeholders (2,76). Active participation at this stage allows for measures to be taken against biased outcomes and ensures ethical use of AI. Particularly, the participation of healthcare workers' unions is critical in this context.

As we mentioned above, awareness of biases stemming from the training data sets or algorithmic assumptions by doctors and cautious interpretation of the results will enhance the quality of healthcare services. Moreover, particularly in healthcare, adopting a participatory governance approach during the development phase of AI systems that allows involvement of healthcare stakeholders will likely reduce the likelihood of generating these biases. This engagement not only fosters transparency but also ensures that the algorithms are more aligned with the nuanced needs of diverse patient populations.

The second stage involves healthcare workers approaching the results produced by AI systems with caution, providing human input to correct any biases or deficiencies. This approach not only prevents AI systems from misleading doctors but also supports doctors in managing complex health data that they might not easily analyze on their own (77). Thus, AI systems enhance the capability of healthcare professionals to manage processes more effectively by providing them with insightful analyses of extensive health data.

Current studies suggest low diagnostic accuracy of chatbots, possibly due to 'hallucinations' and other factors that affect the algorithm output (78). Therefore, it is crucial for healthcare professionals to approach the results produced by AI technologies cautiously, enabling the detection and

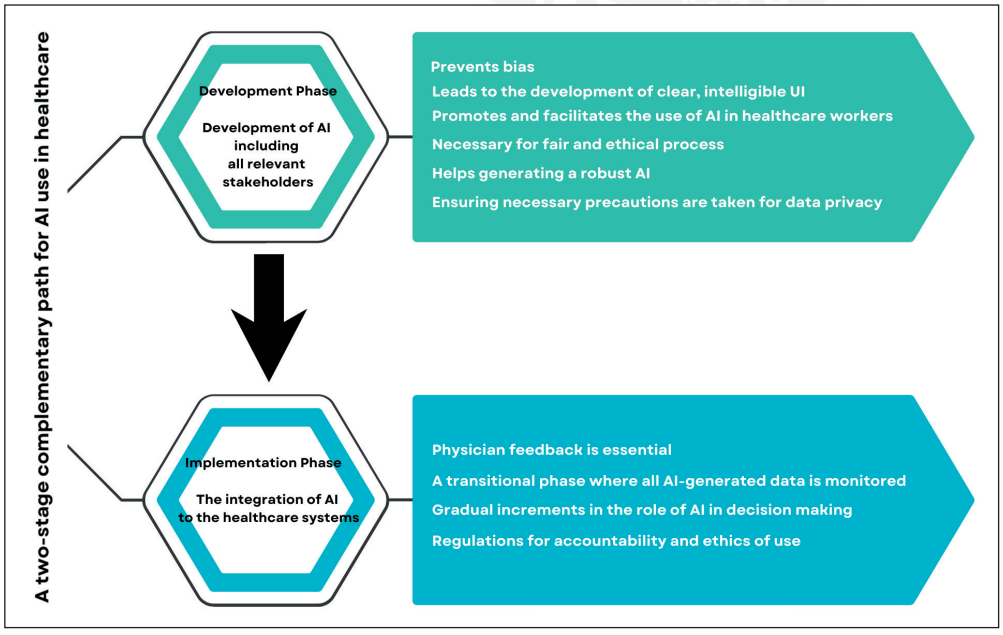


Figure 1. A two-stage complementary path for AI use in healthcare.

correction of errors. This vigilance is essential to minimize the adverse effects and safeguard patient outcomes.

CONCLUSION

Healthcare and medicine are among the primary fields impacted by AI technologies. AI holds significant potential for improving the quality of healthcare services. Indeed, the fact that the initial applications related to AI primarily started in the healthcare sector points to this potential. The digitalization of healthcare and the rapid accumulation of big data provide significant opportunities for the development of AI technologies. AI can help surpass human limitations in collecting, processing, and analyzing these vast datasets quickly and accurately, thereby substantially enhancing the quality of healthcare services (27, 79). Therefore, the focus of this study is not on the potential applications of AI technologies in healthcare, but on how they should be utilized to enhance the quality of healthcare services.

It is well known that every major technological transformation leads to significant changes in the skill sets required for various professions. With these transformations, a considerable number of existing jobs disappear while new professions that require new skills emerge. A similar situation applies to AI technologies. However, while technological transformations post 1970s have spread automation and had the potential to transform existing professions and create new ones, warnings are issued that AI technologies might not have the same potential (28). In other words, if the current path of automation continues, the AI ecosystem might eliminate the need for many professions without demonstrating the same performance in creating new ones. Consequently, significant fluctuations in employment are expected. On the other hand, the professions emerging from AI technologies are expected to require a high level of skill, necessitating advanced education that may include graduate studies. This indicates a shift towards more specialized and higher educational requirements for the workforce engaged with emerging AI-driven sectors.

The rapid development of AI technology in the medical field and its increasingly advanced capabilities in diagnosis and treatment have highlighted the necessity of integrating AI into medical education without delay (80). It is also known that medical school students are willing to take courses related to AI (81). When examining the curricula of different universities offering medical education (such as Stanford University and Harvard University), it is observed that courses on topics like “AI in healthcare, data science, fair AI, human-machine interaction, etc.” have been added to the curriculum to enhance AI literacy (82, 83). In this context, a study exists in the literature that serves as a guide for the integration of AI into medical education curricula, which defines the necessary competencies for medical students to understand the workings of AI, use it responsibly, and develop AI literacy (including clinical applications, ethical and legal frameworks, data analytics, statistics, etc.) (84).

This study proposes a two-stage complementary approach for the use of AI technologies in healthcare. The development phase of AI applications should ensure the fair participation of all healthcare stakeholders. This cooperative approach is crucial for integrating diverse perspectives and expertise, which enhances the robustness and applicability of AI systems in healthcare settings.

The second stage of integrating AI technologies in healthcare is the implementation phase, where a cautious approach to these systems is essential. Despite all precautions taken during the first stage, AI systems might still produce biased outcomes or exhibit hallucinatory behavior during application. Detecting these errors, which can negatively affect diagnosis and treatment processes, and making the necessary corrections is critical. Healthcare workers should act as a ‘filter behind the AI’ (27).

Finally, considering that generative AI systems particularly enhance the productivity of individuals with medium and low skills and shorten training periods for this group (35-37), the use of AI in all training within the healthcare sector could improve the quality of healthcare services by enhancing the quality of human capital in the field. Furthermore, it would also enable the training of a new generation of doctors and healthcare professionals with AI literacy.

AI systems are seen to significantly facilitate doctors’ work by taking over routine tasks and simplifying more complex jobs. In this context, the field of radiology offers significant potential for this collaboration (85). Thus, AI-human interaction can create greater collective intelligence in healthcare (86). This integrated approach ensures that AI supports healthcare professionals without replacing the critical human judgment necessary in medical practice.

The use of AI in healthcare, as outlined, necessitates an enhancement of AI literacy among doctors and other healthcare professionals. Given the rapid development in AI technologies, continuous updating of detailed training specific to AI usage in each healthcare domain is imperative. This requirement for continuous education can trigger significant transformations in decision-making processes within the medical field. At this stage, even if AI systems are not replacing doctors in healthcare, doctors proficient in AI will be preferred over those who lack such skills (27,29). Therefore, AI literacy in healthcare is no longer an option but a necessity.

A similar situation exists in discussions about the use of AI in scientific research and writing scientific papers (87). The opportunities presented by generative AI technologies, especially ChatGPT, have started to be actively utilized by scientists, and papers with ChatGPT as a co-author have even

been published. As in the field of healthcare, the ethical dimension of using AI technologies in this field, particularly regarding who will take responsibility for its contributions, is a topic of ongoing debate (88). While some journals, such as Science, take a firm stance that text, figures, images, or graphics generated by AI can never be used in articles (89), many journals have policies stating that AI cannot be a co-author, but its contributions can be significant and must be explicitly acknowledged in the article (90,91). This approach implies that, similar to the significant contributions of AI in diagnosis and treatment processes in the healthcare field, medical AI systems cannot replace doctors due to the lack of accountability.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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Ergonomi ve Ergonomik Eğitimin Önemi

Ergonomics and the Importance of Ergonomic Education

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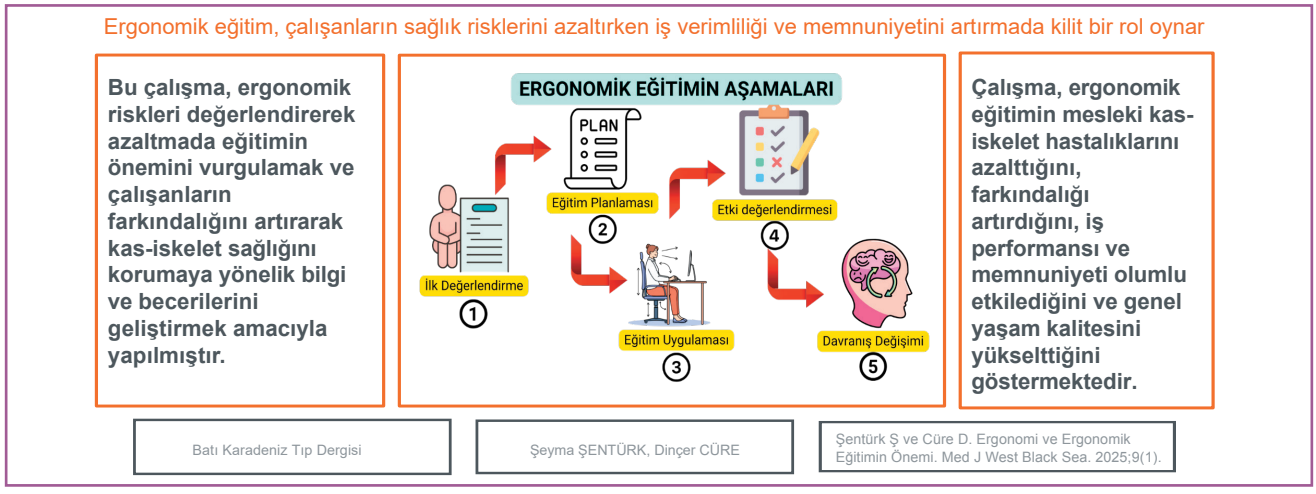
GRAFİKSEL ÖZET



ÖZ

Dünya genelinde saptanmış tüm kas-iskelet sistemi hastalıklarının %30'una yakınının Mesleki Kas İskelet Hastalıklarının oluşturduğu bilinmektedir. İşe bağlı hastalıkların ve iş kazalarının sebep olduğu bütün iş günleri kaybının %34'üne yakınını kas-iskelet sistemi hastalıkları oluşturmaktadır. İş ile alakalı psikososyal, ergonomik, fiziksel ve kişisel faktörlerin mesleki kas iskelet hastalıklarının oluşumuna etkisi bilimsel yollarla ispatlanmıştır. Güncel literatüre baktığımızda endüstrileşmiş ülkelerde mesleki kas iskelet hastalıklarının artışı, çalışanların, işverenlerin, devlet yöneticilerinin, sağlık bakım sistemlerinin ve sigorta şirketlerinin dikkatini fazlasıyla bu konuya çekmektedir. Prevalans ve maliyetteki dikkat çeken artış nedeniyle; risk faktörleri, ergonomik girişimler ve ergonomik eğitimi kapsayan ergonomi programları ve bu bileşenleri içeren rehabilitasyon yaklaşımlarıyla ilgili uygulama ve çalışmalar ivedilik kazanmaya başlamıştır. Önleyici yaklaşımlar ve korunma yolları vasıtasıyla ergonomi konusunda toplum bilinci oluşmakta, iş yerlerinde ergonomik müdahaleler ve ergonomik eğitim hızla yaygınlaşmakta ve uygulanmaktadır. Ergonomik prensiplere göre tasarlanmış fiziksel bir ortamda çalışmanın, sorunları önleyip, iş aktivitelerinde performans artırımı için, bir başına yetersiz olduğu yapılan çalışmalarda güçlü kanıtlarla saptanmıştır. Ergonomik eğitim vererek çalışanların ergonomik davranışlar ve müdahalelerle ilgili bilinçlenmeleri, böylelikle ergonomi farkındalıklarının artırılmasıyla, iş yeri koşulları ve ortamı yeteri kadar ergonomiye sahip olmasa dahi, mesleki kas iskelet hastalıklarının prevalansının azaldığı gözlemlenmiştir. Bu derleme, bu kapsamda çalışanlara ergonomik eğitim verilmesinin önemini, ergonomi programı içerisinde yerini ve ilişkili faktörleri vurgulamakta ve ele almaktadır.

Anahtar Sözcükler: Ergonomi, ergonomik eğitim, mesleki kas iskelet hastalıkları

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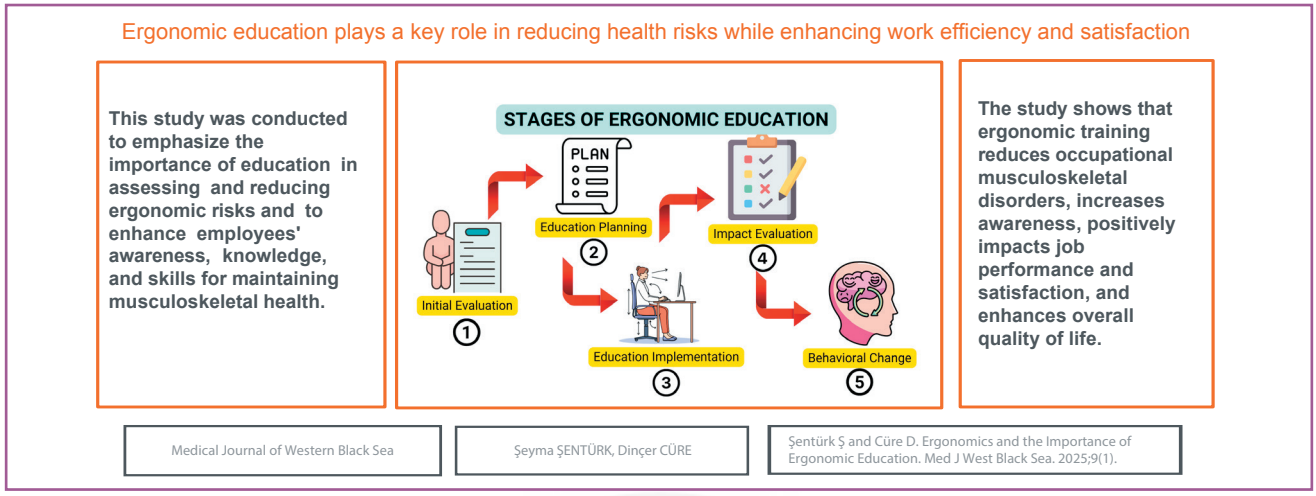
GRAPHICAL ABSTRACT



ABSTRACT

Work-related musculoskeletal disorders comprise an estimated 30% of all musculoskeletal system disorders identified on a global scale. Occupational accidents and disorders constitute 34% of the total number of days lost from work. Scientific evidence supports the notion that work-related psychosocial, ergonomic, physical, and personal factors all contribute to work-related musculoskeletal disorders development. The increase in work-related musculoskeletal disorders in industrialized nations has been attracting the interest of employees, employers, government officials, healthcare systems, and insurance companies, according to recent studies. Practices and research concerning ergonomics programs that incorporate risk factors, ergonomic initiatives, and ergonomic training and rehabilitation approaches have started to gain momentum as a result of the rapid rise in prevalence and costs associated with these components. The general public is becoming increasingly aware of ergonomics through the use of preventative measures and protection techniques, leading to an accelerated expansion and implementation of workplace interventions and ergonomics training. Substantial evidence from research indicates that simply having an ergonomically designed work environment does not effectively prevent problems or improve performance in work-related tasks. Even in the presence of an inappropriate ergonomic working environment and conditions, we observe that ergonomics training decreases employees' awareness of ergonomic behaviors and interventions while simultaneously increasing their awareness of ergonomics. This review examines and discusses the significance of ergonomic training for employees, its integration within ergonomics programs, and other pertinent aspects.

Keywords: Ergonomics, ergonomic education, work related musculoskeletal disorders

GİRİŞ

Disiplinlerarası bir bilim dalı olan ergonomi insan ile kullanılan çalışma ortamı ve araçlar arasındaki ilişkileri bilimsel yöntemle inceleyen uygulama alanlarını kapsamaktadır. Ergonomi, *"İşbilim"* veya *"İnsan Mühendisliği"* olarak da adlandırılır. İş, makine ve insanın birbirleriyle optimum düzeyde uyumlu olması amacıyla, insanın anatomik, fizyolojik, biyomekanik gibi birçok özelliğini göz önüne alarak işlerin ve kullanılan her türlü aracın bu özelliklere göre tasarlanmasını sağlamaktadır (1). Diğer bir tanıma göre ergonomi (veya insan faktörleri mühendisliği), sistem içindeki bireyler ve diğer personellerle arasındaki ilişkileri göz önüne alarak, bireylerin sağlığını, işle ilişkili sistemin verimliliğini, güvenliğini, en iyi hâle getirmek için ilkeleri, bilimsel teorileri, tasarımların verilerini ve metodolojisini uygulamakta olan bir disiplindir (2). Ergonomi programları çerçevesinde, programın temel bileşenleri; iş yeri risk etkenleri değerlendirilmesi, ergonomik eğitim, ergonomik girişimlerdir (3,4) .

Morbidite nedenleri arasında olan Kas İskelet Sistemi Hastalıkları (KİS), sağlıkta önemli bir yer tutmaktadır. Bireylere, topluma ve devletlere ağır bir yük oluşturmaktadır. Bu hastalıklar bireylerin yaşam kalitesini düşürmekte, sakatlık ve fonksiyon kayıplarına neden olup, sağlık harcamalarıyla, sistemler içerisinde çok büyük ölçüde yüke sebep olmaktadır. ABD'de 1995 yılında, kas-iskelet sistemi hastalıkları nedeniyle toplam 3.008.000 hastane yatışı gerçekleşmiş ve bu durumun toplam maliyeti 215 milyar ABD doları olmuştur. (5). Bu harcamalar doğrudan, dolaylı ve görülmeyen harcamalardan oluşmaktadır. Hekimin muayene etmesi, tanı amacıyla yapılan testler, ilaç kullanımları, hastaneye yatışların yapılması gibi durumlar tıbbi bakım maliyetlerini oluşturmaktadır. KİS hastalıklarının doğrudan maliyetlerinin yapılan çeşitli çalışmalarda milyar dolara kadar yük getirdiği bildirilmektedir (6).

Mesleki aktiviteler sırasında fiziksel ve psikososyal risklerle oluşan ağrı, sakatlanma ve disfonksiyonlarla seyir gösteren

KİS hastalıkları çalışan bireylerde görülen yaygın sağlık sorunlarıdır. Çoğunlukla kasları, diskleri, tendonları, ligamanları ve birçok yumuşak dokuyu etkilemektedir. Bu hastalıklarının önemli bir kısmını oluşturan Mesleki Kas İskelet Hastalıkları (MKİH)'nın iş ile ilgili aktivitelere bağlı olarak geliştiği kabul edilmektedir. Meslekle ilişkili faktörlerde bedenin kötü postürlerde kullanımı, iş sırasında tekrarlamalı, zorlamalı hareketler, ergonomi konusunda fiziksel, bilişsel yetersizlikler, davranışsal faktörler gibi nedenler önemli ölçüde yer almaktadır (7).

Yakın zamanda endüstrileşmiş ülkelerde MKİH'nin artışı çalışanların, işverenlerin, devlet yöneticilerinin, sağlık bakım sistemlerinin ve sigorta şirketlerinin dikkatini fazlasıyla bu konuya çekmiştir. Prevalans ve maliyetlerdeki dikkat çeken artış nedeniyle; risk faktörleri, ergonomik girişimler ve ergonomik eğitimi kapsayan ergonomi programları ve bu bileşenleri içeren rehabilitasyon yaklaşımlarıyla ilgili uygulama ve çalışmalar ivedilik kazanmaya başlamıştır. Önleyici yaklaşımlar ve korunma yollarıyla ergonomi konusunda toplum bilinci oluşmakta, iş yerlerinde ergonomik müdahaleler ve ergonomik eğitim hızla yaygınlaşmakta ve uygulanmaktadır (3,4,8). Bu nedenlerle bu derlemenin amacı, ergonominin önemli bir bileşeni olan ergonomik eğitim ve ergonomik eğitimle ilişkili faktörlere vurgu yapmaktır.

MESLEKİ KAS İSKELET SİSTEMİ HASTALIKLARI

Beklenen yaşam ömrünün artmasıyla KİS hastalıklarının prevalansı toplumda artmaktadır. İngiltere'de yapılan bir çalışmada 40 yıl öncesiyle kıyaslanınca sık görülen KİS ağrılarının prevalansının oldukça arttığı gözlemlenmiştir (9). Bu hastalıklar 150'den fazla, farklı şekillerde sendrom ve durumlardan oluşmaktadırlar. Örneğin, fibromiyalji, tendinit, osteoartrit, omuz ve kol ağrıları, sırt ve bel ağrıları gibi birçok hastalığı kapsayabilmektedir. Dünya genelinde 70 yaş ve üzeri bireylerin %40'ında diz osteoartriti kaynaklı ağrılar bulunmaktadır. Osteoartrit tanısı bulunan bireylerin %25'i günlük yaşam aktivitelerini bağımsız yerine getirememektedir. Toplumun %80'inde hayatlarının bir döneminde bel ağrısı şikâyeti görülmekte olup, bu durum epidemik boyutlara ulaşmıştır (10).

Dünya genelinde saptanmış tüm KİS hastalıklarının %30'una yakınını MKİH'nin oluşturduğu bilinmektedir. İşe bağlı hastalıkların ve iş kazalarının sebep olduğu bütün iş günleri kaybının %34'üne yakınını KİS hastalıkları oluşturmaktadır. Dolayısıyla, bunların sebep olduğu tazminat maliyetleri yıl bazında 15-20 milyar dolarlara ulaşmaktadır (11). MİKH içerisinde bel ağrısı yüksek prevalansı ile yer almaktadır. Bununla beraber pek çok hastalık bu grup içerisinde yer almaktadır. Tekrarlayan hareketler ve zorlanmalar ile birikimli travmalar MKİH'ye neden olan başlıca önemli iki etkeni oluşturmaktadır. Bu iki önemli etken nedeniyle yumuşak dokularda, kaslarda, tendonlarda, kemiklerde ve eklem yapılarında değişiklikler oluşmaktadır. Bunların sonucunda, birçok klinik tablo karşımıza çıkmaktadır. Çalışma hayatının uzun sürmesi, bu hastalıkların ortaya çıkmasında önemli bir etken olmakla birlikte, aşırı zorlanma durumlarında daha kısa bir süre içerisinde de gelişebilmektedir (12).

Geçtiğimiz son zamanlarda MKİH'nin gelişmiş ülkelerde maliyetlerinin ve prevalansının yükselmesine paralel olarak yapılan çalışmalarda mali kayıplar, risk faktörleri, iş günü kayıpları gibi konular sık ele alınmaktadır. Bu konuda yapılan çalışmalar hız kazanmıştır. Gelişmiş ülkelerde kanunen MKİH meslek hastalığı olarak kabul edilmektedir. Bu ülkelerde meslek hastalığı tanısı konulmasının ardından, maluliyetler göz önüne alınarak tazminat ödemeleri yapılmaktadır (13). Erken emekliliğin ve maluliyet ödemesi yapılmasının başlıca nedeni meslek hastalıklarıdır. Bu hastalıkların ekonomik olarak yük oluşturmasının ve yasal düzenlemelerin yapılmış olmasının etkisiyle MKİH'yi önlemek amacıyla ergonomik eğitim yaygın olarak karşımıza çıkan yöntemlerden biridir (14).

İşyerlerinde iş sağlığı ve güvenliğinin geliştirilmesi, iş kazaları ve MKİH'den çalışanları korumak günümüzde önem kazanmaya devam etmektedir. Meslek hastalıklarından birisi olan KİS hastalıklarının oluşmasında elzem rolü olan ergonomik risk faktörlerinin değerlendirilmesi, işyerlerinde ergonomik ilkelere uygun olarak uygulamalar yapılması oldukça önem arz etmektedir (15).

Ülkemizde MKİH kanunlarla meslek hastalığı olarak kabul edilmektedir. Meslek hastalığı Sosyal Sigortalar Mevzuatında; "İşin niteliğine göre tekrarlanan bir sebeple veya işin yürütüm şartları yüzünden" meydana gelen hastalıklar olarak tanımlanmıştır (16). Ayrıca, 4857 Sayılı İş Yasasında İş Sağlığı ve Güvenliği ile ilgili yönetmeliklerle MKİH için iş yerlerinde risklerin belirlenmesi, önlenmesi, çalışanın korunması, ergonomik eğitim ve ergonomik müdahalelerin uygulanması konusunda, işverenlerin yükümlülüğü bulunmaktadır (17).

Ülkemizde MKİH'nin görülme sıklığı ve oluşumuna neden olan risk faktörleri üzerine yapılan çalışmalar oldukça yetersizdir. Bu nedenle bu hastalıkların maluliyetinin saptanması ve tazminat ödemelerinde birçok sorun karşımıza çıkmaktadır. Diğer meslek hastalıklarında da aynı durum görülmektedir. Bunlara ek olarak, Kas-iskelet sistemi hastalıklarından korunma ve önleme amacıyla işyerlerinde yapılan müdahaleler ve işveren ile çalışanlara verilen eğitimler konusunda, ayrıca bu hastalıklar nedeniyle iş günü kaybı ve sigorta firmalarının tazminat ödemeleri gibi diğer konularda da verilerin oldukça yetersiz olduğu görülmektedir (15,18).

ERGONOMİK RİSK FAKTÖRLERİ

İş ile alakalı psikososyal ve fiziksel faktörlerin MKİH'nin oluşumuna etkisi bilimsel yollarla ispatlanmıştır. İş dışında kalan faktörler de MKİH oluşumunda rol oynamaktadır (19). Üst ekstremiteler ve belde görülen tekrarlanan ve zorlamalı

Tablo 1. Ergonomik Risk Faktörleri

Tekrarlanan ve zorlamalı hareketler
Kötü ve yanlış postürler
Uzun süre aynı pozisyonda kalma
Titreşim etkileri
İş monotonluğu ve stres
İş arkadaşları desteğinin eksikliği
Yetersiz denetim
Düzensiz veya eksik iş molaları
Sedanter yaşam tarzı
Fiziksel kondisyon yetersizliği
Sigara kullanımı

hareketler, ağırlık taşıma ve strese neden olan iş koşulları gibi etkenler hastalık oluşumunu artırmaktadır. Yapılan çalışmalar düzgün tasarlanan ergonomik müdahale ve girişimler içeren programlarla bu sorunların üstesinden gelinebileceğini bildirmektedir (20).

Ergonomik risk faktörleri Tablo 1'de listelenmiştir. Bu faktörler, çalışanların iş sırasında karşılaştıkları fiziksel ve psikososyal riskleri içermekte ve kas-iskelet sistemi hastalıklarının önlenmesinde kritik bir öneme sahiptir.

Fiziksel ve ergonomik etkenler iş ile bağlantılı etkenlerin başında sayılmaktadır. Bu etkenler arasında tekrarlamalı ve zorlamalı hareketler öne çıkmaktadır. Yine columna vertebralisin ve bedenin kötü ve yanlış pozisyonlarda kullanımı, kötü çalışma postürleri de oldukça etkili olmaktadır. Bu hastalıklardan bel fıtığının oluşmasında diz ve kalçayı kullanmadan bele yüklenerek öne eğilmek, yanlış pozisyon ve postürlerde ağırlık kaldırma ve taşıma aktivitelerinin yapılması, yine bu hastalıklardan olan karpal tünel sendromu oluşumunda bilgisayarla çalışma sırasında el bileğinin aşırı fleksiyonda kullanılması önemli derecede rol oynamaktadır. Çalışırken uzun süre aynı veya yanlış postürde veya pozisyonda kalınması ayrıca titreşim gibi etkenlere maruz kalınması da bu etkenlerin arasında sayılmaktadır (21).

Güncel literatüre baktığımızda psikososyal etkenlerin de bu hastalıkların oluşumunda rol oynadığını görmekteyiz. Çalışanların iş monotonluğu yaşaması, iş memnuniyetsizliği hissetmesi ve sürekli zaman baskısı altında çalışması risk faktörleri olarak kabul edilmektedir. Ayrıca, iş yerinde, iş arkadaşı desteğinin olmaması, yetersiz denetçi bulunması, iş molalarının yetersiz ve eksik olması veya iş molaların bir düzene tabi olmaması ve iş ile ilişkili organizasyonel etkenlerde sorunlar bulunması da risk faktörü olarak kabul edilmektedir. Yine kişinin yaşamında inaktif veya sedanter olması, ileri yaşta olması, aşırı kilolu olması, fiziksel kondüsyonunun yetersiz olması, sigara kullanması gibi kişisel etkenler de bu hastalıkların oluşumuna katkı sağlamaktadır (22).

İşverenler, iş aktiviteleri sırasında kullanılan ekipman ve araçların aynı prensiplerle kullanılması ve seçilmesi, işyerlerini ergonomik prensiplere uygun olarak tasarlanması gibi girişimlerde bulunmalıdır. Bu girişimler MKİH'yi önlemek için yapılması gereken uygulamalar arasında yer almaktadırlar. Bu hastalıkların önlenmesinde birçok girişim, müdahale ve uygulama bulunmakta, risk faktörlerinin önüne geçilmektedir. Yine işverenlerin, ortaya çıkacak bilgilerin kullanımı ışığında işyerlerinde risk değerlendirmesi yapmaları gerekmektedir. Bunun sonucunda bu belirlenen risk faktörlerini kontrol altına almak için birtakım prosedürler oluşturabilmektedirler (20,21). Konuyu örneklendirmek gerekirse; iş duraklarının, araç ve ekipmanlarının tasarlanması ya da tekrar tasarlanması gibi müdahaleler gerekebilmektedir. Bu amaçla mühendislik prosedürleri uygulanmalı, kontroller sağlanmalıdır. Yine çalışanların rotasyonu, iş çeşitliliğinin nasıl artırılacağı, mola sürelerinin artırılması gibi konular dikkate alınmalıdır. Ergonomik prensiplerle ağırlık taşıma teknikleri gibi iş pratiğini içeren eğitimler verilmesi ve iş alanlarının temiz tutulması gibi organizasyonel kontrollerin sağlanması bu uygulamalar içerisinde bulunmaktadır. İşverenlerin titreşim eldiveni ve diz koruyucuları gibi kişisel koruyucu donanımların belirlenmesi ve tedarik edilmesi konularında da uygulama ve müdahalelerde bulunmaları gerekebilmektedir. Bunlar iş ile ilişkili risk faktörlerini en aza indirebilmektedirler (14).

ERGONOMİK EĞİTİM

Ergonomik eğitim ergonomi programlarının önemli bileşenlerinden birini oluşturmaktadır (20,23). Çalışanlarda ve ergonomi ekibinin ergonomik eğitimde amaçlarının başında ergonomik bilinç oluşturulması, iş aktiviteleri sırasında güvenli ve ergonomik açıdan optimum düzeyde iş davranışları geliştirilmesi gelmektedir. Eğitimin içeriğinde KİS hastalıkları, risk faktörleri, erken teşhis ve tedavi, ergonomik risk faktörleri ve çözüm yolları, sağlıklı yaşam davranışları ve alışkanlıkları geliştirme, koruyucu önlemler kapsamında ergonomi, düzgün postür kullanımı ve prensipleri, biyomekanik prensiplerle vücudun kullanımı, egzersizler, fiziksel aktivite yaklaşımları gibi konular bulunmaktadır (19,24).

Bir ergonomik eğitim, prensip olarak çalışanın KİS'de yaralanmalara neden olabilen faktör ve davranışlarını değiştirmesi ve bunlardan kaçınmasını amaçlamaktadır. Dolayısıyla çalışanın MKİH'den korunma yöntemlerini öğrenmesine, çalışanda ergonomik farkındalık sağlanmasına ve oluşmasına odaklanmalıdır (25). Ergonomik prensiplere göre tasarlanmış fiziksel bir ortamda çalışmanın, sorunları önleyip, iş aktivitelerinde performans artırımı için, bir başına yetersiz olduğu yapılan çalışmalarda güçlü kanıtlar taşımaktadır (26). Ergonomik eğitim vererek çalışanların ergonomik davranışlar ve müdahalelerle ilgili bilinçlenmeleri, böylelikle ergonomi farkındalıklarının artırılmasıyla, iş yeri koşulları ve ortamı yeteri kadar ergonomiye sahip olmasa dahi KİS

hastalıklarının prevalansının azaldığı gözlemlenmiştir (27). Ergonomik eğitim süreci, belirli aşamalardan oluşmaktadır ve bu aşamalar Şekil 1'de detaylandırılmıştır.

Ergonomik eğitim verilirken, eğitim esas olarak KİS hastalıklarına neden olan durum ve faktörlerden korunma yollarını öğretmeye odaklanmalı, anlatımının sade, anlaşılır ve açık bir şekilde dile getirilmesi gerekmektedir. Ergonomik eğitim seminer, sunum, ders anlatımı şeklinde verilebileceği gibi poster, broşür verilmesi gibi yazılı materyal yollarıyla da yapılabilmektedir, ayrıca çevrimiçi eğitim gibi sanal yollarla da verilebilmektedir (28). İnsan ve işin optimum düzeyde uyumunu sağlamak isteyen bir bilim dalı olan ergonominin ana amaçları iş koşulların ve fiziksel çevresinin iyileştirilmesi, gerekli olmayan ve yüksek şiddete zorlanmalardan çalışanın sağlığının korunması, çalışma esnasında ortamda ve koşullarda güvenliğin iyileştirilmesi ve işten alınan memnuniyetin yükseltilmesidir. Bu amaçlara uygun müdahale ve girişimlerde bulunulursa, çalışanların bedensel ve psikolojik iyilik durumları artmaktadır, dolayısıyla çalışanların performansı ve işin verimliliği de artmış olacaktır (29,30).

Ergonomik eğitim çeşitli içerikler ve yöntemlerle verilmektedir. Kurumlar veya eğitimciler kendi uzmanlık alanlarını temel alan bilgileri ve deneyimlerini eğitimlere yansıtmaktadırlar. Bazı eğitimlerin etkinlikleri yapılan bilimsel çalışmalarla değerlendirilmiştir. Ergonomik eğitim kapsamında yapılan yasal düzenlemeler, konuyla ilişkili bir hizmet sektörü oluşturmuştur. Eğitim şirketlerinin eğitim konularının başlıcaları sağlık, çevre ve güvenlikten oluşmaktadır. Sağlık ve güvenlik konularında verilen eğitim programlarında ana amaç yaralanmaların önlenmesidir (31). Ergonomik eğitimler, sağlık ve güvenlik eğitimleri kapsamında verilmektedir. Bu çerçevede temel bileşenlerden biridir (32-34).

Şekil 1. Ergonomik Eğitim Aşamaları

Eğer eğitimlerde mühendislik kontrolleri bulunuyorsa eğitimde bu kontrollerin çalışanların anlayacağı şekilde aktarımı sağlanmalıdır. Çalışanlara iş çevresinde yapılacak değişimlerin KİS sorunlarını önlemedeki rolü izah edilmelidir (35). Bir ergonomik eğitim ana hatlarıyla, çalışana ergonomik farkındalık kazandırmaya ve daha önemlisi çalışanın KİS'de yaralanmaya yol açabilen durumlardan kaçınmanın yollarını öğretmeye odaklanmaktadır (25). Eğitimin başarılı olması ve hedefe ulaşması için kişinin özgüveni ve motivasyonu sağlanmalıdır. Kalıcı değişimin olması kişinin aldığı eğitimin gereklerini uygulamasından ve bu şekilde KİS yaralanmalarını önlemesinden geçmektedir. Ergonomik eğitim temel bilimsel prensipleri ve çalışma ortamında düzenin nasıl sağlanacağı ile ilgili teknikleri içermektedir. Böyle bir eğitimde hedef, çalışanı riskli durumlar hakkında bilgilendirmek, bu durumları tespit edebilme yetisini kazandırmak ve çalışanı, örneğin iş ortamını düzenlemek gibi önlemler almaya teşvik etmektir (36).

Ergonomik eğitimlerde beklenen sekonder etki çalışanın herhangi bir sağlık sorunu olmadan daha verimli çalışmasıdır. Herhangi bir ağrı ve rahatsızlık olmaması hali çalışanın iş ortamında daha yüksek iş kapasitesine sahip olmasını sağlamaktadır (37). Ergonomik eğitim çeşitli yöntemlerle sunulmaktadır. Didaktik eğitim katılımcıların ihtiyaç ve taleplerini belirleyen bir eğitmen tarafından ders formatında verilmektedir. Eğitimin sonunda soru cevap bölümü adıyla ayrı bir bölüm yer alabilmektedir (38). Bazı çalışmalar eğitim içeriğini görsel ve medya ürünleri ile desteklemenin öneminden bahsetmektedir (39,40).

Ergonomik eğitim ekseninde, katılımcının taleplerine daha fazla önem vermeyi vurgulayan çalışmalarda grup öğrenme hedeflerini kendi belirlemektedir. Eğitimci ile öğrenen arasında devam eden bir iletişim söz konusu olmaktadır. Eğitim, problem çözme becerisi kazandırma ve pratik uygulamalar şeklinde sunulmaktadır (41). Bunların dışında bilgisayar bazlı eğitim programları da tasarlanmış ve bu programların da kullanıcı ihtiyaçlarına ne derece cevap verdiği değerlendirilmiştir (42).

Ergonomik eğitim programları bilgi düzeyinin artması ve davranış değişikliği ile ilgili sonuçlara odaklanmaktadır. Öğrenilen bilginin davranış değişikliğine aktarımı ya da davranış değişikliğinden önceki aşamaları genellikle daha az konu edilmiştir. Yapılan pilot projelerde ergonomik girişimin kümülatif travma bozuklukları ile ilgili bilgi artışı ve riskli davranışları azaltmadaki etkinliği değerlendirilmiştir (43). Ergonomik eğitim e-posta, poster, 45 dakikalık seminer ve bilgi broşürleri ile sunumlarla da verilebilmektedir. Bu yöntemlerle de katılımcıların sağlık ve güvenli çalışma postürleri konusunda daha bilinçli oldukları, çalışanların iş yerinde değişiklikler yaptıkları saptanmıştır (44).

Bazı araştırmacılar kişiye ve gruba özel eğitim sunmanın önemine değinmişler, kişilerin ihtiyaç duydukları unsurlara

karşı daha duyarlı oldukları ve bu yolla daha hızlı ve etkin bir değişim sağlanabileceğini iddia etmişlerdir. Erişkin öğrenme modellerinin kas iskelet sistem yaralanmalarına uyarlanması olarak adlandırılan bu eğitim yöntemi, genellikle sağlık alanında çalışan profesyoneller tarafından sunulmuş olup pek çoğu test edilmemiştir (38).

Sonuç olarak, eğitimler içerik olarak katılımcıların ihtiyaçlarını tespit edip aynı zamanda o ihtiyaçları karşılamalıdır. Bunun dışında, eğitim içeriğinde görseller ve interaktif uygulamalar yer alabilmektedir. Ergonomik eğitimde, çalışanları riskler hakkında bilgilendirme, riskli durumların tespit edilmesini sağlayabilmek ve çalışanı kendi çalışma ortamını düzenlemeye teşvik etmek hedeflenmektedir (45). Ergonomik eğitim verilmesinden sonra eğitimi alan bireylerin katılım ve uyum sağlaması eğitimin fayda sağlaması için oldukça önem arz etmektedir. Verilen eğitim sonucunda çalışanın özverili davranarak öğrendiklerini iş aktiviteleri haricinde de hayatına aktarması ve hayatında uygulaması eğitimin sürdürebilirliğini ve kalıcılığını sağlamaktadır (46). Ergonomik eğitimin ve girişimlerin KİS'den kaynaklanan hastalıkların prevalansını ve maliyetlerini düşürdüğü, bireylerin yaşam kalitesini artırdığı, iş verimliliği, performansını ve iş ile ilişkili memnuniyeti artırdığı çalışmalarda gösterilmiştir (37).

EGZERSİZ

Fiziksel aktivite gündelik yaşamımız içerisinde iskelet kaslarını kullanarak yaptığımız ve enerji harcaması yapılan tüm hareketler olarak tanımlanmaktadır (47). Fiziksel aktivite, egzersizlerden spor dallarına, hobi aktivitelerinden veya günlük yaşamda yapılan faaliyetlere kadar bütün insanların yaptığı hareketleri içermektedir. Egzersiz boş vakitlerdeki fiziksel aktivitenin alt başlığında sayılan fiziksel uygunluğun bir veya daha fazla bileşeninin korunması veya geliştirilmesini amaçlayan planlanmış, düzenli ve tekrarlı fiziksel aktiviteler olarak tanımlanmaktadır (48).

Fiziksel aktivite eksikliği, yanlış beslenme alışkanlıkları ve yaşam tarzına bağlı stres nedeniyle bireylerin kronik hastalıklara yakalanma riski artmaktadır. Ayrıca bireyler, sosyolojik değişimlerle karşı karşıya kalmakta ve psikolojik baskılarla mücadele etmek zorunda kalmaktadır. (49). Egzersiz, fiziksel ve psikolojik etkileri olan stres faktörünün yönetilmesinde önemli bir yere sahiptir. İnsan bedeninde, biyokimyasal olarak çoğu değişikliklere neden olmaktadır. Egzersiz sırasında norepinefrinin serum kan düzeyi yükselmekte ve bu artış, depresyon durumunda semptomların şiddetini önemli ölçüde azaltmaktadır. Aynı şekilde kanda endorfin düzeyinin artması, ağrı hissinin azalmasında etkilidir. Ruh hâlinin iyileşmesinde etkileri olan endorfinin bunun gibi olumlu etkileri vücutta görülmektedir (50).

Düzenli yapılan egzersizler, kalp damar hastalıklarına bağlı morbiditeyi ve hastalığın şiddetini azaltmakta, bunun yanında obezite, hipertansiyon ve osteoporoz gibi kronik hastalıkların önlenmesinde önemli ölçüde etkili olmaktadırlar. Doğru şiddette, düzenli aralıklarla ve devamlı yapılan egzersizler, pulmoner enfeksiyonların riskini azaltır, immün sistem üzerine olumlu etkisi vardır. Ruhsal hastalıkların örneğin depresyon ve anksiyetenin prevalansını ve semptomlarının şiddetini azaltır, bunun gibi pek çok yararlı etkileri bulunmaktadır (51). Egzersizin aynı zamanda vücut yağ kütlesinin azalmasında, bireyin psikolojik iyilik hâlinin artmasında ve özgüvenin sağlamasında, postür düzgünlüğünün devam ettirilmesi veya iyileştirilmesinde etkileri bulunmaktadır. Egzersiz bireyin stres faktörleriyle başa çıkmasına yardımcı olmakta, dengesini ve koordinasyonunu geliştirmekte, esnekliğini korumakta ve artırmaktadır (52).

Yaşa bağlı artan oksidatif stres ve inflamasyon, çizgili kasların kütlesinde ve fonksiyonun azalmasında rol oynamaktadır. Düzenli egzersiz yaşlanma sürecine katkıda bulunan bu faktörlerin etkilerinin azaltılmasında önemli bir rol oynar. Düzenli fiziksel aktivite ve egzersiz yaşın ilerlemesi ile ilişkili kas metabolizmasının bozulmasını yavaşlatmakta, kas gücü, kuvveti, tonusu ve kütlesini korumakta ve artırmaktadır. Kas hücrelerinin yenilenme kapasitenin düşmesini yavaşlattığı ve kas hücrelerini koruduğuna dair çalışmalarda güçlü kanıtlar bulunmaktadır (53,54). Düzenli egzersiz, kas dengesinin sağlanması ve korunması, aerobik kapasitenin korunması ve iyileştirilmesi, esnekliğin korunması ve geliştirilmesi, kas-eklem stabilitesinin korunması ve iyileştirilmesi, beden farkındalığının artması, postüral düzgünlüğün sağlanması, reflekslerin gelişmesi, reaksiyon zamanının kısalması ve kemik mineral yoğunluğunun korunması ve iyileştirilmesi gibi birçok olumlu sonuç sağlamaktadır (55).

Çalışanlara yönelik, direnç egzersizleri gibi çeşitli egzersiz uygulamaları ve eğitimi, özellikle kas-iskelet sistemi (KİS) şikayetleri veya ağrıları olanlarda olumlu sonuçlar sağlayabilmektedir. Ergonomik eğitim kapsamında verilen egzersizlerin temel amaçları, çalışanların düzgün postür kullanımını teşvik etmek ve bedensel farkındalıklarını geliştirmektir (51,56).

SONUÇ

Ülkemizde MKİH'nin görülme sıklığı ve oluşumuna neden olan risk faktörleri başlığında yapılan çalışmalara ihtiyaç duyulmaktadır. Bu çalışmalar ışığında sorun yaşanan özellikle MİKH gibi birçok hastalıkta maluliyetinin saptanması ve tazminat ödemelerinde düzelme sağlanmış olacaktır. Ayrıca, MKİH'de işyerlerinde korunma ve önleme ile ilişkili yapılan müdahale ve girişimler, işveren ve çalışanlara verilen eğitimler, bu hastalıklar nedeniyle iş günü kaybı ve sigorta tazminatı ödemeleri gibi konularda çalışmalar yapılarak verilerin artırılmasına ihtiyaç duyulmaktadır. Yakın zamanda endüstrileşmiş ülkelerde MKİH'nin artışı, çalışanların, işverenlerin, devlet yöneticilerinin, sağlık bakım sistemlerinin ve sigorta şirketlerinin dikkatini fazlasıyla bu konuya çekmek-

tedir. Prevalans ve maliyetlerde dikkat çeken artış nedeniyle; risk faktörleri, ergonomik girişimler ve ergonomik eğitimi kapsayan ergonomi programları ve bu bileşenleri içeren rehabilitasyon yaklaşımlarıyla ilgili uygulama ve çalışmalar ivedilik kazanmaya başlamıştır. Ülkemizde de bu çalışmaların artırılması gerekmektedir.

Önleyici yaklaşımlarla ve korunma yollarının kullanılmasıyla, ergonomi konusunda toplum bilinci oluşması, iş yerlerinde ergonomik müdahaleler ve ergonomik eğitimin hızla yaygınlaşması ve uygulamalarda yer alması ve artırılması gerekmektedir. Bu hastalıkların ekonomik olarak yük oluşturması ve yasal düzenlemelerin yapılmış olmasının etkisiyle MKİH'yi önlemek amacıyla ergonomik eğitim yaygın olarak karşımıza çıkan yöntemlerden birini oluşturmaktadır. Ergonomik prensiplere göre tasarlanmış fiziksel bir ortamda çalışmak, tek başına sorunları önlememekte, iş aktivitelerinde performans artırımı için ergonomik eğitim verilmesi de önemli bir komponent olarak ergonomik müdahale ve programlarda yer almalıdır.

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Yok.

Yazar Katkı Beyanı

Yazı Fikri: **Şeyma Şentürk,** Tasarım: **Şeyma Şentürk, Dinçer Cüre,** Analiz, Yorum ve Yazım: **Şeyma Şentürk, Dinçer Cüre.**

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ORIGINAL ARTICLE

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Vaccination Indecision in Mothers with Children Aged 0-5 Years

0-5 Yaş Arası Çocuğu Olan Annelerde Aşı Kararsızlığı

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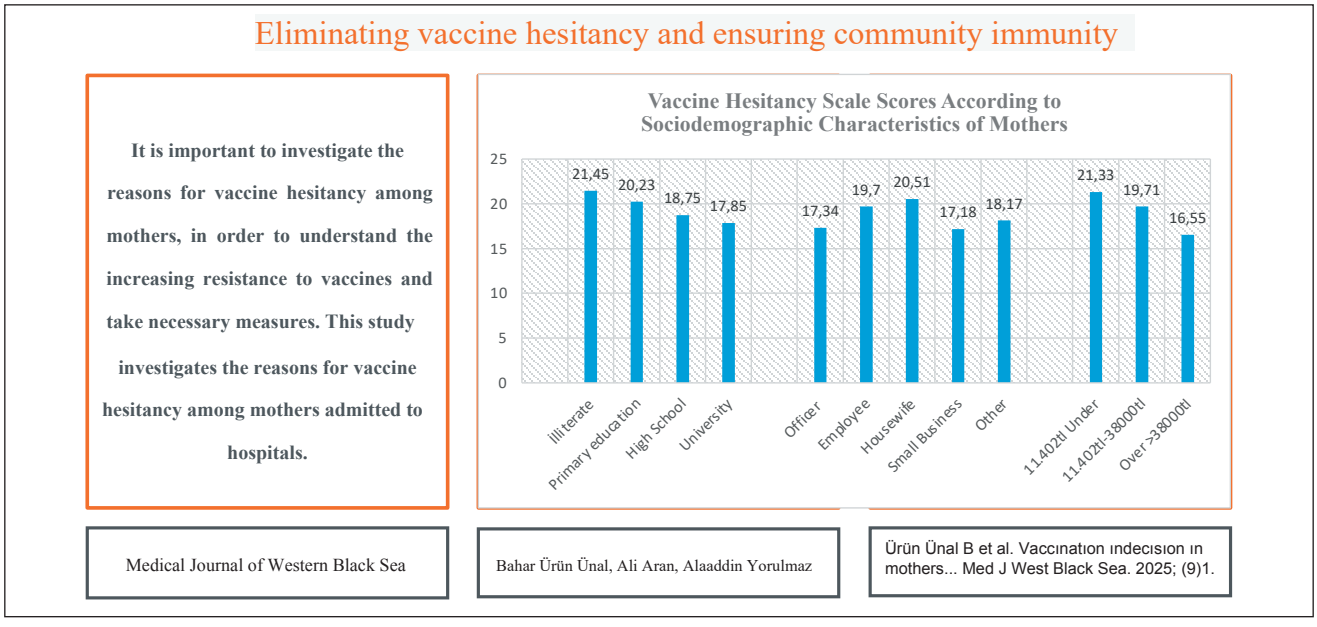
GRAPHICAL ABSTRACT



ABSTRACT

Aim: Vaccines are one of the most effective methods against diseases today. Vaccine hesitancy, defined as a delay in the acceptance or rejection of vaccines despite the availability of vaccination services, is increasing rapidly worldwide. It is important to investigate the reasons for vaccine hesitancy among mothers, in order to understand the increasing resistance to vaccines and take necessary measures. This study investigates the reasons for vaccine hesitancy among mothers admitted to hospitals.

Material and Methods: The Faculty of Medicine Hospital included 250 mothers with children aged 0-5 years, which increased between October-December 2023. The cross-sectional descriptive study literature was scanned and the 10-question survey formula presented was exhausted. In addition, vaccine hesitancy was measured using the 9 question Vaccine Hesitancy Scale.

Results: The study found that the score on the Vaccine Hesitancy Scale increased as the mother's educational status decreased 21.45±8.45 (p=0.012). Additionally, the score was higher for mothers who were housewifes 20.51±7.09 (p=0.001) and for those with lower income levels 21.33±3.72 (p=0.001).

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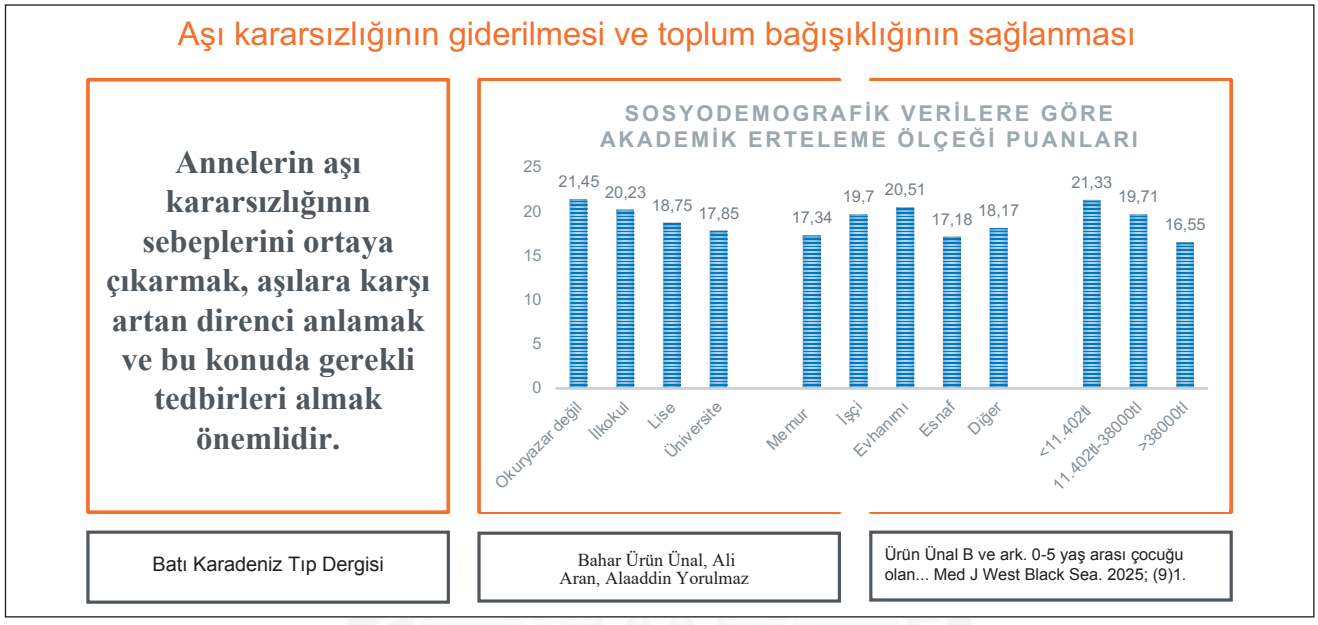
Conclusion: It has been determined that vaccine hesitancy may decrease with an increase in the income and educational status of mothers, as well as directing them towards work. These factors may have an impact on the number of unvaccinated individuals in the community.

Keywords: Vaccine hesitation, behavior, attitude

GRAFİKSEL ÖZET



ÖZ

Amaç: Aşılar günümüzde hastalıklara karşı en etkili yöntemlerden birisidir. Aşı hizmetlerinin mevcut olmasına rağmen aşıların kabulünde veya reddinde gecikme olarak tanımlanan aşı kararsızlığı dünya genelinde büyük bir hızla artmaktadır. Annelerin aşı kararsızlığının sebeplerini ortaya çıkarmak, aşılara karşı artan direnci anlamak ve bu konuda gerekli tedbirleri almak önemlidir. Bu çalışmada hastanelere başvuran annelerin aşı kararsızlığı nedenlerini araştırmak amaçlandı.

Gereç ve Yöntemler: Tıp Fakültesi Hastanesine Ekim-Aralık 2023 tarihlerinde başvuran 0-5 yaş arası çocuğu olan 250 anne dahil edildiği kesitsel tanımlayıcı tipte olan çalışmaya literatür taranarak hazırlanan 10 soruluk anket formu kullanıldı. Ayrıca aşı kararsızlığı, 9 soruluk Aşı Kararsızlığı Ölçeği kullanılarak ölçülmüştür.

Bulgular: Annenin eğitim durumu azaldıkça aşı kararsızlığı ölçeği puanının arttığı 21.45±8.45 (p=0,012), ev hanımı annelerin puanının daha yüksek olduğu 20.51±7.09 (p=0,001), annenin gelir seviyesi azaldıkça aşı kararsızlığı ölçeği puanının daha yüksek olduğu saptandı 21.33±3.72 (p=0,001).

Sonuç: Annelerin gelirinin artırılması, eğitim durumunun yükseltilmesi, çalışma hayatına yönlendirilmesi ile aşı kararsızlığının azalacağı belirlendi. Bu etmenlerin toplumda aşı olmayan kişi sayısına etkili olabileceğini düşünmekteyiz.

Anahtar Sözcükler: Aşı kararsızlığı, davranış, tutum

INTRODUCTION

Vaccines play a crucial role in promoting child health and creating healthy societies. Vaccination programmes are designed to prevent infectious diseases, provide immunisation against them, and reduce mortality and morbidity rates. Public health services strive to achieve individual and social immunity through vaccination, with the goal of maintaining a vaccination rate of at least 95% in the community. Immunisation services are crucial in preventing vaccine-preventable diseases and related disabilities and deaths. They are among the most important and cost-effective public health interventions, both globally and in our country (1).

Childhood immunisation programmes have led to significant reductions in morbidity and mortality among children under 5 years of age. The benefits of immunisation at the community level can only be achieved if a high proportion of children are immunised. Inadequate vaccination in the

community has often been thought to be due to barriers to access to vaccines, but these barriers have now been partially removed. Vaccine instability is recognised as a more important risk factor than access to vaccination (2).

A study analysed the economic impact of vaccines in 73 low- and middle-income countries. The study found that vaccination against 10 vaccine-preventable infectious diseases could prevent approximately 20 million child deaths between 2001 and 2020 and save US$ 350 billion (3).

In recent years, a movement opposing vaccination has emerged in our country. The number of cases of vaccine refusal, which had previously been insignificant, increased significantly in 2015 following a ruling on the issue of "obtaining parental consent for vaccination". Furthermore, anti-vaccine discourses were frequently featured in the media. The number of families who do not wish for their children to be vaccinated has increased significantly in recent years. While there were 183 such families in 2011, this figure had risen to 980 by 2013, 5,400 by 2015 and 12,000 by 2016. By 2018, the number of cases related to vaccine rejection had reached 23,000. The vaccination rate in Turkey, which was 98% in 2016, decreased to 95.2% in 2012. In 2017, 85 cases of measles were reported across the country, with the number of cases reaching 44 in the first three months of 2018. Consequently, while the incidence of measles was 0.01 per hundred thousand population in 2016, it has increased to 0.10 per hundred thousand today. It would appear that the number of individuals refusing vaccination rises in correlation with the number of measles cases (4).

Although vaccines have been successful, there is a growing trend among some individuals to view vaccination as unsafe and unnecessary. The number of unvaccinated children is increasing due to mothers who are undecided about vaccination. This reluctance to vaccinate is beginning to jeopardise the progress made in eliminating and reducing the impact of many infectious diseases (5).

It is a well-established fact that the number of mothers who are undecided about vaccination is significantly higher than the number of mothers who refuse vaccines altogether. This group of mothers is more likely to change their behaviour as they tend to actively seek information about vaccines. Therefore, it is crucial to have a better understanding of how to effectively communicate with undecided mothers and address their concerns. This is essential for translating the scientific benefits of vaccines into practice. In this study, it is important to determine the basic problems and needs of the target audience before communicating with families. Communication should be based on these factors to increase effectiveness (6). The aim of this study is to examine and evaluate the factors that contribute to the indecision of mothers who are undecided about vaccination.

MATERIALS and METHODS

This cross-sectional study included mothers with children aged 0-5 years who applied to Faculty of Medicine, Pediatrics Outpatient Clinic between October and December 2023 and agreed to participate. In calculating the sample size of the study, a national study examining the knowledge and attitudes of parents towards vaccines was used. 486 patients applied to the outpatient clinic in 3 months. 236 patients who refused to participate in the study and did not meet the conditions were not included. The sample size required to eliminate this situation with vaccine advocacy was calculated as a total of 215 people in the Gpower program at 0.05 alpha and 80% power level. Considering the sample losses, the sample size of 215 was increased by 15% (32.2 people ~ 33 people). The study was planned to include at least 248 people and was completed with 250 people.

A questionnaire was administered through face-to-face interviews to assess mothers' knowledge and attitudes towards childhood vaccines. The questionnaire was developed based on a literature review (7). The participants were asked seven questions regarding their sociodemographic characteristics and non-routine vaccines, including the Rotavirus vaccine, Conjugated Meningococcal vaccine, and Haemophilus influenzae Type b vaccine. Additionally, The Vaccine Hesitancy Scale, A nineteen-question survey was administered.

The criteria for inclusion in the study were determined as: residing in the city center, having at least a high school graduate education level, having a child between the ages of 0-5, being able to speak Turkish, being literate, being 18 years old and over, and being willing to participate in the study.When selecting parents to participate in the study, age, number of children, income level, etc. were not taken into consideration. Mothers who did not agree to participate in the study were not included in the study.

At the time of the study, 1 dollar was equivalent to approximately 28.90 Turkish lira. In Turkey, the minimum wage was determined as 11402 liras at the time of the study. This corresponds to approximately 393 dollars.

The Vaccine Hesitancy Scale was developed by Larson and colleagues in 2015 to compare vaccine hesitancy across countries and to assess the development of this situation over time (8). The validity and reliability study of the scale was conducted by Shapiro et al. (9). The validity and reliability study of the Turkish language was conducted by Önal et al. Önal et al. conducted a study on mothers and fathers with children aged 9-16 and suggested that studies be conducted on other age groups(2). Soysal et al. stated in their study that this scale could also be used on mothers and fathers with children under the five age (10).

The scale consists of 9 items. The scale consists of a five-point Likert type (strongly agree/agree/undecided/disagree/strongly disagree) and two sub-dimensions (lack of trust (items 1,2,3,4,6,7,8) and risks (items 5,9). The lowest score that can be obtained is 9, the highest score is 45. The scale score is calculated by reversing the scores in the lack of confidence (1,2,3,4,6,7,8) sub-dimension, which consists of positive propositions, and the risks (5,9), consisting of negative propositions.) sub-dimension is calculated by adding them directly. It is recommended that the evaluation of the scale be made based on the total score. There is no cut-off point in the scale. An increase in the score obtained from the scale indicates an increase in vaccine hesitancy. The Cronbach's alpha values obtained for the sub-dimensions and the entire scale are 0.892 for lack of confidence, risks and the entire scale, respectively; 0.632 and 0.874 were obtained. In the reliability analysis of the scale, which was conducted according to the test-retest method, the correlation coefficient between the first and last measurement was found to be 0.879.

The study was discussed at the Local Ethics Committee Meeting dated 24.10.2023 and was approved by the local ethics committee (Decision no: 2023/504). All data were evaluated with the SPSS (Statistical Package for Social Sciences) for Windows 21.0 statistical package program. Before the analyses, the suitability of the variables to normal distribution was examined using Q-Q plot and Kolmogorov-Smirnov/shapiro-Wilk tests.

Descriptive statistics were given as frequency, percentages, mean and standard deviation. For variables that meet parametric test assumptions, t-test is used to compare scales between two groups, One Way Anova test is used to compare more than two groups, Mann-Whitney U test is used to compare scales between two groups for variables that do not meet parametric conditions, and Kruskal-U test is used to compare more than two groups. The results were evaluated at the 95% confidence interval.

RESULTS

Table 1 presents the sociodemographic characteristics of the participants. The research found that 152 out of 250 mothers with children aged 0-5 who participated in the study were between the ages of 25-35, accounting for 60.8%. Additionally, 59 mothers (23.6%) were primary school graduates, 60 (24%) were high school graduates, and 120 (48%) were university graduates. The study found that 35.2% (n=88) of the participants were civil servants, while 30.8% (n=77) were housewifes. Additionally, 78.4% (n=196) of the participants belonged to nuclear families. The study also revealed that 67.2% (n=168) of the participants had an income between 11,402-38000 TL. Furthermore, 55.6% (n=139) of the participants were mothers or fathers, while 34% (n=85) were mothers or grandmothers who took care of their children.

Table 2 compares the responses given by mothers to the Vaccine Hesitancy Scale. Childhood vaccines are effective for my child's health. Of the 250 mothers with children aged 0-5 who participated in the study, 70% of them strongly agree to the question "Childhood vaccines are important for my child's health." 64% strongly agree to the question "Childhood vaccines are effective." 57.6% of them responded that getting my child vaccinated is important for the health of others in my society. 50.8% of the mothers said that all childhood vaccines provided to our society by the state are beneficial. 33.6% said that they are undecided because new vaccines carry more risks than old vaccines. 35.6% strongly agree to the question "Is the information I receive about vaccines from the vaccination program reliable?" 44.8% of the mothers responded that getting vaccinated is a good way to protect my children from diseases. 38.8% of

Table 1. Sociodemographic characteristics of participants

Variables *	Findings (n=250)	
Mothers Age		
<25	31	(12.4)
25-35	152	(60.8)
>35	67	(26.8)
Educational status of the mother		
Illiterate	11	(4.4)
Primary Education	59	(23.6)
High School	60	(24)
University	120	(48)
Mothers profession		
Officer	88	(35.2)
Employee	41	(16.4)
Housewife	77	(30.8)
Small Business	16	(6.4)
Other	28	(11.2)
Family type		
Extended Family	196	(78.4)
Nuclear Family	48	(19.2)
Divorced Family	6	(2.4)
Mothers income level		
Under 11.402 TL	6	(2.4)
11.402TL-38000 TL	168	(67.2)
Over >38000 TL	76	(30.4)
Person taking care of the child		
Mother or Father	139	(55.6)
Grandmother or grandfather	85	(34)
Caregiver	18	(7.2)
Other	8	(3.2)

*Data were shown as n (%).

Table 2. Mothers' Responses to the Vaccine Hesitancy Scale (n=250)

Mothers' Responses *	I Totally Disagree	I Disagree	I'm Undecided	I Agree	I Totally Agree
Childhood vaccinations are important for my child's health	6 (2.4)	5 (2.0)	25 (10.0)	39 (15.6)	175 (70.0)
Childhood vaccines are effective	5 (2.0)	7 (2.8)	21 (8.4)	57 (22.8)	160 (64.0)
Getting my child vaccinated is important for the health of others in my community	7 (2.8)	5 (2.0)	37 (14.8)	57 (22.8)	144 (57.6)
All childhood vaccines provided to our society by the government are beneficial	8 (3.2)	13 (5.2)	41 (16.4)	61 (24.4)	127 (50.8)
New vaccines carry more risks than old ones	39 (15.6)	46 (18.4)	84 (33.6)	39 (15.6)	42 (16.8)
The information I receive about vaccines from the vaccination program is reliable	8 (3.2)	21 (8.4)	51 (20.4)	81 (32.4)	89 (35.6)
Getting vaccinated is a good way to protect my children from diseases.	4 (1.6)	15 (6.0)	43 (17.2)	76 (30.4)	112 (44.8)
I usually do whatever my doctor or healthcare professional (midwife, nurse, etc.) recommends about vaccinations for my children.	13 (5.2)	17 (6.8)	46 (18.4)	77 (30.8)	97 (38.8)
I am concerned about serious side effects of vaccines	32 (12.8)	58 (23.2)	73 (29.2)	32 (12.8)	55 (22.0)

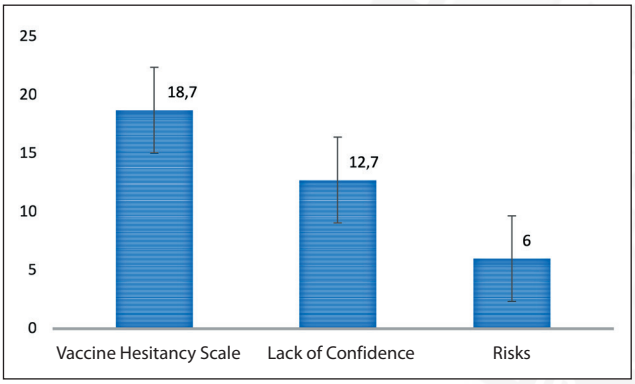


Figure 1: Vaccine Hesitancy Scale

*The scale two sub-dimensions lack of confidence and risks. The mean scores of the subscales were found to be lack of confidence=12.7±4.7 and 6.0±2. The median value of lack of confidence is 12.0 and risks is 6.0.

them strongly agreed that I usually do whatever my doctor or auxiliary health personnel (midwife, nurse, etc.) recommend about vaccines for my children. 73% of them stated that they were worried about the serious side effects of vaccines.

Table 3 compares The Vaccine Hesitancy Scale scores based on participants' sociodemographic characteristics. The results show that as the mother's educational level decreases, The Vaccine Hesitancy Scale score increases significantly (p=0.012). Mothers with primary education had higher Vaccine Hesitancy scores than those with university education. Additionally, a significant relationship was found between mothers' occupation and vaccine hesitancy score (p=0.001). The study found that mothers who were housewifes had a higher vaccine hesitancy score compared to mothers who were civil servants. Additionally, the study found a significant relationship between mothers' income level and vaccine hesitancy score (p=0.001). Specifically, those with an income level of 11.402-38.000 TL had a higher vaccine hesitancy score than those with an income level greater than 38.000 TL (p<0.001). No significant difference was found between the person caring for the child, the mother's age, family type, and vaccine hesitancy score (p>0.05).

Figure 1, the average The Vaccine Hesitancy Scale score of the participants was evaluated as 18.7±5.3. The mean scores of the subscales were found to be lack of confidence = 12.7±4.7 and risks = 6.0±2. The median value of lack of confidence is 12.0 and risks is 6.0. The minimum and maximum value of Lack of Confidence is between 7-35. The risks were in the range of 2-10. The first quarter of the lack of confidence was 10 and the third quarter was 17. The first quarter of the risks was 5 and the third quarter was 7.

DISCUSSION

Childhood vaccines are crucial in preventing infectious diseases in children. Studies have shown that families often lack sufficient knowledge about childhood vaccines (11), which can lead to delayed or incomplete immunisations (5). This puts children at risk of contracting infectious diseases. Families should be informed about the screening programme and vaccines and should be followed up by relevant healthcare institutions.

Table 3. Vaccine hesitancy scale scores according to sociodemographic characteristics of mothers

Variables	Findings (n=250)	p**
Mothers age (year±SD)		
<25 years	22.29±6.07	
25-35 years	18.51±5.48	0.231
>35 years	18.73±4.51	
Educational status of the mother		
Illiterate	21.45±8.45	
Primary education[a]	20.23±5.63	**0.012**
High School	18.75±5.24	**0.024**[ab]
University[b]	17.85±4.66	
Mothers profession		
Officer [a]	17.34±4.38	
Employee	19.70±3.16	
Housewife [b]	20.51±7.09	**0.001**
Small Business	17.18±3.72	**0.001**[ab]
Other	18.17±4.11	
Family type		
Extended Family	18.68±5.46	
Nuclear Family	19.29±5.02	0.760
Divorced Family	18.33±2.80	
Mother's income level*		
11.402 TL Under	21.33±3.72	
11.402 TL-38000 TL[a]	19.71±5.56	**0.001**
Over >38000 TL[b]	16.55±4.11	**<0.001**[ab]
Person taking care of the child		
Mother or Father	19.38±5.72	0.261
Grandmother or grandfather	17.98±4.97	
Caregiver	18.61±3.75	
Other	17.50±4.00	

* The lower limit and upper limit were determined based on the Turkish Statistical Institute's 2023 minimum wage and average poverty line. **SD:** Standart Deviation, **X:** Mean
**One-way ANOVA, *Post hoc* analysis

In our study, it was observed that vaccine hesitancy increased as the education rate of mothers decreased. There are many studies in the literature similar to our results (5,6,12). In a study conducted by Onsomu et al. in Kenya, it was found that the rate of vaccination increased as the level of education increased in the relationship between the level of education of mothers and completion of vaccination of children.5 In a study conducted by Gust et al. in the United States of America in 2001, a positive correlation was found between the increase in the education level of mothers and the completion of immunisations.6 In a study conducted by Hadjipanayis et al. in 18 European countries evaluating the vaccination safety of families, it was found that mothers and fathers with high school graduates and less than high school graduates had higher vaccination instability compared to families with university graduates (12). In contrast to our study, in the study conducted by Gentile et al. on 600 participants in Argentina in 2019, the relationship between vaccine hesitancy and educational status was evaluated significantly. It was concluded that parents with higher education levels had higher vaccine hesitancy (13). It was found that increasing the education level of mothers decreased their ambivalence towards vaccines. Wei et al. found that individuals with low income had a low vaccination rate. However, a study conducted in the United States of America found a correlation between vaccine acceptance and income level, indicating that those with higher incomes may have more difficulty accepting vaccines and may delay vaccination (14,15).

A study conducted in 16 countries, including Turkey, reported that individuals who opposed vaccination were more prevalent in countries with higher income (16). Our study found that ambivalence towards vaccines increased as income level decreased. As with other studies, we observed that difficulties in accessing vaccines may arise, in addition to ambivalence towards vaccines. Increasing income levels can facilitate access to vaccines and decrease ambivalence towards vaccines in direct proportion (17-19).

There may be an inverse relationship between socioeconomic status and vaccine hesitancy, as observed in a study of 614 volunteers in Turkey (17). Difficulties in accessing vaccines, particularly in low- and middle-income countries, have been identified in a publication evaluating 19 studies. This has led to decreased acceptance of vaccination, with some individuals having to wait years to be vaccinated (18). A study evaluating concerns about vaccination in low- or middle-income countries reported concerns about the costs of immunisation services provided by vaccination (19).

According to the results of our study, the Vaccine Hesitancy Scale score was 18,7±5,3. In the study prepared by Aygün and Tortop the mean score of the scale calculated by using all 10 items in the original scale was 2.10±0.36 (20). Due to the limited number of studies conducted with the Vaccine Hesitancy Scale in Turkey, different adaptations, and different number of questions, comparing the mean scores may not show meaningful results. In the study conducted by Çebi and Mandıracıoğlu, The Vaccine Hesitancy Scale was employed to assess vaccine hesitancy among students of vocational schools of health. The resulting vaccine hesitancy score was 32.29 ± 5.1 (21). The findings of the study indicate that students exhibit vaccine hesitancy. In the study conducted with the participation of university students in Mersin, the vaccine hesitancy scores were found to be 21.10 ± 5.3 (22). The results of the study indicated that

the vaccine hesitancy scale scores were lower than those observed in previous studies. The lower scores observed in our study can be attributed to several factors. Firstly, the medical faculty hospital in question is located in the city centre, which may have influenced the results. Secondly, the study was conducted in a single centre, which may have introduced a degree of bias. Thirdly, families may have social, cultural and personal differences, which could have affected the results.

In a similar study, 4.2% of the participants he answered the question "vaccinations are important for his health" by saying "I strongly disagree." In our study, it was 4.4%. It is seen that 5% of the participants stated that getting vaccinated is not important for the health of other people in the society. It is seen that it is 4.8% in our study. It was understood that 18.1% of the participants thought that all vaccines in the vaccination program offered to the society by the state were beneficial. It was determined that 75.2 in our study. 25.8% of the students stated that the new vaccines were more risky than the old vaccines. It was evaluated as 34.2 in our study. 38.1% of the participants reported that they found the information they received about vaccines credible and reliable. This rate was evaluated as 68% in our study. It was determined that 63.4% of the participants saw getting vaccinated as a good way to protect themselves from disease. It was evaluated as 75.2 in our study. 65.7% of the participants reported that they generally followed the recommendations of their doctor or health institution about vaccines. It was 69.6 in our study. It was understood that 31.2% of the students thought that vaccines had serious side effects. It was observed that it was 34.8 in our study (23).

The small number of studies conducted in Turkey made it difficult to compare the scale score. Furthermore, it should be noted that one of the limitations of the study is that the data is based on personal declarations. The routine vaccination schedule of the Ministry of Health was not included. Therefore, no information was provided about non-routine vaccination. Since the mothers' ages were asked in categories, the mean or median was not determined.

This study evaluates the factors that contribute to mothers' hesitancy towards childhood vaccines and their willingness to receive non-routine childhood vaccines. The importance of full childhood vaccinations in protecting children against infectious diseases is well-established. The study findings indicate that vaccine hesitancy increases as the education level of mothers decreases. Increasing the education level of mothers can reduce vaccine hesitancy and increase vaccination rates in society. However, vaccine hesitancy is more common among housewifes than civil servants. Additionally, a mother's income level can also be a factor in vaccine hesitancy. As income levels decrease, mothers become more hesitant towards vaccines. However, increasing their income and creating employment opportunities for housewifes can reduce this hesitancy and increase demand for vaccines. Access to vaccines has also improved in recent years, leading to higher vaccination rates in society. It is important to investigate the reasons for mothers' hesitancy and offer solutions to improve herd immunity. Solution suggestions in the form of advertisements and banners can be created to raise awareness among families about non-routine vaccinations. Solution suggestions in the form of advertisements and banners can be created to raise awareness among families about non-routine vaccinations. Contacting families and providing them with information can also be helpful. This will increase the vaccination rate and ensure community immunity against infectious diseases.

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None.

Author Contributions

Concept: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz,** Design: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz,** Data Collection or Processing: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz,** Analysis or Interpretation: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz,** Literature search: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz,** Writing: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz,** Approval: **Bahar Ürün Ünal, Ali Aran, Alaaddin Yorulmaz.**

Conflicts of Interest

The authors declare that there is no conflict of interest.

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Ethical Approval

The study has been approved by Selçuk University Ethics Committee (approval number: 2023/504).

Review Process

Extremely and externally peer-reviewed and accepted.

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ÖZGÜN ARAŞTIRMA

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Tiroid Hormonlarının Prematüre Bebeğin Postnatal Büyümesine Etkisi

The Effect of Thyroid Hormones on the Postnatal Growth of the Premature Infant

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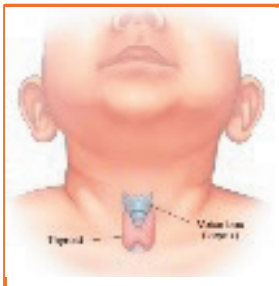
GRAFİKSEL ÖZET

Prematüre bebeklerin büyümesi konjenital hipotiroidi olup olmamasına bakılmaksızın mutlaka ilk tiroid stimülan hormon ve serbest tiroksin düzeyleri ile değerlendirilmelidir.



- Prematüre bebeklerde konjenital hipotiroidinin büyümeye olan etkisi tam olarak bilinmemektedir.

- Çalışmamızda çok düşük doğum ağırlıklı prematüreler retrospektif olarak değerlendirildi.
- Tiroid stimülan hormon düzeyi ve konjenital hipotiroidi durumuna göre hastaların özellikleri karşılaştırıldı.

- Prematüre bebeğin büyümesi konjenital hipotiroidi ile ilişkili değildi.
- Ancak yüksek tiroid stimülan hormon düzeyi olan hastaların kilo alımları ve baş çevresi büyümesinin daha geride olduğu bulundu.

Batı Karadeniz Tıp Dergisi | Ufuk Çakır, Cüneyt Tayman | Çakır U, Tayman C. Tiroid hormonlarının... Med J West Black Sea. 2025;9(1).

ÖZ

Amaç: Hipotiroidi büyüme üzerine olumsuz etkilidir. Ancak prematüre bebeklerde konjenital hipotiroidinin (KH) büyümeye olan etkisi tam olarak bilinmemektedir. Çalışmamızın amacı çok düşük doğum ağırlıklı (ÇDDA: ≤1500g) prematüre bebeklerde KH'nin büyümeye olan etkisinin değerlendirilmesidir.

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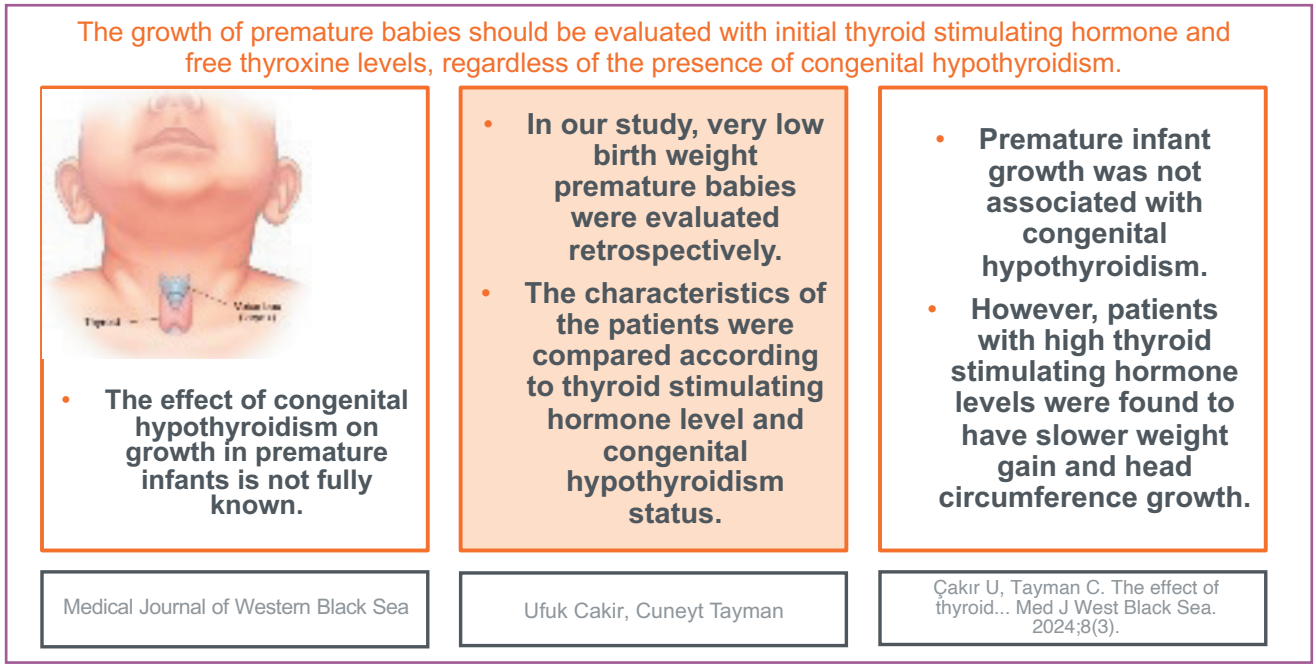
Gereç ve Yöntemler: Çalışmamıza ÇDDA olan prematüre bebekler retrospektif olarak dahil edildi. Hastalar tiroid fonksiyon testlerine göre KH olan ve olmayan olarak iki gruba ayrıldı. Konjenital hipotiroidi olan ve olmayan gruplar kilo alımı, baş çevresi, demografik ve klinik özellikleri açısından karşılaştırıldı. Serum tiroid stimülan hormon (TSH) düzeyi <6, 6-20 ve >20 uIU/L göre hastaların özellikleri karşılaştırıldı.

Bulgular: Konjenital hipotiroidi olan 46 hasta, KH olmayan 307 hasta olup çalışmaya toplam 353 hasta dahil edildi. Kilo alımı ve baş çevresindeki büyüme açısından KH olan (sırasıyla, 115,5±33,9 g/hafta ve 0,60±0,19 cm/hafta) ve olmayan gruplar (sırasıyla, 119,4±34,8 g/hafta ve 0,60±0,19 cm/hafta) arasında istatistiksel fark tespit edilmedi (sırasıyla, p=0,467, p=0,276). Serum TSH düzeyi >20 uIU/L olan hastalarda kilo alımının (108,3±24,9 g/hafta) TSH düzeyi <6 ve 6-20 uIU/L olan hastalara göre (sırasıyla, 121,2±34 g/hafta ve 117,9±37,4 g/hafta) anlamlı olarak düşük olduğu bulundu (p=0,040). Serum TSH düzeyi 6-20 ve >20 uIU/L olan hastalarda baş çevresi büyümesi (sırasıyla, 0,60±0,19 cm/hafta ve 0,60±0,20 cm/hafta) TSH düzeyi <6 uIU/L olan hastalara (0,65±0,19 cm/hafta) göre anlamlı olarak düşük bulundu (p=0,034).

Sonuç: Çalışmamızda KH ile prematüre bebeğin büyümesi ilişkili bulunmadı. Ancak yüksek TSH düzeyi olan hastaların kilo alımları ve baş çevresi büyümesinin daha geride olduğu bulundu.

Anahtar Sözcükler: Büyüme, baş, tiroid bezi, yenidoğan

GRAPHICAL ABSTRACT



ABSTRACT

Aim: Hypothyroidism effects negatively on growth. But the effect of congenital hypothyroidism (CH) on preterm newborns are still not known. In this study, we aimed to evaluate the effect of congenital hypothyroidism on very low birth weight (VLBW: ≤1500 g) preterm newborn.

Material and Methods: We retrospectively analyzed the data of VLBW preterm newborns. The patients were divided into two groups, with and without CH, according to thyroid function tests. We compared the demographic features, clinical data, weight gain and head circumference of preterm newborns who were classified into 2 groups: ones with CH and without CH. Characteristics of the patients were compared according to thyroid stimulating hormone (TSH) levels <6, 6-20 and >20 uIU/L.

Results: A total of 353 preterm newborns were enrolled into the study 46 in CH and 307 in control group. No statistically significant difference was found between with CH (115.5±33.9 g/week and 0.60±0.19 cm/week, respectively) and without CH groups (119.4±34.8 g/week and 0.60±0.19 cm/week, respectively) in weight gain and head circumference change (p=0.467, p=0.276, respectively). We found that, weight gain in preterms who had TSH >20 uIU/L (108.3±24.9 g/week), were lower than preterms who had TSH <6 and 6-20 uIU/L (121.2±34 g/week and 117.9±37.4 g/week, respectively) (p=0.040). Head circumference change was lower in preterm who had TSH 6-20 and >20 uIU/L (0.60±0.19 cm/week and 0.60±0.20 cm/week, respectively) than preterms who had TSH <6 uIU/L (0.65±0.19 cm/week) (p=0.034).

Conclusion: Our study did not show any relationship between growth of preterm newborns and CH. But preterm newborns who had higher TSH levels were shown to have lesser weight gain and head circumference change.

Keywords: Growth, head, newborn, thyroid gland

GİRİŞ

Konjenital hipotiroidi (KH) yaklaşık 2000-4000 yenidoğandan bebekten birini etkilemektedir (1,2). Prematüre bebeklerde ise KH sıklığı daha yüksektir (3). Tiroid hormonlarının hemen her organ sistemi üzerinde önemli etkileri vardır. Normal büyüme ve nörolojik gelişim üzerine de tiroid hormonları önemli rol oynamaktadır. Erken ve etkili bir şekilde tespit edilip tedavi edilmeyen KH'nin nörobilişsel gelişim üzerinde olumsuz etkileri olabilir. Yenidoğan döneminde KH'yi tanımlamak ve tedavi etmek için KH patofizyolojisinin anlaşılması gereklidir. Ayrıca, KH teşhisi ve tedavisi, özellikle yüksek riskli olan prematüre bebeklerde iyi klinik sonuçların sağlanması için kritik öneme sahiptir (2).

Konjenital hipotiroidi olan yenidoğanların çoğu doğumda normaldir, hiçbir belirti ve semptom göstermez. Ancak bu hastaların takibinde yapılan çalışmalarda, tanıda ve tedavide gecikmenin veya hiç tedavi edilmemesi durumunda, ciddi nörolojik bozuklukların yanı sıra, fiziksel gelişimde de olumsuz sonuçlara yol açtığı gösterilmiştir (1).

Prematüreler üzerinde yapılan bazı çalışmalarda, KH ile prematüre osteopenisi, intraventriküler kanama (İVK), respiratuvar distres sendromu, prematüre retinopatisi, mortalite ilişkisi değerlendirilmiştir ve KH ile bu morbiditeler arasında bir ilişki bulunmamıştır (4-11). Tiroid hormonları, insülin, büyüme hormonu, glukokortikoidler, insülin benzeri büyüme faktörü-1, diğer hormonlarla birlikte vücut protein metabolizmasını düzenler, dolayısıyla büyüme ve gelişme ile ilgili süreçlerle yakından bağlantılıdırlar (12).

Konjenital hipotiroidili yenidoğanların büyümesi hakkında tartışmalı sonuçlar vardır. Erken tedavinin, ilk levotiroksin dozunun, tiroid hormon düzeylerinin normal büyümeye etkisi konusunda da yine belirsizlikler vardır (1,13,14). Özellikle prematüre bebeklerde KH ve tiroid hormonlarının büyüme üzerine etkisi konusunda çalışmalar yetersizdir.

Tiroid hormonları büyüme için son derece önemli olmasına rağmen prematüre bebeğin postnatal büyüme parametreleri ile KH ilişkisi belirsizdir. Dolayısıyla çalışmamızın hipotezine göre prematüre bebek postnatal büyüme sürecinde tiroid hormon düzeylerinden etkilenebilir. Bu yüzden çalışmamızda prematüre bebeğin postnatal büyümesine KH ve tiroid hormonlarının etkisinin değerlendirilmesi amaçlanmıştır.

GEREÇ ve YÖNTEMLER

Hastaların Seçimi ve Etik Onam

Çalışmamıza Haziran 2021 – Kasım 2021 tarihleri arasında yenidoğan yoğun bakım ünitemizde (YYBÜ) yatan çok düşük doğum ağırlıklı (ÇDDA: ≤1500 g) prematüre bebekler dahil edildi. Çalışmaya başlamadan önce Ankara Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu'na başvuruldu ve etik onam alındıktan sonra (tarih: 05/12/2017, karar no: 148/2017) çalışma yürütüldü. Çalışmaya alınan hastaların veri kayıtları retrospektif olarak gerçekleştirildi. Çalışma Helsinki Deklarasyonu prensiplerine uygun olarak yapıldı.

Çalışma Protokolü

Türk Neonatoloji Derneği kılavuzlarına uygun olarak YYBÜ'ye yatan tüm prematüre bebeklerde tiroid stimülan hormon (TSH) ve serbest tiroksin (sT4) düzeyleri postnatal 7. günde bakıldı (3). Eğer hastada 7 gün içinde eksitus gelişirse, TSH ve sT4 düzeyleri belirlenemediği için çalışmaya alınmadı. Ek olarak, doğum ağırlığı >1500 g olan, majör konjenital anomalisi, ciddi İVK (≥3 evre) ve hidrosefalisi olan bebekler çalışmaya alınmadı.

Serum TSH düzeyi >20 uIU/L olan hastalar KH kabul edilip tedavi başlandı. Serum TSH düzeyi 6-20 uIU/L arasında ise ve sT4 düzeyi 0,62-1,18 ng/dL arasında ise 1 hafta sonra TSH ve sT4 kontrolü yapıldı. Kontrolde TSH 6-20 uIU/L ise KH kabul edilip tedavi başlandı. İlk bakılan serum TSH düzeyi 6-20 uIU/L arasında ve sT4 <0,62 ng/dL ise KH için tedavi başlandı. Serum TSH düzeyi <6 uIU/L ve sT4 düzeyi 0,62-1,18 ng/dL arasında olması durumunda normal tiroid fonksiyonları olarak kabul edildi (3).

Konjenital hipotiroidizm tespit edilen hastalara levotiroksin 8-12 mcg/kg/gün dozunda başlandı. Uygun levotiroksin dozunu belirlemek için tedavi sonrası normal TSH ve sT4 düzeyini sürdürecek şekilde düzenli aralıklarla (2-4 kez/ayda) serum TSH ve sT4 bakıldı. Konjenital hipotiroidizm tespit edilen hastalar tiroid bezi agenezisi açısından tiroid ultrasonografisi ile değerlendirildi (3). Çalışmaya dahil edilen hastalar KH olup tedavi başlanan ve KH olmayan olarak iki gruba ayrıldı. Ayrıca TSH düzeyi <6 uIU/L, 6-20 uIU/L ve >20 uIU/L olan hastalar üç ayrı grup olarak karşılaştırıldı.

Tiroid Fonksiyon Testlerinin Değerlendirilmesi

Postnatal 7. günde venöz kandan elde edilen serum örneklerinden sT4 ve TSH düzeyleri elektrokemilüminesans immünoassay yöntemini kullanan Roche e601 (Roche diagnostic GmbH, Mannheim, Germany) analizörü ile analiz edildi. Testlerin fonksiyonel duyarlılığı ise 0,014 µIU / mL ve tespit etme limiti 0,005 uIU / ml idi.

Beslenme ve Büyümenin İzlemi

Yenidoğan yoğun bakıma yatan tüm prematüre bebekler Türk Neonatoloji Derneği önerilerine uygun olarak enteral ve parenteral beslenmektedir (15,16). Yatışında normal şartlar altında gebelik haftasına göre 70-120 ml/kg/gün başlanan günlük toplam mayi miktarı yaklaşık 20 ml/kg/gün şeklinde artırılarak 180 ml/kg/gün mayi civarına ulaşılmaktadır. Prematüre bebek için günlük kalori hedefi 120-140 kkal/kg/gün ve protein hedefi ise 3,5-4,5 g/kg/gün olarak belirlendi. Tüm hastaların yatışından taburculuk gününe kadar günlük vücut ağırlığı takibi ve haftada en az 2 kez baş çevresi ölçümü yapıldı. Yani tüm hastaların kilo ve baş çevresi verileri yatışı

boyunca elde edildi. Elde edilen veriler g/hafta ve cm/hafta olarak değerlendirildi.

Demografik Özellikler ve Tiroid Fonksiyon Testleri

Tüm bebeklerin gebelik haftası (GH), doğum ağırlığı (DA), cinsiyet, antenatal steroid tedavisi, gebelik haftasına göre düşük doğum ağırlığı [small for gestational age (SGA); <10. persentil] (17), geç neonatal sepsis varlığı (>72 saat) (18), tam oral beslenmeye geçiş zamanı, yatış süresi, haftalık kilo alımı, haftalık baş çevresi büyümesi, sT4 ve TSH düzeyleri kayıt edildi. Konjenital hipotiroidi olan ve olmayanlar ile TSH düzeyi <6 uIU/L, 6-20 uIU/L ve >20 uIU/L olan hastalar demografik ve klinik özellikler açısından karşılaştırıldı.

İstatistiksel analiz

Verilerin istatistiksel analizinde SPSS (Statistical Package for the Social Sciences) 18.0 (versiyon 18, SPSS Inc., St. Louis, MO, USA) istatistiksel paket programı kullanıldı. Elde edilen verilerin normal dağılımını değerlendirmek için grafiksel olarak histogram ve Shapiro- wilk testi kullanıldı. Sürekli değişken olması durumunda t testi veya Mann- Whitney U testi kullanıldı. Nominal değişkenler için Pearson χ 2 testi uygulandı. Sonuçlar ortalama ± standart sapma olarak verildi. Kategorik değişkenlerdeki sonuçlar frekans ve yüzde dağılımı olarak ifade edildi. Normal dağılıma uyan ikiden fazla grubun karşılaştırılmasında ANOVA kullanıldı. ANOVA testi sonucu anlamlı çıkan değişkenlere ikili alt grup karşılaştırması için Post-Hoc test yapıldı. Çalışmamızda yapılan güç analizine (G-Power Version 3.1.9.6. Statistical power) göre %80 güçle ve %95 güven aralığında her grupta en az 34 hasta olması gerektiği belirlenmiştir. Yüksek TSH düzeyleri bağımsız risk faktörü olarak kilo alımı ve baş çevresi üzerine etkisinin değerlendirilmesi için logistik regresyon analizi ile değerlendirildi. Analiz sonucunda p <0,05 ise istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Çalışma döneminde toplam 663 hasta yatışı oldu. Doğum ağırlığı >1500 g olan 284 hasta çalışmadan dışlandı. Doğum ağırlığı ≤1500 g olan 379 hastadan yatış sonrası 7 gün içinde eksitus gelişen 17 hasta, majör konjenital anomalisi olan 4 hasta, ciddi İVK (≥3 evre) ve hidrosefalisi olan 5 hasta çalışmaya alınmadı. Çalışma döneminde dahil etme kriterlerine uygun toplam 353 hasta dahil edildi. İlk TSH düzeyi >20 uIU/L olan 38 hasta ve ilk TSH düzeyi 6-20 uIU/L olan 72 hastanın kontroldeki TSH düzeyi >6 uIU/L olan 8 hasta ile birlikte toplam 46 hasta KH tanısı aldı ve tedavi başlandı. İlk TSH düzeyi 6-20 uIU/L olan 72 hastanın 64 tanesinin kontrol TSH değeri <6 uIU/L olup geçici TSH yüksekliği %18,1 olarak (64/353) olarak bulundu. Konjenital hipotiroidi olan 46 hasta, KH olmayan 307 hasta olup, ÇDDA prematüre bebeklerde KH sıklığı %13 (46/353) olarak bulundu. Yapılan tiroid ultrasonografi sonucunda hiçbir hastada tiroid agenezisi tespit edilmedi. Konjenital hipotiroidi olan ve olmayan gruplar arasında demografik ve klinik özellikler açısından sonuçlar benzer bulundu (p>0,05). Konjenital hipotiroidi olan grupta yatış süresi olan 75,9±35,3 gün, KH olmayan grupta yatış süresi olan 69,7±24,6 gün kilo ve baş çevresi izlemi yapıldı. Birincil sonuç olarak, kilo alımı ve baş çevresinde büyüme açısından da KH olan ve olmayan gruplar arasında istatistiksel fark tespit edilmedi (sırasıyla, p=0,467, p=0,276). Konjenital hipotiroidi grubunda KH olmayan gruba göre sT4 düzeyi anlamlı olarak düşükken TSH düzeyi ise anlamlı olarak yüksek bulundu (sırasıyla, p<0,001, p<0,001) (Tablo 1).

İkincil sonuç olarak, tiroid hormon düzeylerine göre hastalar değerlendirildiğinde, serum TSH düzeyi >20 uIU/L olan hastalarda kilo alımının TSH düzeyi ≤20 uIU/L olan hastalara göre anlamlı olarak düşük olduğu bulundu (p=0,040). Serum TSH düzeyi ≥6 uIU/L olan hastalarda baş çevresi büyümesi TSH düzeyi <6 uIU/L olan hastalara göre anlamlı olarak düşük bulundu (p=0,034). TSH düzeyi <6 uIU/L, 6-20 uIU/L ve >20 uIU/L olan üç ayrı grubun diğer demografik ve klinik özellikler açısından sonuçları benzer bulundu (p>0,05). Serum TSH düzeyi >20 uIU/L olan grupta, TSH düzeyi ≤20 uIU/L olanlara oranla sT4 düzeyi anlamlı olarak düşük bulundu (p<0,001) (Tablo 2, Şekil 1). Lojistik regresyon analizi ile de yüksek TSH düzeyinin kilo alımı ve baş çevresi büyümesi ile ilişkili olduğu gösterildi (sırasıyla, OR 1,772, %95 CI 1,470-3,772, p<0,001 ve OR 1,977, %95 CI 1,613-3,819, p<0,001).

Tablo 1. Konjenital hipotiroidi durumuna göre demografik ve klinik özellikler

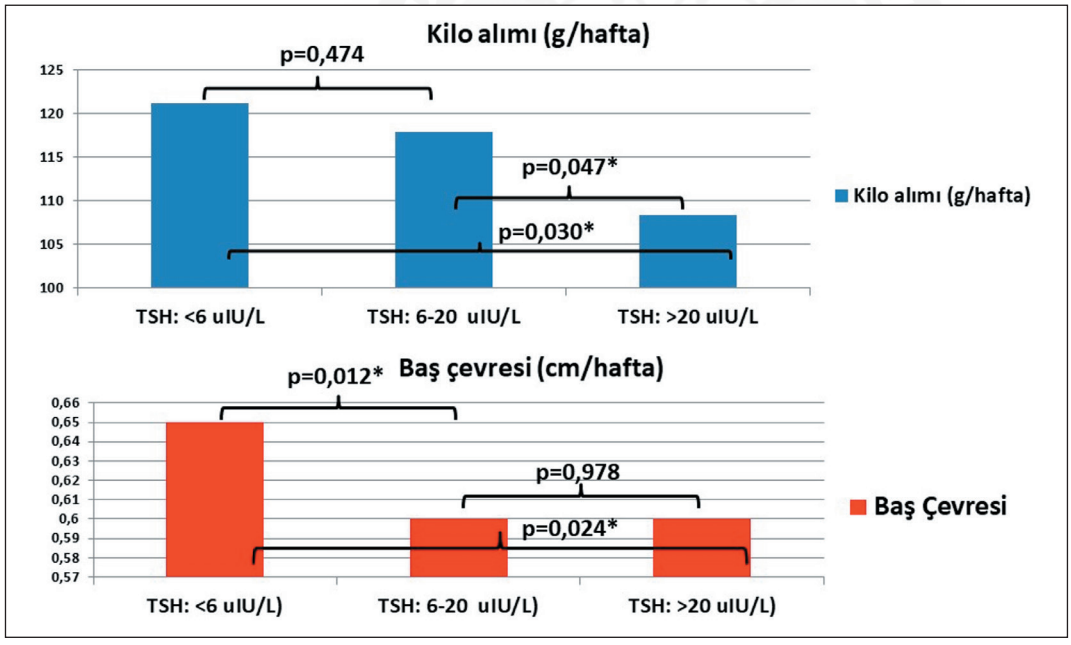
Değişkenler	Konjenital hipotiroidi olan (n=46)	Konjenital hipotiroidi olmayan (n=307)	*p**
Gebelik haftası, hafta [a]	29,5±1,1	29,7±1,2	0,188
Doğum ağırlığı, g [a]	1154±217	1182±222	0,416
Erkek cinsiyet, [b]	22 (47,8)	152 (49,5)	0,190
Antenatal steroid tedavisi, [b]	29 (63)	212 (69)	0,598
SGA, [b]	4 (6,6)	28 (9,1)	0,109
Sepsis, [b]	16 (34,7)	71 (23,1)	0,165
Kilo alımı, g/hafta [a]	115,5±33,9	119,4±34,8	0,467
Baş çevresi, cm/hafta [a]	0,60±0,19	0,64±0,19	0,276
Tam oral beslenmeye geçiş zamanı, gün [a]	17,6±7,1	16,3±7,0	0,239
Yatış süresi, gün [a]	75,9±35,3	69,7±24,6	0,070
sT4, ng/dl [a]	0,78±0,32	1,11±0,31	<0,001
TSH, uIU/L [a]	35,51±24,44	4,49±3,23	<0,001

***SGA:** gebelik haftasına göre düşük doğum ağırlığı, **sT4:** serbest tiroksin, **TSH:** tiroid stimülan hormon
[a] ortalama ± standart sapma, [b] n (%), *Student's t-test.

Tablo 2. Tiroid stimülan hormon sonuçlarına göre demografik ve klinik özellikler

Değişkenler	<6 uIU/L TSH (A) (n=220)	6-20 uIU/L TSH (B) (n=95)	>20 uIU/L TSH (C) (n=38)	*p**	*p*** A ve B	*p*** A ve C	*p*** B ve C
Gebelik haftası, hafta [a]	28,2±1,12	28,2±1,10	27,7±1,07	0,102	0,867	0,182	0,078
Doğum ağırlığı, g [a]	1093±219	1054±227	1055±220	0,279	0,157	0,327	0,981
Erkek cinsiyet, [b]	110 (50)	48 (50,5)	16 (42,1)	0,096	0,932	0,210	0,065
Antenatal steroid tedavisi, [b]	153 (69,5)	64 (67,3)	24 (63,1)	0,756	0,905	0,459	0,551
SGA, [b]	18 (8,1)	11 (11,6)	3 (7,8)	0,090	0,377	0,086	0,059
Sepsis, [b]	48 (21,8)	27 (28,4)	12 (31,5)	0,487	0,762	0,311	0,251
Kilo alımı, g/hafta [a]	121,2±34	117,9±37,4	*108,3±24,9*	***0,040***	0,474	***0,030***	***0,047***
Baş çevresi, cm/hafta [a]	0,65±0,19	0,60±0,19	0,60±0,20	***0,034***	***0,012***	***0,024***	0,978
Tam oral beslenmeye geçiş zamanı, gün [a]	16,5±5,7	17,6±29,5	18,4±7,4	0,173	0,095	0,080	0,759
Yatış süresi, gün [a]	68,9±22,5	70,6±29,5	73,6±36,1	0,190	0,103	0,066	0,644
sT4, ng/dl [a]	1,10±0,32	1,09±0,32	0,82±0,34	***<0,001***	0,950	***<0,001***	***<0,001***
TSH, uIU/L [a]	2,84±1,63	8,87±2,50	40,68±23,80	***<0,001***	***<0,001***	***<0,001***	***<0,001***

SGA: gebelik haftasına göre düşük doğum ağırlığı, **sT4:** serbest tiroksin, **TSH:** tiroid stimülan hormon
[a] ortalama ± standart sapma, [b] n (%). *ANOVA, **Post –Hoc



Şekil 1. Tiroid stimülan hormon sonuçlarına göre kilo alımı ve baş çevresi büyümesi
*p <0,05 istatistiksel olarak anlamli kabul edildi. **TSH:** tiroid stimülan hormon

TARTIŞMA

Prematüre bebeklerdeki KH'nin kilo alımı ve baş çevresi büyümesi üzerine etkisini değerlendirmek amacıyla gerçekleştirdiğimiz çalışmamızda KH olan hastalarda KH olmayanlara göre kilo alımı ve baş çevresi açısından fark tespit edilmemiştir. Serum TSH düzeyi >20 uIU/L olanlarda kilo alımının ve TSH düzeyi >6 uIU/L olanlarda ise baş çevresinde artışın daha düşük olduğu bulundu.

Tiroid hormonu, gebeliğin ilk üç aylık döneminden başlayarak ve yaşamın ilk birkaç yılı boyunca beyin gelişiminde kritik bir rol oynar. Bu dönemde hipotiroidizmin ciddi nörogelişimsel sonuçları olabilir (2). Nörogelişim dışında somatik büyüme içinde tiroid hormonları gereklidir. Tiroid hormonları osteoblastlar dışında diğer birçok dokudaki hücrelerde de DNA sentezi üzerindeki uyarıcı etkisi ile büyümeyi doğrudan etkiler (12). Dolayısıyla hızlı büyüme sürecinde olan

ve doğum sonrası YDYBÜ'de yatan prematüre bebeklerde KH'nin büyümeye etkisi değerlendirilmelidir. Çalışmamızda KH olan ve olmayan ÇDDA prematüre bebeklerin YDYBÜ'de geçirdikleri zaman boyunca benzer kalori ve protein hedeflerinde, benzer kilo alımı ve baş çevresi büyümesine sahip oldukları bulundu. Bazı çalışmalarda neonatal tarama ile saptanan KH hastalarının büyük çoğunluğunun normal büyüme gösterdiği bildirilse de, KH'nin erken saptanması ve tedavisi ile büyüme geriliğinin önlendiği bilinmektedir (19,20).

Eğer KH geç tanı alır ve geç tedavi edilirse hastaların büyüme ve gelişimi de geride kalmaktadır. Konjenital hipotiroidi tanısı ne kadar erken konulur ve tedavi edilirse hipotiroidiye bağlı gelişim geriliği önlenmiş olur. Grant tarafından 361 KH hastasının 4 yaşa kadar takibinin yapıldığı çalışmasında, erken tedavi başlananların büyümeyi yakalamasının daha iyi olduğu bulmuştur. Ayrıca, büyümeyi yakalamada erken tedavi yaşı dışında tedavi dozu ve hastalığın şiddetinin de etkili olduğunu bildirmiştir (19). Çalışma hastalarımızın sonuçlarına göre, KH tanısını alıp tedavisinin erken başlanması nedeniyle KH'nin büyümeyi olumsuz etkilemediği sonucuna varılabilir.

Bazı çalışmaların sonuçlarına göre, KH tedavisinin başlangıç yaşı ve ilk levotiroksin dozunun boy uzaması ve kilo alımı ile baş çevresinin ise yalnızca ilk levotiroksin dozu ile ilişkili olabileceği gösterilmiştir (1,21). Bir çalışmaya göre, yenidoğan taraması ile teşhis edilen ve yeterli miktarda günlük levotiroksin dozu ile hemen tedavi edilen KH hastaları normal olarak büyümektedir ve normal yetişkin boyuna ulaşmaktadır (22). Bu yönüyle sonuçlarımıza benzerlik göstermektedir. Ancak yüksek doz levotiroksin başlanmasının sadece yüksek TSH düzeyini daha erken dönemde düşürdüğü gösterilmiştir (14). Yüksek doz levotiroksinin 4 yaşta büyüme ve kemik gelişimine etkili olmadığı sadece zekâya olumlu etkili olduğunu gösteren verilerde mevcuttur (1,23). Çalışmamızda KH olan hastalara levotiroksin dozu standart 8-12 mcg/kg/gün aralığında başlanmıştır. Üst limit doz ve alt limit dozdan alan hastaların verilerine ulaşılamadığı için tedavi dozuna bağımlı büyüme değerlendirilememiştir. Dolayısıyla KH tanı yaşı, tedaviye başlama zamanı ve tedavi dozu ile kısa ve ileri dönem sonuçlar değerlendirilememiştir.

Çalışmamızın diğer ana sonucuna göre, TSH düzeyi >20 uIU/L olan hastalarda kilo alımının, TSH düzeyi >6 uIU/L olan hastalarda ise baş çevresindeki büyümenin daha az olduğu tespit edildi. Heidari ve ark. 760 KH incelediği çalışmasında, vücut ağırlığı ve baş çevresindeki büyümenin tanı anındaki serum TSH konsantrasyonundan etkilendiğini bulmuştur (1). Sonuçlarımıza benzer şekilde tanı anında daha yüksek olan TSH düzeylerine sahip bebeklerin kilo alımı ve baş çevresi büyümesinin olumsuz etkilendiği rapor edilmiştir. Ayrıca KH için tedavi başladıktan sonra serum TSH düzeylerinin normale gelme süresi ile büyümesi arasında bir ilişki tespit edilmediği de bildirilmiştir (1). Çalışmamızda KH hastalarının TSH düzeyi normalleşme zamanı verisi değerlendirilememiştir. Bain ve Toublanc'in gerçekleştirdiği çalışmada ise çocukluk yaş grubunda standart boydan daha kısa olan hastaların öyküsünde KH tanısının olduğu ve yenidoğan döneminde TSH normalleşme yaşının önemli ölçüde geciktiği rapor edilmiştir. Ayrıca yetişkinlikte daha uzun boyu etkileyen ana faktörlerin KH tedavisine başlama yaşı ve tedaviye uyum olduğunu belirtmişlerdir (24).

Çalışmamızın ve literatürdeki az sayıda çalışmanın sonuçlarına göre KH olan hastaların kısa dönemde somatik büyümesini etkileyen ana faktörlerin, tanı anında TSH düzeyi, tedaviye başlama yaşı ve tedavi dozu olduğu söylenebilir. Sonuçlarımızda olduğu gibi özellikle TSH düzeyleri >20 uIU/L olanlarda TSH düzeyleri ≤20 uIU/L olanlara oranla anlamı olarak sT4 düzeyleri daha düşüktür. Aslında ilk TSH yüksekliğini etkileyen en önemli parametre birincil olarak düşük sT4 düzeyleridir. Dolayısıyla yüksek TSH'nın büyümeye olumsuz etkisi olduğu kadar düşük sT4'ünde büyümeye olumsuz etkisi vardır. Yüksek TSH ve düşük sT4'e bağlı olarak KH tanısı konulan hastaların kısa dönemde büyüme etkilenmediği sonuçlarımıza göre söyleyebiliriz. Sonuç olarak, yüksek TSH ve düşük sT4 düzeyi sonucunda doğrusal büyüme ve DNA sentezi yetersiz olur. Bu yüzden KH tedavisine erken başlamak büyümeyi hatta ileriki dönemde nörogelişimi olumlu etkileyebilir (1,12,19). Bu yüzden KH tanılı hastalar ilk TSH düzeylerinin yüksekliklerine göre daha riskli olabileceği ve bu hastaların kısa dönemde kilo alımı ve baş çevresi etkilenebilir. Ayrıca bu hastalar uzun dönemde gelişimsel olarak risk altında olabilir. Hastaların kısa ve uzun vadede riskleri sadece KH olup olmamasına göre değerlendirilmemelidir. Ayrıca ilk TSH ve sT4 düzeyleri ve izlemdeki normalleşme süreçleri ile gelişimsel sonuçlar değerlendirilmelidir. Bu hipotezi desteklemek için daha geniş vaka serilerinin olduğu, tiroid hormonlarının daha sık ve uzun dönemde izlendiği, somatik büyümeye ek olarak nörogelişimin de değerlendirildiği çalışmaların yapılması gereklidir.

Çalışmamızda az sayıda KH vakasının değerlendirilmesi, retrospektif olması ve tek merkez verileri olmasından dolayı kısıtlılıklar vardır. Annede tiroid hastalığı, tiroid ilaç kullanımı, tiroid antikor düzeyi, postnatal serum TSH ve sT4 izlem sonuçlarımız mevcut değildi.

Sonuç olarak, KH tek başına büyümeyi etkileyip etkilemediği net değildir. Ancak serum TSH düzeyleri arttıkça büyümenin olumsuz etkilendiği söylenebilir. İleride yapılacak randomize prospektif çalışmalarda, büyümeyi etkileyen diğer faktörlerle birlikte tiroid hormonları ve KH'nin değerlendirilmesi daha değerli bilgiler verebilir.

Teşekkür

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Yazar Katkı Beyanı

Fikir ve Tasarım: **Ufuk Çakır,** Veri toplama veya işleme: **Ufuk Çakır,** Analiz veya Yorumlama: **Cüneyt Tayman,** Literatür taraması: **Ufuk Çakır,** Makalenin Yazılması: **Ufuk Çakır,** Onay: **Cüneyt Tayman.**

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Hakemlik Süreci

Kör hakemlik süreci sonrası yayınlanmaya uygun bulunmuştur.

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ORIGINAL ARTICLE

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Factors Affecting Internet Addiction and Health-Promoting Behaviors in Adolescents: A Cross-Sectional Study

Ergenlerde İnternet Bağımlılığı ve Sağlığı Geliştirici Davranışları Etkileyen Faktörler: Kesitsel Bir Çalışma

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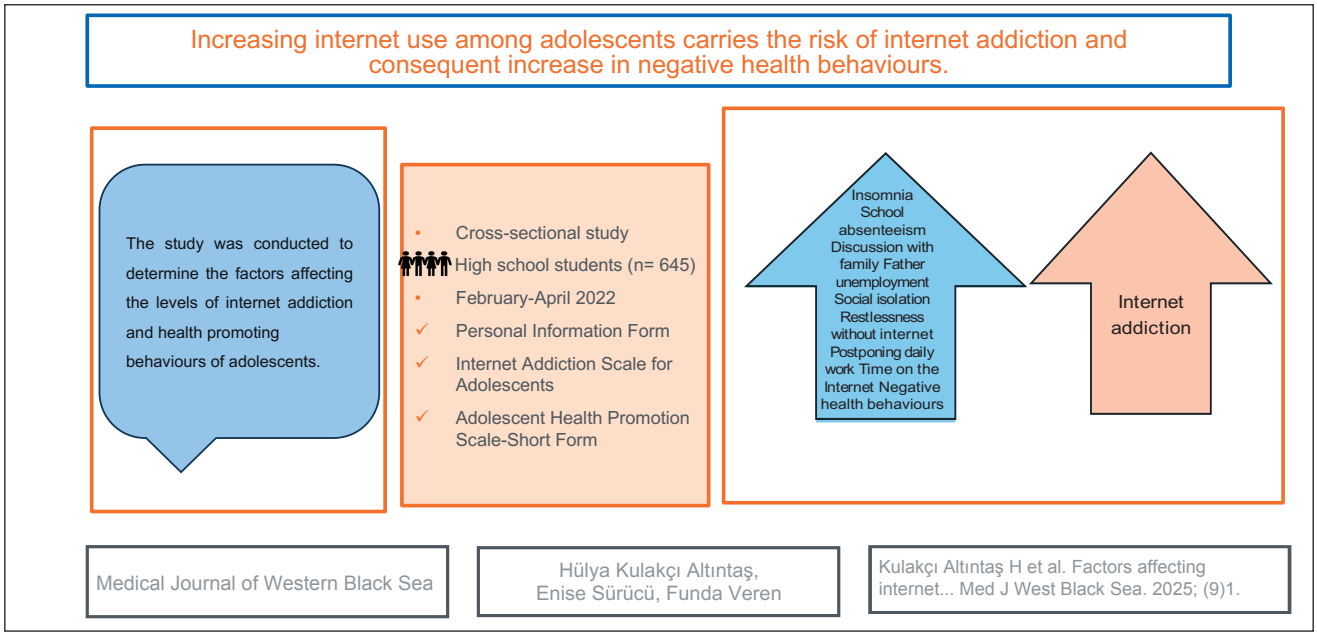
GRAPHICAL ABSTRACT



ABSTRACT

Aim: This study was designed to determine the internet addiction and health-promoting behavior levels of adolescents and evaluate the factors affecting these variables.

Material and Methods: A cross-sectional design was used in the study, which included students at a high school located in a city in Turkey (n= 645). Data were collected using a Personal Information Form, the Internet Addiction Scale for Adolescents, and the Adolescent Health Promotion Scale-Short Form.

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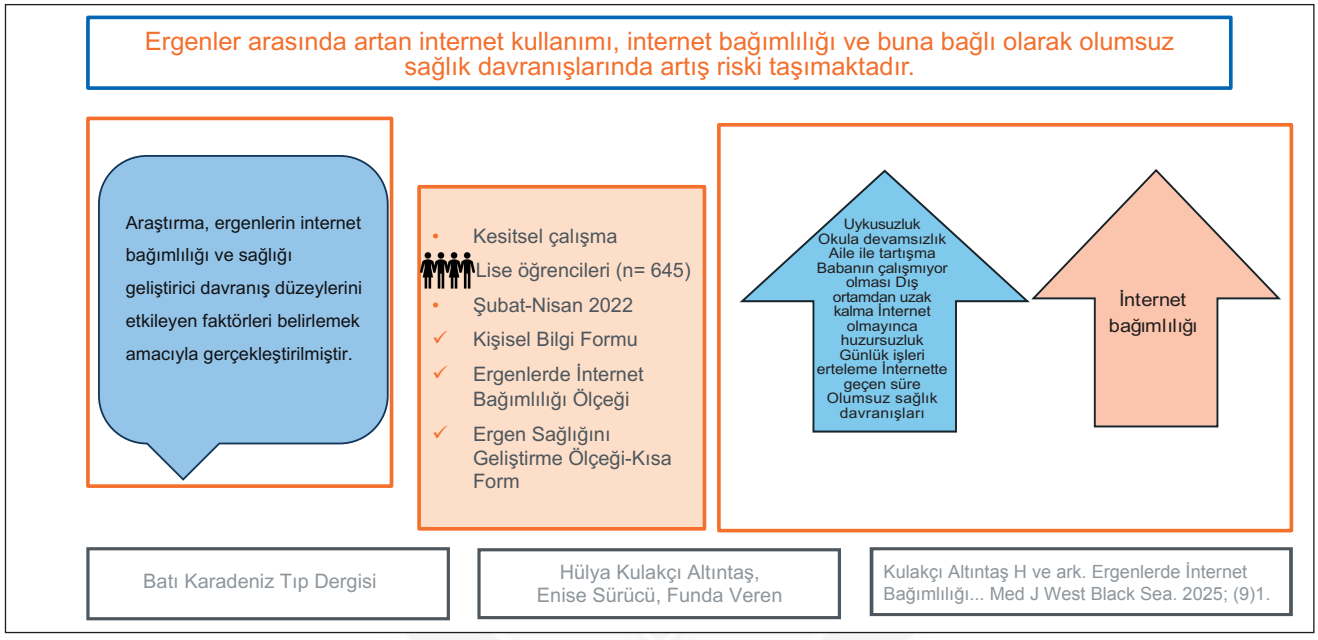
Results: The mean Internet Addiction Scale for Adolescents score of the participants was 20.98±6.75, while their mean Adolescent Health Promotion Scale-Short Form score was 69.76±13.34. It was found that experiencing insomnia due to time spent on the internet, being absent from school due to time spent on the internet, arguing with family members due to time spent on the internet, father not working, preferring to spend time on the internet instead of going out with others, feeling restless when not connected to the internet, postponing daily tasks while on the internet, daily time spent on the internet and non-health promoting behaviours significantly increased internet addiction levels.

Conclusion: It was found that as participants spent more time on the internet instead of the outdoor environment and their internet addiction levels increased, their health-promoting behaviours decreased. Increasing internet use among adolescents carries the risk of increasing internet addiction and decreasing health-promoting behaviours in the future.

Keywords: Adolescent, adolescent behavior, internet addiction, health promotion

GRAFİKSEL ÖZET



ÖZ

Amaç: Bu çalışma ergenlerin internet bağımlılığı ve sağlığı geliştirici davranış düzeylerini belirlemek ve bu değişkenleri etkileyen faktörleri değerlendirmek amacıyla planlanmıştır.

Gereç ve Yöntemler: Türkiye'nin bir ilinde bulunan bir lisedeki öğrencilerin (n= 645) dahil edildiği araştırmada kesitsel desen kullanılmıştır. Veriler Kişisel Bilgi Formu, Ergenlerde İnternet Bağımlılığı Ölçeği ve Ergen Sağlığını Geliştirme Ölçeği-Kısa Form kullanılarak toplanmıştır.

Bulgular: Katılımcıların Ergenlerde İnternet Bağımlılığı Ölçeği puan ortalaması 20.98±6.75, Ergen Sağlığını Geliştirme Ölçeği-Kısa Form puan ortalaması 69.76±13.34 olarak hesaplanmıştır. İnternette geçirilen zaman nedeniyle uykusuzluk yaşamanın, internette vakit geçirme nedeniyle okula devamsızlık yapmanın, internette geçirilen zaman nedeniyle aile üyeleriyle tartışmanın, babanın çalışmıyor olması, başkalarıyla dışarı çıkmak yerine internette vakit geçirmeyi tercih etmenin, internete bağlı olmadığında huzursuz hissetmenin, internetteyken günlük işleri ertelemenin, internette geçirilen günlük sürenin ve sağlığı geliştirici olmayan davranışların internet bağımlılık düzeylerini anlamlı olarak artırdığı bulunmuştur.

Sonuç: Katılımcılar dış ortam yerine internette daha fazla zaman geçirdikçe ve internet bağımlılık düzeyleri arttıkça, sağlığı geliştirici davranışlarının azaldığı tespit edilmiştir. Ergenler arasında internet kullanımının artması, ileride internet bağımlılığını artırma ve buna bağlı olarak sağlığı geliştirici davranışları azaltma riski taşımaktadır.

Anahtar Sözcükler: Ergen, ergen davranışı, internet bağımlılığı, sağlığı geliştirme

INTRODUCTION

Adolescence is the physically healthiest period of human life (1). However, adolescents are particularly vulnerable to the risk of internet addiction during this period. This vulnerability is often accompanied by acquiring bad habits by imitating adults, neglecting health-promoting behaviors, high social demands, and risky behaviors that play an important role in social acceptance (2).

Internet addiction is defined as excessive preoccupation with the internet, increased use of the internet for satisfaction, feeling aggression and tension when no internet access is available, and the negative effects of excessive internet use on work, social, and family life (3). In the literature, 5.1-80.2% of adolescents worldwide have been reported to have internet addiction (4, 5). This ratio ranges within 1.3-22.1% in Turkey, and this result reveals that almost one in every five adolescents are an internet addict (6, 7). In a relevant study, it was reported that nearly half of 348 problematic internet users, who demanded help for internet addiction in Hong Kong between 2012 and 2017, were12 to 17 years old (8). It was also determined that in the literature, internet addiction has been studied in the context of different variables including sleep (4), psychological factors (4), sociophobia (9), loneliness (10), attention deficit and hyperactivity disorder (11), and social coping (12).

Health-promoting behaviors constitute a concept including attitudes and habits that affect health (13). This concept also includes parameters such as nutrition, social support, undertaking health responsibilities, satisfaction with life, exercise, and stress management. Negative life behaviors such as unhealthy eating habits and inadequate physical activity, which began in high-income populations and have had a global impact so far, pose a long-term threat for adolescent health (1). On the other hand, the risk of adopting an unhealthy lifestyle is 2.29-fold more among adolescents with internet addiction (13). Studies investigating the relationship between internet addiction and health-promoting behaviors and evaluating the effects of internet addiction on health-promoting behaviors have focused on dimensions including nutrition (14), social support (15), physical activity (16), and quality of life (5). However, the creation of time- and cost-effective strategies with a high level of evidence against internet addiction is only possible with the identification of the factors with negative effects on all aspects of health- promoting behaviors. In this context, a limited number of studies was found in the relevant literature to evaluate internet addiction and health- promoting behaviors holistically (2, 17).

It is highly important to continuously update data on research regarding the internet use behaviors of adolescents against the rate of development and change in technology and identify health-promoting behaviors during this critical period when adolescents create their health capital. Since different factors may play a role in internet addiction and health-promoting behaviors under different socioeconomic conditions, at different places, and at different times, it has been suggested that preventive factors that pose a risk of internet addiction and unfavorable health-related behaviors among adolescents will be beneficial (18,19).

Therefore, this study was carried out to evaluate internet addiction, health-promoting behaviors, and affecting factors in adolescents.

MATERIALS and METHODS

Study Design and Participants

The population of this cross-sectional study included students of a high school located in a city center in Turkey (n= 645). The minimum required sample size was calculated as 574 participants based on a similar study in the literature (20) according to adolescent health promotion mean scores, with α=0.05, 1-β=0.90, and d= 0.135. The inclusion criteria were the agreement of the student to participate in the study and the consent of the parents of the student. The exclusion criteria were the presence of any psychiatric disorder and a visual or hearing impairment. All students of the aforementioned high school were invited to participate in the study. Among those, the parents of 45 students did not give consent for their participation. Thus, a total of 600 students were enrolled. Eleven students filled out data collection instruments incompletely or incorrectly. The study was completed with 589 students. The participation rate was 91.3%.

Procedures

This study was completed in accordance with the tenets of the Declaration on Helsinki. Ethical approval was obtained from the Human Research Ethics Committee of Zonguldak Bülent Ecevit University (09.11.2021/99622-335), and written permission was received from the Provincial Directorate of National Education (E-45865702-604.01.01-408326869/07.01.2022). Written informed consent was obtained from the families of the students. Verbal consent was received from the students.

Data were collected between 15 February and 22 April 2022. After the necessary permissions were obtained, the school administrators were met, and days and hours suitable for data collection were determined. Informed consent forms were sent to parents with the students in closed envelopes. The students were told to deliver the envelope to their teachers the next day. The students who were allowed to participate in the study by their parents were informed about the purpose of the study. Those who were willing to participate were given the data collection instruments, and

data collection was completed based on the self-reports of the participants under the supervision of the researchers. The application of the data collection instruments took approximately 20 minutes.

Measures

A personal information form, the Internet Addiction Scale for Adolescents, and the Adolescent Health Promotion Scale-Short Form were used to collect the data in this study (21, 22). Permission was granted from the developers of the Internet Addiction Scale for Adolescents and the Adolescent Health Promotion Scale-Short Form for their use.

Personal Information Form

This form was prepared by the researchers after their review of the relevant literature, and it included questions evaluating the demographic characteristics of the students and their internet and technological device use characteristics (2, 17).

Internet Addiction Scale for Adolescents

This scale was developed by Tas (2019) to identify internet addiction among adolescents. It consists of 9 items and a single factor. Scale items are assessed by a Likert-type grading method with the response options of "1=never, 2=rarely, 3=sometimes, 4=generally, and 5=always". The lowest and highest scores that can be obtained from the scale are 9 and 45. There is no inversely scored item in the scale. High scores show high levels of internet addiction. The Cronbach's alpha coefficient of the scale was reported as 0.81 (22). Cronbach alpha coefficient was calculated as 0.84 in this study.

Adolescent Health Promotion Scale-Short Form

The Adolescent Health Promotion Scale-Short Form was developed by Chen et al. in 2014 (23). This scale consists of 6 subscales and a total of 21 items. Its subscales are nutrition (items 1, 2, and 3), social support (items 4, 5, 6, and 7), health responsibility (items 8, 9, 10, and 11), life appreciation (items 12, 13, 14, and 15), exercise (items 16, 17, and 18), and stress management (items 19, 20, and 21). Each item is scored on a Likert-type scale with the response options of "1=never, 2=sometimes, 3=occasionally, 4=mostly, and 5=always". The score of any specific subscale is calculated by the sum of the scores of all items in that subscale, and the total scale score is calculated by the sum of all subscale scores. The lowest and highest scores that can be obtained from the scale are 21 and 105. Higher scores indicate more positive health-promoting behaviors. Among the reported internal consistency coefficients of the scale, McDonald's omega was 0.90, and Cronbach's alpha was 0.91 (23). The validity and reliability study of the Adolescent Health Promotion Scale-Short Form was carried out by Inci and Celik in 2021(21). The internal consistency coefficients of the Turkish version were 0.54-0.78 for McDonald's omega and 0.56-0.78 for Cronbach's alpha in terms of the subscales, and both McDonald's omega and Cronbach's alpha were reported to be 0.88 for the overall scale (21). In this study, Cronbach's alpha coefficients for the subscales were found to be between 0.51 and 0.77, and Cronbach's alpha for the overall scale was determined as 0.86.

Data Analysis

The sample size needed to conduct the study was calculated via the G*Power version 3.1.9.4 program. The data collected in the study were analyzed using the SPSS 25.0 (Statistical Package for the Social Sciences, Chicago, Illinois). Descriptive statistics including mean data, standard deviations and percentages were used to describe demographic data and the internet addiction and health-promoting behaviors scores. Multiple regression analysis was conducted to assess the influence predictors of internet addiction and health-promoting behaviors. To determine the factors affecting internet addiction and health-promoting behaviors, the independent variables found significant in the univariate analyses and were suitable for the model were included in the model simultaneously using the "enter" method, and the multiple regression analysis was applied. Class, age, grade point average, daily time spent on the internet, internet addiction, and health-promoting behaviors were continuous variables. Categorical data were coded as 0 or 1 for the multiple regression analysis. The analysis results were standardized by model summary R, R^2, adjusted R^2, and F, and they are presented as β and standard error values. Statistical significance was assessed based on the threshold of $p<0.05$.

RESULTS

The mean age of the participants was 15.84±1.22, with a range of 13-18, and 54.7% of the participants were female (Table 1). It was determined the participants spent a mean time of 3.94±1.96 hours per day (Min:0.50, Max:15) on the internet.

Internet addiction levels and predictive factors

The mean Internet Addiction Scale for Adolescents score of the participants was 20.98±6.75. As a result of the analysis, a significant regression model was found ($F(9,558)= 78.412$, $p <0.001$), and 55% of the total variance in the dependent variable was found to be explained by the independent variables ($adjR^2=0.551$). Accordingly, internet addiction was positively and significantly associated with experiencing insomnia due to time spent on the internet is positive and significant ($\beta=0.212$, $t(558)= 6.747$, $p<0.001$); being absent from school due to spending time on the internet is positive and significant ($\beta=0.093$, $t(558)= 3.173$, $p<0.01$); arguing with family members due to time spent

Table 1: Sociodemographic and descriptive characteristics of the participants.

Variables	Findings (n=589)	
Class (n=589)		
9th grade	138	(23.4)
10th grade	153	(26.0)
11th grade	143	(24.3)
12th grade	155	(26.3)
Age (year±SD, Min.- Max.)	15.8±1.2	(13-18)
Gender (n=587)		
Female	321	(54.7)
Male	266	(45.3)
Education level of the mother (n=586)		
Illiterate	5	(0.9)
Literate with no formal degree	123	(21.0)
Elementary school	105	(17.9)
Secondary school	213	(36.3)
High school	140	(23.9)
Employment status of the mother (n=580)		
Employed	205	(35.3)
Unemployed	375	(64.7)
Education level of the father (n=579)		
Illiterate	4	(0.7)
Literate with no formal degree	57	(9.8)
Elementary school	82	(14.2)
Secondary school	274	(47.3)
High school	162	(28.0)
Employment status of the father (n=574)		
Employed	523	(91.1)
Unemployed	51	(8.9)
Order of the child in the family (n=588)		
Oldest child	321	(54.6)
Middle child	127	(21.6)
Youngest child	140	(23.8)
Family type (n=589)		
Nuclear family (mother, father, and children)	496	(84.2)
Extended family (mother, father, children, and relatives)	60	(10.2)
Broken family (absence of mother or father)	33	(5.6)
Grade point average (Last semester) (Mean±SD, Min.- Max.)	84.2±7.7	50-100

Data were shown as n (%).
min-max=minimum-maximum values.

on the internet is positive and significant (β=0.265, t(558)= 8.865, p<0.001); father not working (β=0.059, t(558)= 2.087, p<0.05); preferring to spend time on the internet instead of going out with others is positive and significant (β=0.124, t(558)= 4.167, p<0.001); feeling uneasy when not connected to the internet positively and significantly (β=0.208, t(558)= 6.722, p<0.001); postponing daily tasks while on the internet was positively and significantly associated (β=0.178, t(558)= 6.059, p<0. 001); daily time spent on the internet positively and significantly (β=0.199, t(558)= 6.398, p<0.001), health-promoting behaviours level negatively and significantly (β=-0.083, t(558)= -2.762, p<0.01) (Table 2). The independent variables of mother's education level, father's education level, family type, father's internet use status, mother's internet use status and grade point average were excluded from the model since they did not show significant predictive power.

Health-promoting behaviors level and its predictive factors

The mean Adolescent Health Promotion Scale score of the participants was 69.76±13.34. Their mean scores on the subscales were found to be 9.55±2.21 for nutrition, 14.24±3.48 for social support, 13.07±3.80 for health responsibility, 14.52±3.56 for life appreciation, 8.68±3.36 for exercise, and 9.70±2.83 for stress management. As a result of the analysis, a significant regression model was found (F (4,576)= 22.310, p<0.001), and 13% of the variance in the dependent variable was found to be explained by the independent variables (adjR^2=0.128). Accordingly, having a computer of one's own positively and significantly (β=0.089, t(576)= 2.287, p<0.05); preferring to spend time on the internet instead of going out with others is negatively and significantly (β=-0.095, t(576)= -2.327, p<0.05); daily time spent on the internet negatively and significantly (β=-0.125, t(576)= -2.836, p<0.01); internet addiction level negatively and significantly (β=-0.235, t(576)= -5.173, p<0.001) (Table 3). Postponing daily tasks while on the internet, experiencing insomnia due to time spent on the internet, being absent from school due to spending time on the internet, arguing with family members due to time spent on the internet, feeling uneasy when not connected to the internet independent variables were excluded from the model since they did not predict the results at a significant level. Figure 1 summarizes the factors affecting the internet addiction levels and health-promoting behaviors of the participants.

DISCUSSION

There has been an increase in the time adolescents spend online due to their preference of the world on the internet, which can be accessed via many channels, as a leisure time activity today (24). As indicated in many studies related to this subject, time spent on the internet poses a risk factor

Table 2: Predictors of internet addiction.

Independent variables	B	SE	Beta β	t	p	VIF
Constant	14.646	1.270		11.528	0.000*	
Experiencing insomnia due to time spent on the internet	2.896	0.429	0.212	6.747	0.000*	1.242
Being absent from school due to spending time on the internet	3.621	1.141	0.093	3.173	0.002*	1.078
Arguing with family members due to time spent on the internet	3.535	0.399	0.265	8.865	0.000*	1.133
Father's employment status	1.394	0.668	0.059	2.087	0.037*	1.021
Preferring to spend time on the internet instead of going out with others	2.131	0.511	0.124	4.167	0.000*	1.115
Feeling uneasy when not connected to the internet	2.898	0.431	0.208	6.722	0.000*	1.211
Postponing daily tasks while on the internet	2.657	0.438	0.178	6.059	0.000*	1.092
Daily time spent on the internet	0.691	0.108	0.199	6.398	0.000*	1.226
Health-promoting behaviours level	-0.041	0.015	-0.083	-2.762	0.006*	1.140
R	0.747					
R^2	0.558					
AdjR^2	0.551					
F	78.412					
Model (p)	0.000*					
Durbin watson	1.880					

SE: standard error of coefficient, β:standardized regression coefficient, **R^2:** proportion of variation in dependent variable explained by regression model, **p:** the level of statistical significance, *p<0.05.

Table 3: Predictors of health-promoting behaviors.

Independent variables	B	SE	Beta β	t	p	VIF
Constant	81.864	1.925		42.519	0.000*	
Having a computer of one's own	2.495	1.091	0.089	2.287	0.023*	1.010
Preferring to spend time on the internet instead of going out with others	-3.245	1.395	-0.095	-2.327	0.020*	1.107
Daily time spent on the internet	-0.845	0.298	-0.125	-2.836	0.005*	1.283
Internet addiction level	-0.464	0.090	-0.235	-5.173	0.000*	1.369
R	0.366					
R^2	0.134					
AdjR^2	0.128					
F	22.310					
Model (p)	0.000*					
Durbin watson	2.067					

SE: standard error of coefficient, β:standardized regression coefficient, **R^2:** proportion of variation in dependent variable explained by regression model, **p:** the level of statistical significance, *p<0.05.

for addiction, and an increase has been observed in addiction levels as this time increases (25). Adolescents use their time on the internet mostly in non- academic contexts including chatting, entertainment, games, social network connections, shopping, and monetization tools (6). In addition to the risk of internet addiction, this non-academic use also causes an increase in school success and school absenteeism rates (26, 27). The adolescents included in this study were found to have moderate levels of internet addiction based on their responses to the measurement instrument that was used. In addition to this, further analyses yielded evidence that daily time spent on the internet and absenteeism from school to spend time on the internet increase internet addiction levels. Especially school nurses should provide information to adolescents about the advantages of phones without an internet connection, alternative forms of communication, and leisure time activities to reduce the time they spend on the internet. Similarly, encouraging the use of stimulating applications in screen time control (e.g., timers, notifications, restrictions) can be beneficial. With the

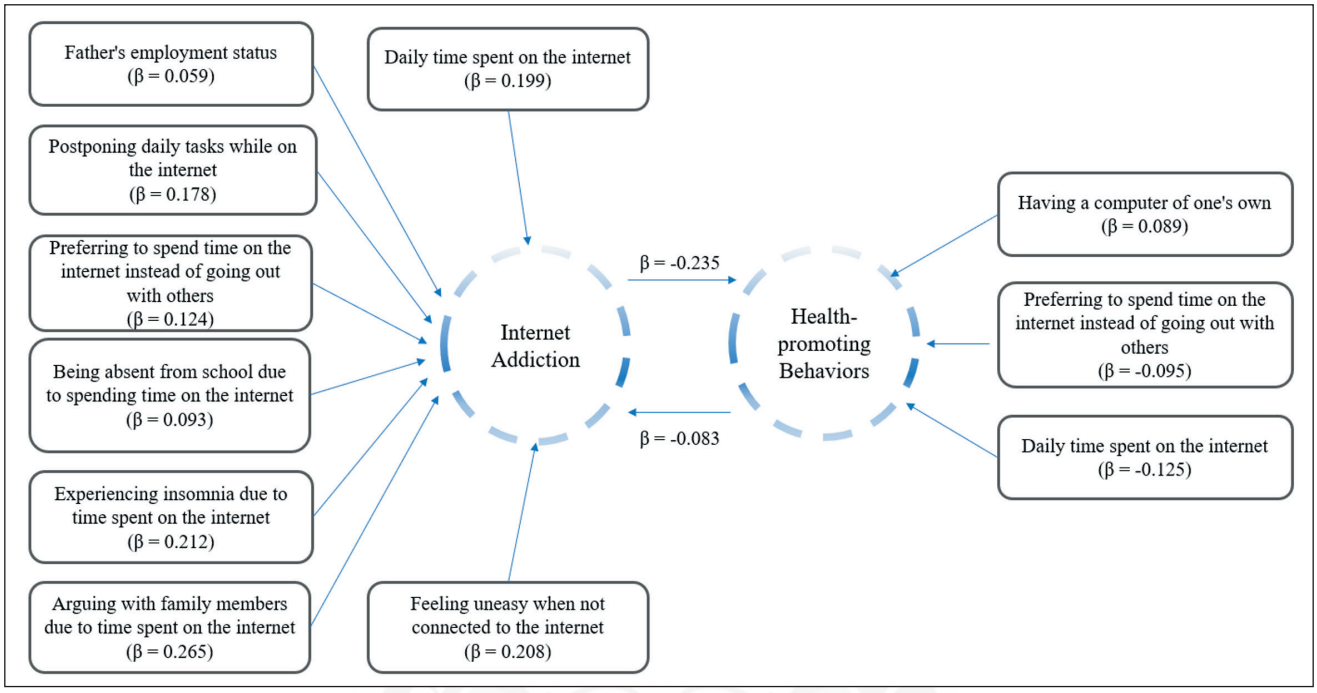


Figure 1: Predictive factors of internet addiction and health-promoting behaviors.

help of these applications, adolescents can review their internet usage habits, set their own limits and gain motivation to reduce their screen times.

Sleep problems due to time spent on the internet are another factor affecting internet addiction (4). Regarding this subject, it was found by Kocas and Sasmaz (2018) that high school students with internet addiction had 2.31 times lower quality of sleep (28). Moreover, insufficient sleep was found to lead to higher levels of media exposure (29). In this study, four of every 10 adolescents were reported to experience sleep problems due to their prolonged use of the internet. In addition, an increase in school absenteeism was also observed on the basis of sleep problems (30, 31). In this study, further analyses confirmed that sleep deprivation due to time spent on the internet and school absenteeism due to time spent on the internet increased internet addiction. Awareness training on sleep hygiene to be provided by school nurses is important for enhancing the sleep quality of adolescents and regulating their sleep cycles. It will be useful to include information about pre-sleep habits, sleep environment, sleep duration, and sleep disorders in the content of this training. Mobile applications that can monitor and control sleep durations can also contribute to the sleep hygiene of adolescents. These applications can help adolescents monitor their sleep patterns, achieve sleep goals, and recognize sleep problems. It is thought that improving sleep hygiene will reflect positively on the academic and health indicators of adolescents.

The internet environment provides virtual social support when the adolescent cannot receive sufficient support from social support mechanisms that are important in the development of self-esteem such as family, friends, and teachers (20). The search for virtual social support is increasing, especially among adolescents who have internet addiction in their families and those who have arguments with their families regarding the purpose and duration of their internet use (8, 32). This situation causes social withdrawal and alienation from outdoor activities in adolescents (33) and paves the way for the transfer of social relationships to the virtual world (34). In addition, familial problems tire the adolescent psychologically and he/she searches for external support mechanisms (35). According to the results of a study, adolescents whose fathers are unemployed have an increased risk of having problems related to internet addiction. It is thought that the resulting negative picture is sustained by adolescents spending their time indoors or maintaining their online presence when they are outdoors. In fact, individuals with internet addiction have difficulty in transitioning to their daily work (36) and there is an increase in their desire to use the internet while they are busy with daily work (37). In the management of this issue with ineffective approaches such as blocking internet access, a state of deprivation is experienced, as in other types of addiction (38), and aggressive behaviors can be exhibited at later stages (39). At the same time, the time spent in front of the screen has a negative effect on each dimension of health-promoting behaviours, especially asocialisation and decreased physical activity in

adolescents (40). Further analyses conducted in this study provided important evidence that having arguments with the family due to the time spent on the internet, adolescents whose fathers do not work, the desire to connect to the internet instead of participating in social activities, disrupting daily tasks due to the time spent on the internet and feeling uneasy when not connected to the internet increase the effects of internet addiction. Accordingly, there is a need for different arguments about what adolescents can put in place of the internet in their lives. In line with the current need, it is recommended to plan activities such as including social responsibility projects that will increase the interaction of adolescents with the environment in school health programs and the establishment of technology detox days.

Health-promoting behaviors are based on the concepts of protection from diseases, early diagnosis/treatment, and rehabilitation. The control of health-promoting behaviors is under the responsibility of individuals, and peer relationships and the social environment are determinants in the formation of these behavior patterns. In this period, while adolescents are striving to have knowledge about every subject with their efforts to form an identity, their self-control and cognitive control are in the developmental stage on the other hand (41). Here, adolescents transition from parent-controlled health practices to the period of taking personal health responsibilities. For this reason, adolescence has critical importance for the acquisition of health-promoting behaviors. Although the measurement tools used in the literature are different, the common view is that the health-promoting behaviors of adolescents are not at the desired level (17). In this study, adolescents were found to have moderate levels of health-promoting behaviors based on the measurement tool used. Many relevant studies have also reported that adolescents have moderate levels of health-promoting behaviors (42).

The increasing popularity of internet use creates an obstacle to practicing health- promoting behaviors among adolescents as in all age groups. In this study, the finding that health-promoting behaviors and internet addiction mutually and negatively affected each other negatively was important. Previous studies in the literature have revealed that there is a relationship between internet addiction and risky health behaviors (4, 43), and internet usage negatively affects the health-promoting behaviors of adolescents (2). For instance, Tran et al. reported that Vietnamese adolescents with internet addiction experienced self-care problems, and their rates of having difficulties in performing daily routines were higher (5). In the study by Hendekci and Aydin Avci, it was determined that nutritional exercise behaviors of adolescents were negatively affected as their internet addiction levels increased; however, those who used the internet for information and educational purposes had healthy diets and meal plans (14). In a different study, it is also stated that technology-based health applications provide motivational support for health-enhancing behaviours (44). The increase in time spent on the internet every day, which was found in this study, also showed a negative effect on health-promoting behaviors, as well as increasing internet addiction levels. Similarly, it was found that bringing a tablet with a mobile internet connection to a gym decreased the physical activity intensity of adolescents by 17% and increased their sedentary behaviors by 54% in the study by Kobak et al. (16). In addition, further analyses in this study revealed that having one's own computer had a positive effect on health-promoting behaviours. The findings obtained in this study indicated that the inadequacy of parents and adolescents in terms of digital literacy is the source of the problem. Therefore, in order to bring the health-promoting behaviours of adolescents to the desired level, the time spent online should be reduced, effective leisure time management should be established and the time spent online should be supported with controlled and health-promoting content. Studies in which online and leisure time management is enriched with health-promoting activities and practices and strengthened with social support mechanisms such as family and friends are important in terms of continuity and applicability.

In this study, the form of internet use was not questioned, and a distinction between generalized and specific internet use was not made. Therefore, there may have been differences among the participants regarding how and for what they used the internet. In the study, the level of internet addiction was determined using a self-report scale rather than clinical and diagnostic measures, and this may have created social acceptability bias. Since the study did not include a community-based group, it is not possible to generalise the results due to the influence of socio-cultural and economic factors on internet addiction and health-promoting behaviours.

According to the results of this study, it was determined that adolescents have moderate level of internet addiction and moderate level of health promoting behaviours and these two concepts affect each other negatively. It was found that experiencing insomnia due to time spent on the internet, absenteeism from school due to time spent on the internet, arguing with family members due to time spent on the internet, father not working, preferring to spend time on the internet instead of going out with others, feeling restless when not connected to the internet, postponing daily tasks while on the internet, daily time spent on the internet and non-health promoting behaviours significantly increased internet addiction levels. It was found that as the time the participants spent on the internet instead of spending time outside and internet addiction levels increased, their health-promoting behaviours decreased significantly, while having a personal computer significantly increased health-promoting behaviours.

According to the results of this study, with an increase in internet use and a decrease in health-promoting behaviors, there is a risk of internet addiction rising to high levels in the future. To reach the Sustainable Development Goals and Healthy People 2030 goals, it is necessary to take urgent measures against internet addiction in adolescents and encourage health-promoting behaviors. It is recommended to establish early and preventive measures such as adolescent-specific prevention programs, education, skill development, behavioral change, and intervention strategies for these two problems that threaten global health, and it is recommended to encourage the participation of families in these programs. It is thought that especially in school health services, short and medium-term action plans developed by a multidisciplinary team under the leadership of a school health nurse will provide effective results in the long term. For future research, qualitative or representative cohort studies in which the effect of internet addiction on health-promoting behaviors is evaluated within the sociocultural structure and according to different forms of internet usage are recommended.

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Author Contributions

Concept: **Hülya Kulakçı Altıntaş, Enise Sürücü, Funda Veren,** Design: **Hülya Kulakçı Altıntaş, Enise Sürücü, Funda Veren,** Data collection and processing: **Hülya Kulakçı Altıntaş, Enise Sürücü, Funda Veren;** Analysis and interpretation: **Hülya Kulakçı Altıntaş, Enise Sürücü, Funda Veren,** Literature search: **Enise Sürücü, Funda Veren,** Writing: **Hülya Kulakçı Altıntaş, Enise Sürücü,** Approval: **Hülya Kulakçı Altıntaş, Enise Sürücü, Funda Veren.**

Conflicts of Interest

The authors have no confict of interest to declare.

Financial Support

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Ethical Approval

This study was completed in accordance with the tenets of the Declaration on Helsinki. Ethical approval was obtained from the Human Research Ethics Committee of Zonguldak Bülent Ecevit University (09.11.2021/99622-335), and written permission was received from the Provincial Directorate of National Education (E-45865702-604.01.01-408326869/07.01.2022). Written informed consent was obtained from the families of the students. Verbal consent was received from the students.

Review Process

Extremely and externally peer-reviewed.

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ÖZGÜN ARAŞTIRMA

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Farklı Egzersiz Kapasite Testlerinin İnterkostal Kas Oksijenizasyonu Üzerine Etkisi

Examining the Effect of Different Exercise Capacity Tests on Intercostal Muscle Oxygenation

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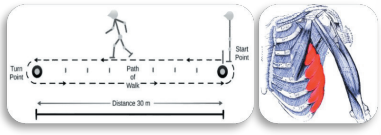
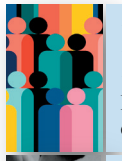
GRAFİKSEL ÖZET

6DYT'nin uygulama kolaylığı ve egzersiz kapasitesini göstermedeki başarısı dolayısıyla daha fazla tercih edilebilecek bir alan testi olduğu söylenebilir.



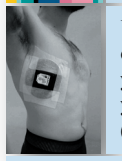
Çalışmamızın amacı;

- **Artan hızda mekik yürüme (AHMYT) ve altı dakika yürüme (6DYT) testleri sırasında meydana gelen intercostal kas oksijenizasyonu değişimi**
- **Bu değişimin hemodinamik yanıtlar üzerine etkilerini belirlemek,**
- **Test başarılarını karşılaştırmaktır.**



- **18-35 yaş**
- **BKİ<25 kg/m²**
- **Sağlıklı bireyler**

Katılımcılar randomize edilerek iki gruba ayrıldı.



Uygulama süresince kas oksijenizasyonunu ölçmek için yedinci interkostal boşluğa yakın kızılötesi spektroskopi (MOXY) cihazı yerleştirildi.

- **Solunum fonksiyon testi ile solunum fonksiyonları**
- **Modifiye Borg Skalası ile dispne**
- **Taşınabilir tansiyon aleti ile kan basıncı**
- **Parmak oksimetresi ile kalp hızı ve oksijen saturasyonu**

- **AHMYT ve 6DYT'nin olgular üzerindeki hemodinamik yanıtları ve yardımcı solunum kas oksijenizasyonu yanıtları veya başka bir deyişle zorlanma dereceleri benzerdir.**
- **Olgular 6DYT'yi daha iyi tolere edebilmekte, test süresi AHYT'ye göre 6 dk ile sınırlanmış olmasına rağmen daha uzun mesafelerde yürüyebilmekte, daha az dispne şikayeti yaşamaktadır.**

Batı Karadeniz Tıp Dergisi

Eylem Çinkılıç , Enise Sert , İrem Çayır, Sema Nur Günaydın, Zeynep Betül Özcan, Esra Pehlivan

Çinkılıç E ve ark. Farklı Egzersiz Kapasite ... Med J West Black Sea. 2025;9(1).

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ÖZ

Amaç: Egzersiz kapasitesi, kardiovasküler durumdan, kas oksijenizasyonundan ve yardımcı solunum kaslarının fizyolojik özelliklerinden etkilenebilmektedir. Bu çalışmanın amacı, klinikte sık kullanılan artan hızda mekik yürüme (AHMYT) ve altı dakika yürüyüş (6DYT) testleri sırasında meydana gelen intercostal kas oksijenizasyonu değişimi ve hemodinamik yanıtlar üzerine etkilerini belirlemek, test başarılarını karşılaştırmaktır.

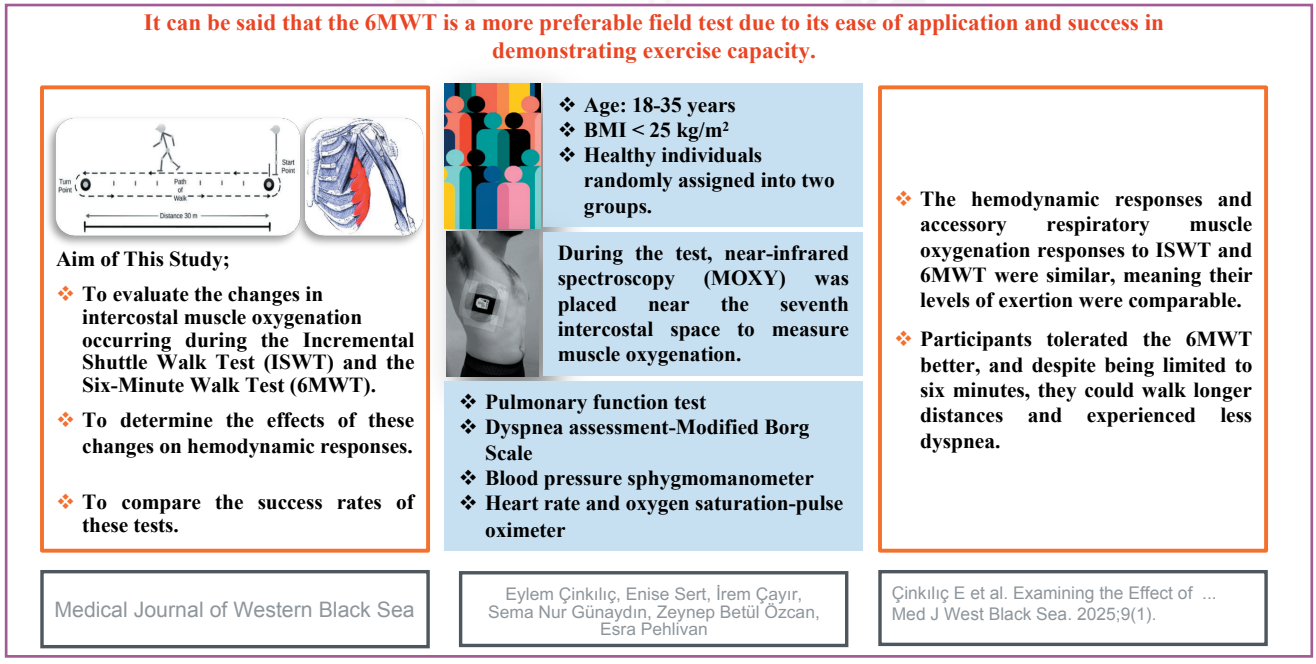
Gereç ve Yöntemler: Çalışmaya 18-35 yaş arası ve beden kütle indeksi <25 kg/m² olan sağlıklı bireyler dahil edildi. Katılımcılar randomize edilerek iki gruba ayrıldı. İlk gruba 6DYT, ikinci gruba ise AHMYT yapıldı. 30 dakikalık arınma süresinden sonra gruplar çaprazlanarak, ilk gruba 6DYT ve 2. gruba AHMYT uygulandı. Solunum fonksiyon testi ile solunum fonksiyonları, modifiye Borg skalası ile dispne, taşınabilir tansiyon aleti ile kan basıncı, parmak oksmetresi ile kalp hızı ve oksijen saturasyonu değerlendirildi.

Bulgular: Olguların testler öncesi istirahat değerleri; kalp hızı (p=0,096), sistolik kan basıncı (p=0,054), diastolik kan basıncı (p=0,081), yorgunluk seviyesi (p=0,058), dispne seviyesi (p=0,067), SpO2 değeri (p=0,089) ölçüldü. Testlerin, başlangıç ve bitiş saturasyon, kalp hızı, kan basıncı yanıtları, kas oksijen saturasyonu ve total hemoglobin miktarları benzerken, AHMYT bitiş kalp hızı değeri istatistiksel olarak anlamlı olmamakla birlikte daha yüksekti (p=0.005). Benzer biçimde bitiş dispne seviyesi ve toplam test süresi AHMYT'de daha fazla (p=0,000), yürüme mesafesi ise 6DYT'de daha fazlaydı (p=0,000).

Sonuç: 6DYT ve AHMYT testlerinin sağlıklı olgularda oluşturdukları hemodinamik yanıtlar ve kas oksijenizasyonu değişimleri benzerdir. Olgular AHMYT'de daha fazla nefes darlığı hissetmekte ve kalp hızı yanıtları daha fazla olabilmektedir. Diğer taraftan AHMYT'de daha uzun sürelerde yürümelerine rağmen, 6DYT'de daha uzun mesafelerde yürüyebilmektedir.

Anahtar Sözcükler: Altı dakika yürüme testi, artan hızda mekik yürüme testi, interkostal kas oksijenizasyonu, kas oksijenizasyonu, MOXY

GRAPHICAL ABSTRACT



ABSTRACT

Aim: Exercise capacity can be affected by cardiovascular status, muscle oxygenation and physiological properties of accessory respiratory muscles. The aim of this study is to determine the effects of intercostal muscle oxygenation changes and hemodynamic responses during the increased speed shuttle walking (ISWT) and six-minute walk (6MWT) tests, which are frequently used in the clinic, and to compare the test successes.

Material and Methods: Healthy individuals between the ages of 18-35 and with a body mass index <25 kg/m² were included in the study. Participants were randomized and divided into two groups. 6MWT was performed on the first group and ISWT was performed on the second group. After the 30-minute washout period, the groups were crossed and 6MWT was applied to the first group and ISWT was applied to the second group. A near-infrared spectroscopy (MOXY) device was placed in the seventh intercostal space to measure muscle oxygenation during the application. Respiratory functions were evaluated with a pulmonary function test, dyspnea with the modified Borg scale, blood pressure with a portable sphygmomanometer, heart rate and oxygen saturation with a finger oximeter.

Results: Resting values of the cases before the tests; heart rate (p=0.096), systolic blood pressure (p=0.054), diastolic blood pressure (p=0.081), fatigue level (p=0.058), dyspnea level (p=0.067), SpO2 value (p=0.089) were measured. While the initial and final saturation, heart rate, blood pressure responses, muscle oxygen saturation and total hemoglobin amounts of the tests were similar, the AHMYT final heart rate value was higher, although not statistically significant (p = 0.005). Similarly, the end dyspnea level and total test time were higher in AHMWT (p=0.000), and the walking distance was longer in 6MWT (p=0.000).

Conclusion: The hemodynamic responses and muscle oxygenation changes produced by 6MWT and ISWT tests in healthy subjects are similar. Patients feel more shortness of breath and heart rate responses may be greater in ISWT. On the other hand, although they walk for longer periods in ISWT, they can walk longer distances in 6MWT.

Keywords: Intercostal muscle oxygenation, MOXY, muscle oxygenation, shuttle walk test at increased speed, six minute walk test

GİRİŞ

Egzersiz testleri bireylerin fonksiyonel egzersiz kapasitesinin belirlenmesinde, hastalık prognozunu tahmin etmek amacıyla, klinik araştırma sonuçlarının yorumlanmasında ve tedavi yanıtının değerlendirilmesinde kullanılmaktadır. Egzersiz testlerinin, laboratuvar ve alan testleri olarak çeşitleri mevcuttur (1).

Alan testleri kronik solunum hastalıklarında, hastaların fonksiyonel egzersiz kapasitelerinin belirlenmesi ve egzersiz performansını sınırlayan dispne, yorgunluk, desaturasyon gibi faktörlerin saptanması amacıyla sıkça kullanılan testlerdir. Az teknik ekipman gerektirmesi, uygulanması ucuz ve kolay olması nedeniyle artan hızda mekik yürüme testi (AHMYT) ve altı dakika yürüme testi (6DYT), alan testleri arasında en yaygın kullanılan testlerdir. 6DYT, fonksiyonel egzersiz kapasitesini ölçen, yapısal geçerliliği yüksek, egzersiz performansı ve fiziksel aktivite ölçekleri ile yüksek düzeyde ilişki gösteren bir testtir. Kullanım kolaylığı sağlaması açısından ve submaksimal efor gerektirdiğinden en sık tercih edilen alan testidir (2). Artan hızda mekik yürüme testinde semptom sınırlı olarak maksimal kapasite değerlendirilir, günlük yaşam aktivitelerinde maksimal yanıtın belirlenmesinde daha duyarlı ölçüm yapılmasını sağlar (3). Tepe oksijen tüketimi (Pik VO_2) tayini için kullanılabilir ve Pik VO_2 ile korelasyonu 6DYT'ye göre daha iyidir. Ancak maksimal yüklenimli bir test olmasından dolayı, uygulanması daha zor bir yöntemdir (4).

Kas oksijenasyonu, metabolik solunumun bir sonucu olarak hedef doku içindeki oksijen akışını ifade eder ve aerobik kapasite, artan akciğer ventilasyonu, solunum hızı ile doğrudan ilişkilidir (5). Kas oksijenizasyonu, kalpten ve akciğerlerden oksijenli kanın verilmesi ve lokal kas içindeki mitokondri tarafından oksijen alımıdır. Son yıllarda kasın oksijen düzeyi yakın kızılötesi spektroskopisi (Near-Infrared Spectroscopy, NIRS) adı verilen bir teknoloji ile ölçülmektedir. NIRS, ışığının dokulardan geçerken kromofor molekülleri (oksihemoglobin (O2Hb) ve deoksihemoglobin (HHb), sitokrom-c oksidaz (CCO), miyoglobin gibi) tarafından uğradıkları absorbsiyon miktarının ölçüldüğü bir tekniktir (6). Moxy taşınabilir bir NIRS sensörüdür.

Literatüre bakıldığında, AHMYT ve 6DYT karşılaştıran çalışmalar mevcuttur fakat bu çalışmalarda egzersiz performansını ve dispne gibi semptomlarla ilişkili olabilen önemli bir yardımcı solunum kası olan intercostal kasların oksijenizasyonunun değişimi incelenmemiştir. Bu çalışmada amacımız farklı egzersiz kapasitesi testlerinin intercostal kas oksijenizasyonu üzerindeki etkilerini belirlemek, değişen yardımcı solunum kası oksijenizasyonu, hemodinamik yanıtları ve egzersiz test başarısını ortaya konulmasıdır. Çalışmamız bu yönüyle özgündür ve literatüre katkı sağlayacaktır. Klinikte sık kullanılan bu egzersiz testlerinin hangisinin gerçekleştirilmesi gerektiği kararının alınabilmesi ve test başarısını etkileyen faktörlerin belirlenmesi için çalışmamızın klinik pratik bilgi sağlayacağı kanaatindeyiz.

GEREÇ ve YÖNTEMLER

Çalışma prospektif, çapraz kontrollü klinik çalışmadır ve Ekim 2023 - Haziran 2024 tarihleri arasında Sağlık Bilimleri Üniversitesi Hamidiye Sağlık Bilimleri Fakültesi Fizik Tedavi ve Rehabilitasyon Bölümünde gerçekleştirilmiştir. Çalışmaya yerel üniversite etik kurulu tarafından 19.01.2024 tarih ve 23\685 sayı ile etik kurul onayı alındı ve çalışma Helsinki Deklerasyonuna uygun olarak gerçekleştirildi. Katılımcılardan uygulama öncesi yazılı bilgilendirilmiş onam alındı.

Örneklem Büyüklüğü

Çalışmanın örneklem büyüklüğü hesabı G-power Analiz programı kullanılarak yapıldı. Tip 1 hata miktarı 0.05 testin gücü 0.95 iken aralarındaki etki farkını bulabilmesi için minimum olgu sayısının 32 olması gerektiği tespit edildi (7).

Çalışmaya 18-35 yaş aralığında olan ve beden kütle indeksi <25 kg/m² olan sağlık bireyler dahil edildi. Sigara içicisi olan, egzersiz testlerinin yapılmasına engel olabilecek herhangi bir sistemik, ortopedik, kardiyopulmoner hastalığı olan, tanısı konulmuş herhangi bir solunumsal, vasküler ve kalp hastalığı bulunan bireyler dışlandı.

Çalışma Yöntemi

Katılımcılar çalışmaya katılmanın riskleri ve yararları konusunda bilgilendirildi ve gönüllü onam formunu imzaladılar. Katılımcıların yaş, cinsiyet, boy, kilo, vücut kütle indeksi,

medeni durumu, alkol ve sigara kullanımları dahil olmak üzere demografik bilgileri alındı. Çalışma öncesi olgulara solunum fonksiyon testi, nefes darlığı değerlendirmesi, kan basıncı, kalp atım hızı ve saturasyon değerlendirmesi yapıldı. Olgular 6DYT ve AHMYT olmak üzere 2 gruba randomize edildi. Egzersiz testleri öncesinde değerlendirmeler yapıldıktan sonra interkostal kas üzerine MOXY cihazı yerleştirilerek, 6DYT grubu 6DYT ile, AHMYT Grubu ise AHMYT ile test edildi. En az 30 dakikalık bir arınma süresinden sonra gruplar çaprazlanarak uygulamalar diğer egzersiz testi yapılarak tekrarlandı**.** Arınma süresinin uzunluğu, en az 30 dk olmak üzere ve olgulara yorgunluk durumları RPE Borg skalası ile yapılan sorgulamaya göre belirlendi (8).

Çalışma Sonuç Ölçümleri

Solunum Fonksiyon Testi: Solunum fonksiyon testi, (oncomed parmak tipi) masaüstü spirometri cihazı Cosmed Pony Fx (Italy) kullanılarak Amerika Toraks Derneği kılavuzuna göre gerçekleştirildi. Test katılımcılara, herhangi bir kimyasal maddenin bulunmadığı kapalı bir ortamda, oturur pozisyonda ve burun mandalı kullanılarak yapıldı. Her bir katılımcı için en az üç ölçüm yapılarak en iyi değerler çalışmaya alındı (9).

Modifiye Borg Skalası (mBorg): Sıklıkla efor dispne şiddetini ve istirahat dispne şiddetini değerlendirmek amacıyla kullanılan bir ölçektir. Derecelerine göre dispne şiddetini tanımlayan on maddeden oluşur. Modifiye Borg Skalasında dispne şiddetinin tanımlanıyor olması hastalar açısından daha kolay uygulanmasını sağlamaktadır (5). Olgulara egzersiz testi başlangıcında ve test bitişinde mBorg skalası gösterilerek, skala anlatıldı ve dispne seviyelerinin puanlanması istendi.

Kan basıncı, Kalp atım hızı ve SaO_2 değerlendirilmesi: Kan basıncı (mmHg), testlerin başlangıcından hemen önce ve bitişinden hemen sonra oturur pozisyonda kişinin bileğinden Omron marka tansiyon aleti ile, saturasyon (%) ve kalp atım hızı (atım/dk) ise testlerin yapıldığı süre boyunca parmak oksimetre cihazı (Oncomed parmak tipi) ile ölçüldü.

Kas Oksijenizasyonun Değerlendirilmesi: Kas oksijenizasyon ve total hemoglobin miktarı egzersiz testleri süresince yakın kızıl ötesi spektroskopi cihazı (MOXY, Yakın kızılötesi spektroskopi) ile ölçüldü. Cihaz, anterior aksiller çizgideki yedinci interkostal boşluktaki interkostal kasa yerleştirildi (3). Ölçüm parametreleri kas oksijen saturasyonu ve total hemoglobin miktarının ortalaması idi.

6 Dakika Yürüme Testi: Kapalı ortamda 30 m uzunluktaki koridorda uygulandı, altı dakikalık sürede hastanın yürüdüğü mesafe, oksijen satürasyonu, kalp hızı, dispnedeki değişim kaydedildi. Bunun için teste başlamadan önce oksijen satürasyonu, kalp hızı, tansiyon arteriyel ve Borg skalasına göre dispne düzeyi kaydedildi (10).

Artan Hızda Mekik Yürüme Testi: Bu test hasta teste devam edemeyene kadar sürdürülen giderek artan hızda 10 m aralıklı iki koni arasında yürünen ve iki koni arasındaki her bir 10 metrelik gidişin bir mekik olarak sayıldığı egzersiz testidir. Hastanın nefes darlığı nedeniyle teste devam edemediği, kalp hızının maksimum beklenen kalp hızının yüzde seksen beşine ulaştığı veya max test süresi olan 20 dakikalık testi tamamladığı noktaya kadar devam ettirildi (11).

İstatistiksel Analiz

Verilerin analizi SPSS 25 paket programı kullanılarak gerçekleştirildi. Kategorik değişkenler için yüzde ve frekans değerleri; nicel değişkenler için ise medyan, minimum ve maksimum değerleri sunuldu. Verilerin normal dağılıma uygunlukları Shapiro-Wilk testi ile belirlendi. Gruplar arası karşılaştırmalarda Mann Whitney U testi kullanıldı. Araştırmada tip I hata oranı (α) 0,05 olarak kabul edildi.

BULGULAR

Araştırmaya yaş ortalaması 21,6±4,0 yıl olan 32 kişi dahil edildi. Katılımcıların tamamı sigara ve alkol kullanmamaktaydı ve ek hastalıkları yoktu (Tablo 1).

Tablo 1: Olguların Demografik ve Klinik Özellikleri

Demografik Özellikler	**(n=32)**
Yaş (yıl) Medyan (Min-Maks)	22,00 (19-26)
Vücut Kütle İndeksi (kg/m²) Medyan (Min-Maks)	23,25 (17,20-24,90)
Cinsiyet, n (%)	
Kadın	22 (68,8)
Erkek	10 (31,3)
Sigara içme durumu, n (%)	
Evet	0
Hayır	32 (100)
Alkol kullanma durumu, n (%)	
Evet	0
Hayır	32 (100)
Medeni durum, n (%)	
Evli	0
Bekar	32 (100)
Ek hastalık, n (%)	
Evet	0
Hayır	32 (100)
Solunum Fonksiyon Testi	
1.Saniye Zorlu Ekspirasyon Hacmi	2,87 (0,79-4,75)
Zorlu Vital Kapasite	3,52 (2,40-6,71)
1.Saniye Zorlu Ekspirasyon Hacmi / Zorlu Vital Kapasite	77,50 (32,00-92,00)
6 Dakika Yürüme Testi, m	526 (420-670)
Artan Hızda Mekik Yürüme Testi, m	400 (200-920)

Katılımcılar alkol ve sigara kullanmayan bireyler arasından seçilmiştir. Katılımcıların yaş ortalaması 22, VKİ (kg/ m²) ortalama 23,25 olarak hesaplanmıştır. Çalışmaya katılan 32 kişinin 6DYT(m) ortalama değeri 526(420-670) ve AHMYT(m) ortalama değeri 400(200-920) bulunmuştur.

Olguların, testlerin başlangıç ve bitiş SpO2, kalp hızı, kan basıncı, mBorg yorgunluk skorları, kas oksijenizasyon değerleri ve total hemoglobin seviyeleri benzerdi (p>0,05). Bitiş kalp hızı değeri AHMYT'de istatistiksel olarak anlamlı ve yüksekti (p=0.005). Benzer biçimde olguların test sonu dispne skorları AHMYT'de daha yüksekti (p=0,000). 6DYT yürüme mesafesi 526,50 m iken AHMYT 400 m idi (p=0,000). 6DYT süresi medianı 6 dk iken, AHMYT süresi 7 dk idi (p=0,000) (Tablo 2).

TARTIŞMA

Egzersiz kapasitesi ve egzersiz test başarısı pek çok faktöre bağlıdır. Solunum kaslarının fizyolojik özellikleri de egzersiz performansını etkileyebilir. Çalışmada klinikte en sık kullanılan alan testlerinden olan 6DYT ve AHMYT'de meydana gelen hemodinamik yanıtlar ve kas oksijenizasyon seviyelerinin karşılaştırılması hedeflenmiştir. Çalışmadan elde edilen verilere göre her iki testte meydana gelen hemodinamik yanıtlar ve kas oksijenizasyon seviyeleri benzerdir. AHMYT sırasında olgular daha fazla dispne hissedebilmekte, diğer taraftan 6 dakikadan daha uzun sürelerde testi devam edebilmektedir. Yürüme mesafeleri bakımından ise 6DYT yürüme mesafesinin, AHMYT ye göre daha fazla olduğu tespit edilmiştir.

Çalışmamızda submaksimal bir egzersiz testi olan 6DYT ve maksimal bir egzersiz testi olan AHMYT sırasında ölçülen kas oksijenizasyon düzeyi değişimlerinin benzer olduğu tespit edilmiştir. Test süresi açısından bakıldığında AHMYT'nin altı dakikadan daha fazla sürelerde devam edilmiş olmasına ve iş yükünün daha fazla olmasına rağmen kas oksijenizasyon düzeylerinin benzer olması, olguların genç ve sağlıklı olgulardan seçilmiş olmasından kaynaklanabilir.

Yakın kızılötesi spektroskopiyle triseps surae doku oksijen doygunluğu için referans değerlerini inceleyen bir çalışmada, 30 ila 79 yaş aralığındaki sağlıklı bireylere, arteriyel oklüzyon manevrası ve artan hızda mekik yürüme testi sırasında ve sonrasında doku oksijen satürasyonu değerlendirmeleri

Tablo 2: Altı Dakika Yürüme Testi ve Artan Hızda Mekik Yürüme Testi Parametreleri

	6DYT	AHMYT	Z	P
SpO_2 (%)				
Başlangıç	98 (91-99)	97,50 (91-99)	-0,013	0,089
Bitiş	96,50 (83-99)	96,50 (85-99)	-0,030	0,076
Kalp hızı (atım/dk)				
Başlangıç	94 (56-133)	93 (56-130)	-0,004	0,096
Bitiş	116 (55-162)	138,00 (78-172)	-1,088	0,005
Sistolik Kan Basıncı (mmHg)				
Başlangıç	120,50 (100-157)	120,00 (99-153)	-0,059	0,054
Bitiş	128 (103-182)	129,00 (91,00-189,00)	-0,014	0,088
Diastolik Kan Basıncı (mmHg)				
Başlangıç	80 (53-112)	80,50 (64,00-110,00)	-0,022	0,081
Bitiş	84 (69-115)	83,50 (54,00-111,00)	-0,066	0,050
mBorg Yorgunluk				
Başlangıç	0,00 (0-1)	0,00 (0-1)	-0,055	0,058
Bitiş	0,50 (0-8)	1,00 (0-6)	-0,053	0,059
mBorg Dispne				
Başlangıç	0,00 (0-2)	0,00 (0-2)	-0,041	0,067
Bitiş	0,00 (0-3)	1,00 (0-7)	-3,052	0,000
Yürüme Mesafesi (m)	526,50 (420-670)	400,00 (200-920)	-3,026	0,000
Test süresi, dk	6,00	7,00 (5-12)	-4.383	0,000
SmO_2 Avaraged				
Başlangıç	66,00 (35,00-92,00)	65,00 (25,00-92,00)	-0,074	0,045
Bitiş	62,00 (12,00-94,00)	58,00 (24,00-99,00)	-1,034	0,017
SmO_2 Live				
Başlangıç	65,50 (35,00-92,00)	65,50 (25,00-95,00)	-0,035	0,072
Bitiş	62,00 (12,00-95,00)	58,50 (24,00-99,00)	-1,025	0,021
THB (g)				
Başlangıç	12,11 (11,08-12,77)	12,16 (11,37-12,78)	-0,007	0,094
Bitiş	12,10 (11,09-12,74)	12,26 (11,07-12,92)	-0,067	0,050

6DYT: Altı Dakika Yürüme Testi, **AHMYT:** Artan Hızda Mekik Yürüme Testi, **SmO_2:** Kas Oksijen Satürasyonu, **SpO_2**: Kan Oksijen Satürasyonu, **THB:** Total Hemoglobin

yapılmıştır. Sonuç olarak ise, erkeklerde SpO_2 değerlerinin daha düşük, istirahatte deoksijenasyon ve reoksijenasyon (Tx-reox) oranlarının daha yüksek, ilerleyen efor sırasında ise Tx-reox daha yüksek olduğu tespit edilmiştir (12). Bahsi geçen çalışmadan farklı sonuçlar elde etmiş olmamızın nedeninin bu çalışmadan farklı olarak intercostal kasların oksijenizasyonunun değerlendirilmiş olması olabilir.

Çalışmamızda kas oksijenizasyonu intercostal kaslarda yapılmıştır. Bu kas grubunun seçilmiş olmasının nedeni, başlıca yardımcı solunum kaslarından biri olması ve egzersizde bu kas grubunun aktivite seviyesinin artmasıdır (13). Yapılan bir çalışmada sekiz kürekçide artımlı kürek egzersizi sırasında NIRS yöntemini kullanarak aynı anda vastus lateralis ve biceps brachi kaslarının oksijenizasyonundaki değişiklikler karşılaştırılmıştır. Çalışma sonucunda kürek çekme egzersizi sırasında biceps brachinin vastus lateralisten daha düşük oksijenlenme seviyesine sahip olduğu görülmüştür (14). Deneyimli arazi koşucularında kardiyopulmoner egzersiz testi sırasında interkostal kas oksijenizasyonunun incelendiği bir çalışmada, test sırasında meydana gelen kas oksijen saturasyonu değişiminin anlamlı bulunmadığı bildirilmiştir (15). Yüksek seviye rekabet maraton koşucularında yapılan başka bir çalışmada, interkostal kasların oksijenizasyonuyla vastus lateralis kasının oksijenizasyonu ölçülmüştür. Sonuç olarak artan maksimal egzersiz sırasında interkostallerde dokunun oksijenlenmesinin doğrudan solunum hızı ile ilişkili olduğu ve vastus lateralis'in dokularının oksijenlenmesinde interkostallere göre daha çok deoksijenizasyona uğradığı gözlemlenmiştir. Araştırmacılar yüksek düzeyde rekabetçi maraton koşucularında, artan egzersiz sırasında m. intercostales deoksijenizasyonunun doğrudan aerobik kapasite ve artan akciğer ventilasyonu ve solunum hızı ile ilişkili olduğunu tespit etmiştir (5). Literatüre göre vücut kan dağılımının eforla değiştiği ve özellikle aktif kaslarda oksijen ve kan akımının artacağı bilinmektedir (16). Bahsi geçen çalışmalarda ise farklı sonuçlar beyan edilmektedir. Çalışmamızda olgularda yardımcı solunum kas aktivitesinde vasküler yanıt oluşturacak düzeyde bir zorlanma oluşmamış olabilir.

İnterkostal kasların oksijenizasyonunda değişiklik tespit edilmemiş olmasının nedenlerinden biri de cihazın bu kasların oksijenizasyonunu ölçmeye uygun bir cihaz olup olmadığı sorusunu akla getirebilir. Egzersiz sırasında intercostal kas oksijenizasyonunun MOXY cihazıyla ölçümünün güvenirliğini inceleyen bir çalışmada, 15 maraton koşucusu 7 gün aralıklarla iki farklı ölçüm yapılarak değerlendirilmiştir. Bu iki ölçüm bir test-tekrar test çalışmasıdır. Taşınabilir NIRS güvenilirliği düşük yoğunluklu egzersiz sırasında (dinlenme ve VT1) iyi ve yüksek yoğunluklu egzersiz sırasında (VT2 ve maksimum) mükemmel gözlemlenmiştir. Çalışma sonucunda egzersiz sırasında artan solunum çabasının, MOXY cihazı kullanılarak yeterince kaydedilebileceğini gösterilmiştir (17). Çalışmamızda cihazın intercostal aralığa yerleştirilmesinde ve burada sabit tutulmasında bir zorluk yaşanmamıştır.

Yapılan egzersiz alan testlerinin yürüme mesafesinde, borg dispne bitiş ve test süresi değerlerinde anlamlı farklılık gözlemlenmiştir. Olgular günlük yaşam pratiğine daha yakın tempoda gerçekleştirilen 6DYT'de daha uzun mesafelerde yürüyebilmektedir. Üstelik bunu daha kısa sürede gerçekleştirebilmektedir. Testler sırasında hemodinamik yanıtların ve kas oksijenizasyon değişimlerinin benzer olmasına rağmen, yürüme mesafesinde oluşan bu farklılığın, AHMYT'de daha fazla meydana gelen dispne algısından kaynaklanabilir. Literatürde sağlıklı kişilerde bu alan testlerinin çalışmamızdaki ölçüm parametrelerinin karşılaştırılmasına rastlamadık. Diğer taraftan çalışma sonuçlarımıza paralel olarak, yaşlı aktif erişkinlerde yapılan bir çalışmada AHMYT'nin, 6DYT yürüme mesafesi kadar sürdürülemediği bildirilmiştir (18). Bu çalışmada yürümenin biyoenerjetiği karşılaştırılmış, AHMYT VO_2 tepe değerlerinin, 6DYT VO_2 tepe değerlerinden daha yüksek bulunmuştur (18).

Egzersiz testlerinde oksijen saturasyonu ana takip parametrelerindendir. Artan hızda mekik yürüme testi ve 6DYT'nin karşılaştırıldığı bir makalede AHMYT'den sonra SpO_2'deki düşüşün, 6DYT'deki düşüşe göre daha fazla olduğu bildirilmiştir. SpO_2'deki değişiklik AHMYT sonrası SpO_2'deki değişiklik ile korele olurken 6DYT deki korelasyon zayıf bulunmuştur. Çalışmada oksijen saturasyonu %90'ın altı olan hasta sayısı her iki yürüme testinden sonra benzerdir (19). Çalışmamızdaki olguların sağlıklı genç bireylerden oluşmasına rağmen, her iki test sırasında da desaturasyon yaşanan olgular mevcuttur. Fakat egzersiz testlerindeki saturasyon seviyeleri karşılaştırmasında bir farklılık tespit edilmemiştir. Bu durum testlerin iş yükünden bağımsız olarak altta yatan farklı klinik özelliklerin etkili olabileceğini ve benzer olgularda desaturasyonun görülmüş olabileceğini akla getirmektedir.

Çalışmamızın birtakım sınırlılıkları bulunmaktadır. Çalışma kapsamında sadece interkostal kasların kas oksijenizasyonu ölçülmüştür. Alt ekstremite veya farklı yardımcı solunum kaslarında eş zamanlı ölçümlerin yapılmamış olması bir sınırlılıktır. Bir başka görece limitasyonumuz testlerin herhangi bir kronik hastalığı olmayan gençlerde yapılmış olmasıdır. Çalışma sonuç ölçümlerinde istatistiksel olarak anlamlı seviyelerde farklılığın tespit edilmemiş olmasının nedeni, olgularda yeterli zorlanma derecelerinin oluşmamış olması olabilir. Fakat çalışmamızın ana amacının bu iki alan testi özelinde elde edilen yanıtlara odaklanmış olduğu unutulmamalıdır.

Çalışmamızdan elde edilen verilere göre AHMYT ve 6DYT'nin olgular üzerindeki hemodinamik yanıtları ve yardımcı solunum kas oksijenizasyonu yanıtları veya başka bir deyişle zorlanma dereceleri benzerdir. Fakat olgular 6DYT'yi daha iyi tolere edebilmekte, test süresi AHYT'ye

göre 6 dk ile sınırlanmış olmasına rağmen daha uzun mesafelerde yürüyebilmekte, daha az dispne şikâyeti yaşamaktadır. Sonuç olarak bahsi geçen avantajlar göz önünde bulundurulduğunda 6DYT'nin uygulama kolaylığı ve egzersiz kapasitesini göstermedeki başarısı dolayısıyla daha fazla tercih edilebilecek bir alan testi olduğu söylenebilir.

Teşekkür

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Yazar Katkı Beyanı

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Hakemlik Süreci

Kör hakemlik süreci sonrasında yayınlanmaya uygun görülmüştür.

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ORIGINAL ARTICLE

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Awareness of Patients Who Will Undergo ^{18}F-FDG PET/CT Imaging About Ionizing Radiation Exposure

^{18}F-FDG PET/BT Çekimi Yapılacak Hastaların İyonize Radyasyon Maruziyeti Hakkındaki Farkındalığı

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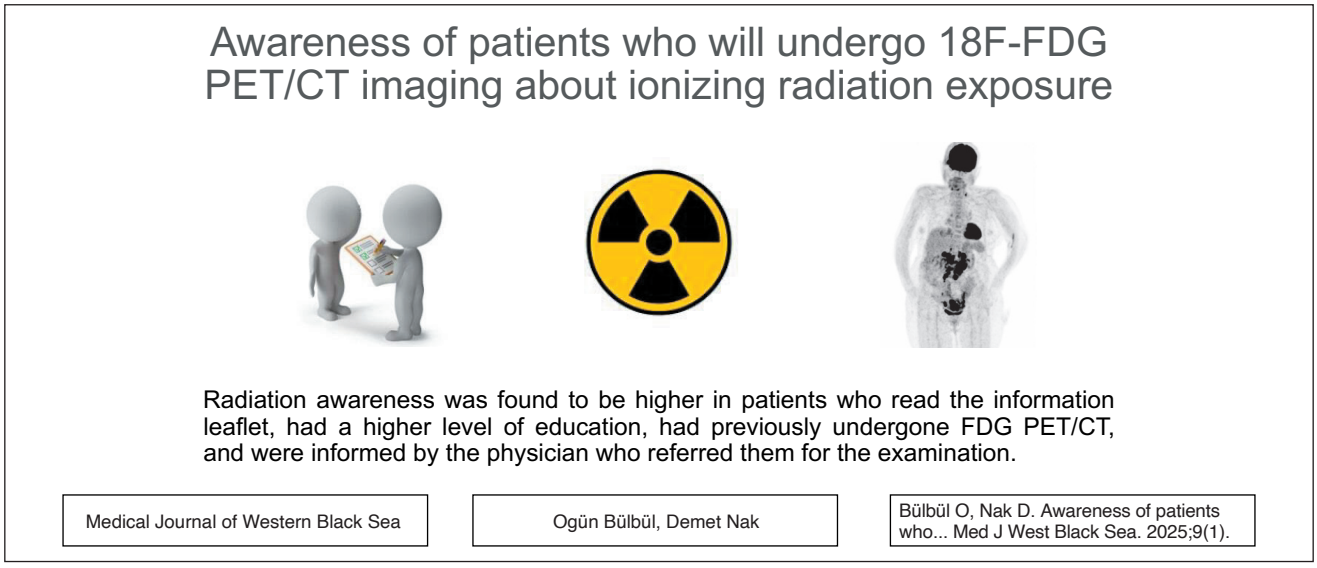
GRAPHICAL ABSTRACT



ABSTRACT

Aim: The use of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) is rising. This study aimed to investigate the awareness of patients undergoing FDG PET/CT about the ionizing radiation exposure related to the examination.

Material and Methods: One hundred and eleven patients who applied to our department for FDG PET/CT were asked the survey questions before FDG injection. Patients were asked to choose the most appropriate answer among the options. The effect of some factors on the patient's responses was investigated. Chi-square and Fisher's exact test were used for statistical analysis.

Results: Approximately eighty-one percent of the patients who read the information leaflet (78/96) and 40% of the patients who did not (6/15) knew what radiation is (p=0.001). Eighty percent of patients with an education level of high school and above (16/20) and 42.9% of patients of secondary school and below (39/91) knew how long FDG would affect the people around them (p=0.011). Approximately 40% of

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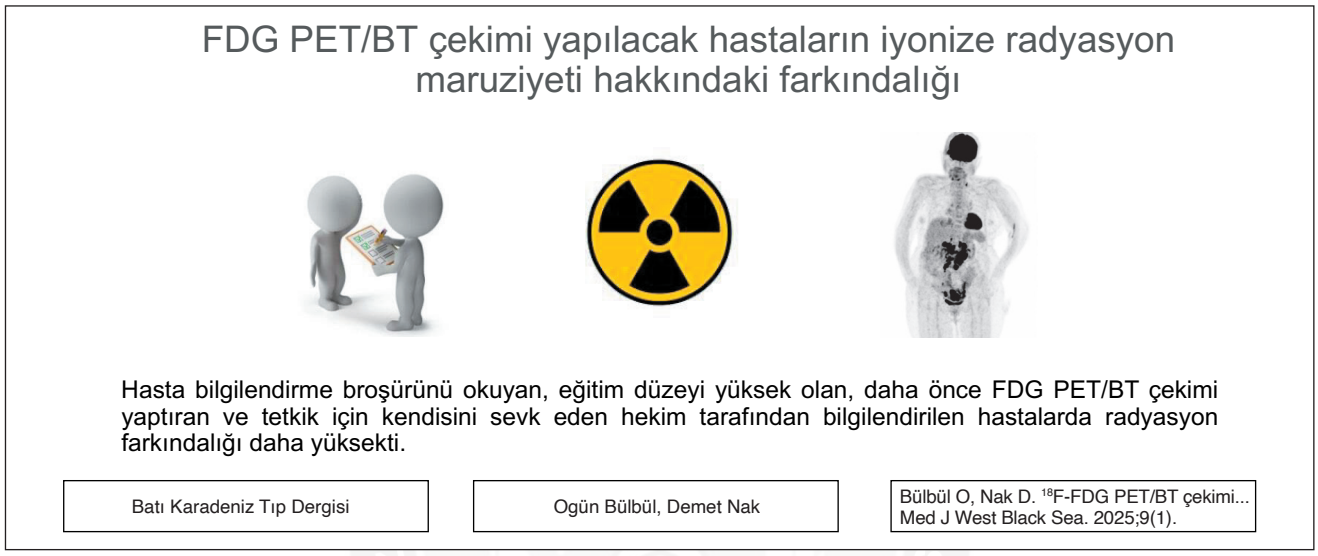
the patients who were informed about the test by their physician (21/52) and 25.5% of those who were not (12/47) were aware that repeated radiation exposure increases the risk of cancer development (p=0.021). Approximately 54% of patients (60/111) reported radiation exposure in magnetic resonance imaging, 34.2% (38/111) in ultrasonography, and 81.1% (90/111) in FDG PET/CT.

Conclusion: According to our study's results, radiation awareness was found to be higher in patients who read the information leaflet, had a higher level of education, had previously undergone FDG PET/CT, and were informed by the physician who referred them for the examination.

Keywords: Awareness, ^{18}F-fluorodeoxyglucose, ionizing radiation, positron emission tomography/computed tomography.

GRAFİKSEL ÖZET



ÖZ

Amaç: ^{18}F-florodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı tomografinin kullanımı artmaktadır. Bu çalışmadaki amacımız FDG PET/CT çekimi yapılacak hastaların tetkike bağlı iyonize radyasyon maruziyeti hakkında farkındalığını araştırmaktır.

Gereç ve Yöntemler: Departmanımıza FDG PET/CT çekimi için başvuran hastalara FDG enjeksiyonu yapılmadan önce anket soruları soruldu. Hastalardan kendilerine en uygun cevabı seçenekler arasından seçmesi söylendi. Bazı faktörlerin hastaların radyasyon hakkındaki sorulara verdikleri cevaplar üzerine etkisi araştırıldı. İstatistiksel analiz için ki-kare ve Fisher's exact test kullanıldı.

Bulgular: Bilgilendirme formunu okuyan hastaların yaklaşık %81'i (78/96), okumayanların %40'ı (6/15) radyasyonun ne olduğu hakkında bilgi sahibiydi (p=0.001). Eğitim seviyesi lise ve üstü olan hastaların %80'i (16/20), ortaokul ve altı olan hastaların ise %42.9'u (39/91) FDG'nin etraftaki insanları ne kadar süre etkileyeceğini biliyordu (p=0.011). FDG PET/CT çekim endikasyonu koyan doktorun tetkik hakkında bilgilendirdiği hastaların yaklaşık %40'ı (21/52), bilgilendirmediği hastaların ise %25.5'i (12/47) tekrarlayan radyasyon maruziyetinin kanser gelişim riskini artırdığını biliyordu (p=0.021). Hastaların yaklaşık %54'ü (60/111) manyetik rezonans görüntülemede, %34.2'si (38/111) ultrasonografide radyasyon maruziyeti olduğunu söyledi, %18.9'u (21/111) FDG PET/BT'de radyasyon maruziyeti olmadığını söyledi.

Sonuç: Çalışmamızın sonuçlarına göre bilgilendirme broşürünü okuyan, eğitim düzeyi yüksek olan, daha önce FDG PET/CT çektiren ve tetkike yönlendiren hekim tarafından bilgilendirilen hastaların radyasyon farkındalığı daha yüksek bulunmuştur.

Anahtar Sözcükler: Farkındalık, ^{18}F-florodeoksiglukoz, iyonize radyasyon, pozitron emisyon tomografisi/bilgisayarlı tomografi

INTRODUCTION

Medical imaging is widely used for the diagnosis of many diseases. Some of these imaging modalities (such as computed tomography (CT)) lead to exposure to ionizing radiation. The frequency of use of medical imaging has increased over the years (1). Medical imaging has become the primary source of artificial radiation exposure for the human body (2). The importance of this is that ionizing radiation exposure is associated with the development of malignancy (3-8). Among medical imaging, CT is the most commonly used medical imaging method, and its use is increasing mostly (9). Therefore, CT appears to be the most severe cause of artificial radiation exposure. ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is a molecular imaging modality that has been frequently used in the imaging of cancer patients in recent years (10). FDG PET/CT is a hybrid medical imaging modality with functional information about tissues provided by FDG molecule and anatomical correlation/attenuation correction provided by CT. FDG causes ionizing radiation exposure by positron decay, and CT causes X-ray exposure. Therefore, FDG PET/CT is a significant source of artificial radiation exposure in cancer patients. Since FDG PET/CT is mainly used in cancer patients, ionizing radiation exposure is not avoided, considering the benefit-harm balance. However, the ionizing radiation content of FDG PET/CT in pediatric patients and patients with prolonged survival (such as Hodgkin's lymphoma and breast cancer) deserves more attention.

Many studies in the literature have shown that patients do not have sufficient information about radiation exposure due to medical images (2,11-14). Surprisingly, some physicians consider magnetic resonance imaging (MRI) and ultrasonography (US) to contain ionising radiation (15). In addition to the developments in the field of medical imaging, the lack of awareness of patients and physicians about ionizing radiation may also be one of the reasons for the increased frequency of use of medical imaging. This study aimed to investigate the awareness of patients undergoing FDG PET/CT that this examination is a source of ionising radiation exposure.

MATERIALS and METHODS

This study was approved by the local ethics committee (Decision no: 2024/121). The ethics committee did not deem it necessary to obtain informed consent from the patients for this study. However, patients signed an informed consent form for FDG PET/CT examination.

Patients

All patients who came to our department for FDG PET/CT between 1 April 2024 and 30 June 2024 were asked whether they would like to participate in a verbal survey questioning some demographic information and the ionising radiation content of FDG PET/CT. Inclusion criteria for the study: 1- Patient's agreement to participate in the survey, 2- Patients whose medical condition was suitable for understanding and answering the questions were asked the questions. Exclusion criteria from the study: 1- Patients' unwillingness to participate in the survey, 2- Patients whose medical condition was not suitable for understanding and answering the questions. The full version of the survey is available in the supplementary material. Questions related to patients' awareness of radiation include:

- Have you had a FDG PET/CT scan before? If yes, how many FDG PET/CT scans have you had before?
- Did you read the patient information leaflet or did someone else read the patient information leaflet to you before you came for FDG PET/CT?
- Do you have information about what radiation is?
- Do you have information about the effects of radiation on the human body?
- Do you know that FDG PET/CT will cause ionizing radiation exposure to your body?
- Did the physician who referred you for FDG PET/CT explain to you that PET/CT will cause radiation exposure to your body?
- Does repeated radiation exposure increase the risk of developing cancer?
- Which examinations cause radiation exposure?
- Do you know how long the radioactive substance fluorodeoxyglucose (FDG) injected into your body for the PET/CT scan can affect the people around you?
- Do you know how long it takes for the radioactive substance fluorodeoxyglucose (FDG), which is injected into your body for the PET/CT scan, to be present in your body in such small quantities that it almost disappears?
- Are you aware of the ways in which the radioactive substance FDG (fluorodeoxyglucose) which is injected into your body for the PET/CT scan can contaminate the environment?

The patients' responses to the questions related to radiation were evaluated based on their declarations. For example, if the patient answered 'yes' to the question 'Do you have information about what radiation is?', no further questions were asked to the patient to question the reliability of this answer.

Statistical Analysis

Demographic data of the patients were presented by descriptive statistical methods. The patients' responses to the questions were described in frequency tables. The effects of nominal variables such as gender and educational status on the answers to the questions were evaluated by Pearson

chi-square analysis and Fisher's exact test. For statistical analysis, SPSS 24 software (IBM Corp., Armonk, NY, USA) was used. P<0.05 was accepted as statistically significant at a 95% confidence interval.

RESULTS

Approximately fifty-two (47%) patients were female and 59 (53%) were male in the study. The mean age of patients was 64 ± 12 years. The educational level of 82% of the patients was secondary school and below, while 18% of them were high school and above. FDG PET/CT was performed previously in 53.2% of the patients. Detailed information about the patients is given in Table 1.

The percentages of patients answering 'yes' to questions 9, 10, 11, 14, 16, 17, and 18, which asked whether radiation and its effects were known or not, were approximately 77%, 54%, 64%, 30%, 50%, 41%, and 34%, respectively.

Approximately 81% of the patients who read the information leaflet and 40% of those who did not, were aware of what radiation is (Question 9, p=0.001) (Figure 1 and Table 2). Approximately fifty-four percent of the patients who read the leaflet and 20% of those who did not know how

Table 1. Detailed patient characteristics.

	Sonuç (n=111)
Age (Years) (Mean ± standardized deviation)	64 ± 12
Gender, n (%)	
- Female	52 (46.8)
- Male	59 (53.2)
Educational level, n (%)	
- Illiterate	20 (18.0)
- Primary school	54 (48.6)
- Secondary school	16 (14.4)
- High school	15 (13.5)
- University and above	6 (5.5)
Previous FDG PET/CT imaging, n (%)	
- Yes	59 (53.2)
- No	52 (46.8)
Referring department, n (%)	
- Non-surgical departments	102 (91.9)
- Surgical departments	9 (8.1)

FDG: ^{18}F-fluorodeoxyglucose, **PET/CT:** positron emission tomography/computed tomography

Table 2. The effect of reading the patient information leaflet, educational level, and previously undergoing FDG PET/CT on patient awareness about radiation in PET/CT.

		Reading the patient information leaflet			p-value
		Yes	No	Unsure	
Knowing what radiation is, n (%)	Yes	78 (81.2)	11 (11.5)	7 (7.3)	**0.001**
	No	6 (40.0)	4 (26.7)	5 (33.3)	
		Reading the patient information leaflet			**p-value**
		Yes	No	Unsure	
Knowing how long FDG affects people around the patient, n (%)	Yes	52 (54.2)	33 (34.4)	11 (11.4)	**0.048**
	No	3 (20.0)	9 (60.0)	3 (20.0)	
		Knowing how long FDG affects people around the patient			**p-value**
		Yes	No	Unsure	
Educational level, n (%)	High school and above	16 (80.0)	3 (15.0)	1 (5.0)	0.011
	Secondary school and below	39 (42.9)	39 (42.9)	13 (14.2)	
		Knowing how long FDG affects people around the patient			**p-value**
		Yes	No	Unsure	
Previously undergoing FDG PET/CT, n (%)	Yes	39 (66.1)	16 (27.1)	4 (6.8)	0.011
	No	16 (30.8)	26 (50.0)	10 (19.2)	
		Knowing that repeated radiation exposure increases the risk of cancer development			**p-value**
		Yes	No	Unsure	
Information provided by the referring physician, n (%)	Yes	21 (40.4)	2 (3.8)	29 (55.8)	0.021
	No	12 (25.5)	6 (12.8)	29 (61.7)	
	Unsure	0 (0.0)	3 (25.0)	9 (75.0)	

FDG: ^{18}F-fluorodeoxyglucose, **PET/CT:** positron emission tomography/computed tomography,

long FDG affects people in the neighborhood (Question 17, p=0.048) (Figure 2 and Table 2). Approximately 39% of the patients younger than 75 years and 50% of the older patients knew the approximate time after which FDG would be almost non-existent in the body (Question 10, p=0.040). Eighty percent of patients with an education level of high school and above and 42.9% of patients with an education level of secondary school and below knew how long FDG would affect the people around them (Question 9, p=0.011) (Figure 3 and Table 2). Approximately 65% of patients with high school education and above and 35% of patients with secondary school education and below knew approximately how long it would take for the FDG to disappear from the body (Question 10, p=0.048). Approximately 7% of patients who had undergone FDG PET/CT and six percent who had not had FDG PET/CT had correct knowledge about the radiation doses of FDG PET/CT and thoracoabdominopelvic CT (The radiation doses of both examinations are close to each other (16)). Approximately 66% of patients who had previously undergone FDG PET/CT and 31% of those who had not had FDG PET/CT knew how long FDG would affect people around them (Question 9, p=0.001) (Figure 4

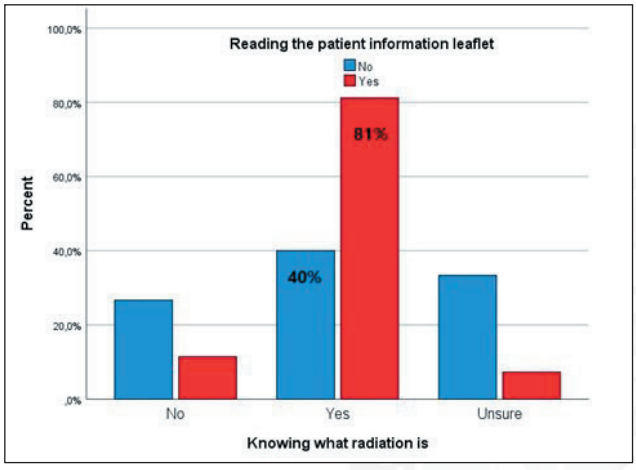


Figure 1: The effect of reading the patient information leaflet on knowing what radiation is. Eighty-one percent of the patients who read the information leaflet and 40% of those who did not were aware of what radiation is (p=0.001).

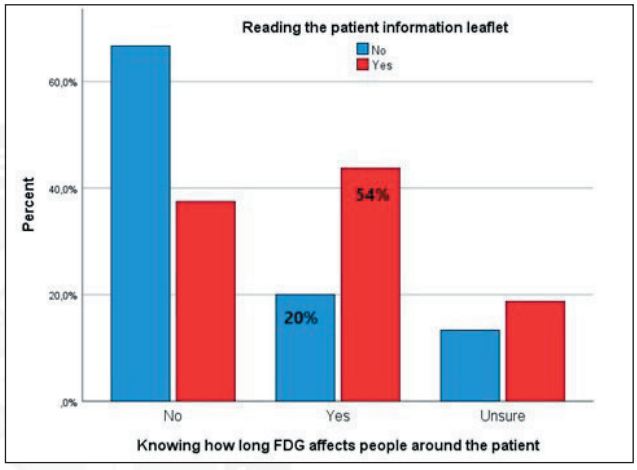


Figure 2: The effect of reading the patient information leaflet on knowing how long FDG affects people around the patient. Fifty-four percent of the patients who read the leaflet and 20% of those who did not know how long FDG affects people in the neighborhood (p=0.048).

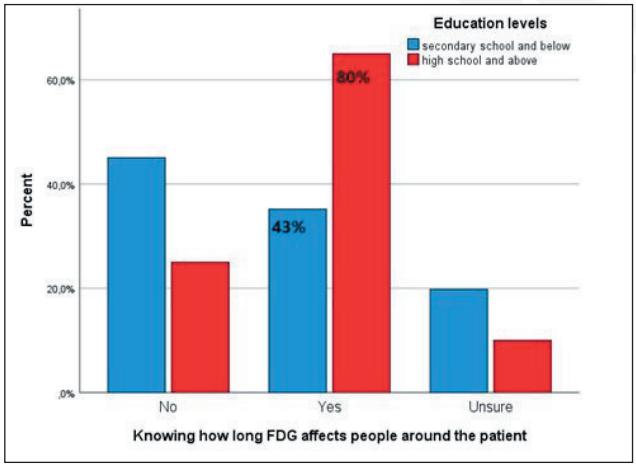


Figure 3: The effect of educational levels on knowing how long FDG affects people around the patient. Eighty percent of patients with an education level of high school and above and 43% of patients with an education level of secondary school and below knew how long FDG would affect the people around them (p=0.011).

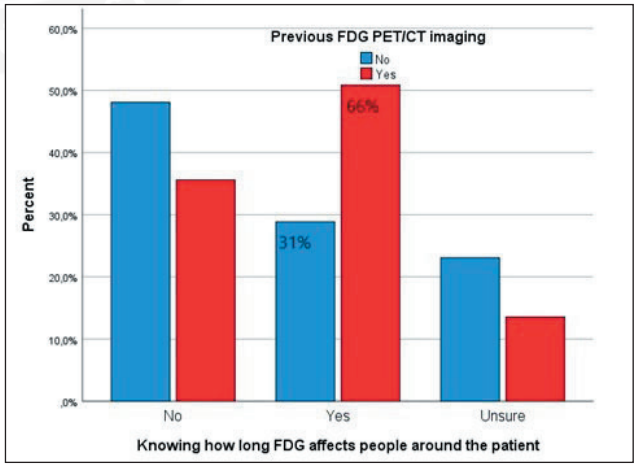


Figure 4: The effect of previously undergoing FDG PET/CT on knowing how long FDG affects people around the patient. Sixty-six percent of patients who had previously undergone FDG PET/CT and 31% of those who had not had FDG PET/CT knew how long FDG would affect people around them (p=0.001).

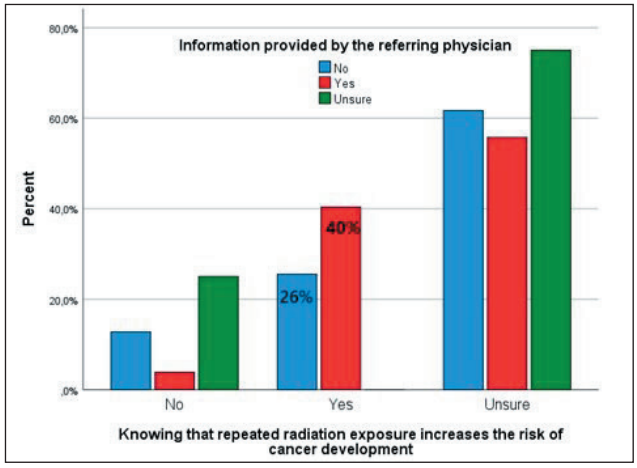


Figure 5: The effect of being informed by the referring physician on knowing that repeated radiation exposure increases the risk of cancer development. Forty percent of the patients who were informed about the test by the physician indicating FDG PET/CT, and 26% of the patients who were not informed knew that repeated radiation exposure increases the risk of cancer development (p=0.021).

and Table 2). Approximately 40% of the patients who were informed about the test by the physician indicating FDG PET/CT, and 25.5% of the patients who were not informed knew that repeated radiation exposure increases the risk of cancer development (Question 6, p=0.021) (Figure 5 and Table 2). Patients informed by the physician had a higher percentage of correct answers to Question 16 and Question 17 (Question 16, approximately 66% vs. 30%, p=0.011; Question 17, approximately 58% vs. 23%, p=0.014). Approximately 48% of patients referred for FDG PET/CT by surgical departments and approximately 33% of patients referred by nonsurgical departments reported having information about the effects of radiation on the human body, but this difference was not statistically significant. This is probably because there were 102 patients referred by internal and nine patients referred by surgical departments in our study. There was no statistically significant difference between the answers given by male and female patients to the questions in this study. Results that were not statistically significant were not presented as tables.

Approximately 47% of patients reported no radiation exposure in X-ray, 45% in CT, 19% in PET/CT, and 74% in mammography. Approximately 54% of patients reported radiation exposure in MRI, 34% in US.

DISCUSSION

Many studies have shown that patients do not have sufficient information about radiation exposure in medical imaging (2,11-14). In this study, we investigated the knowledge of patients undergoing FDG PET/CT about radiation exposure and the effects of some factors on this situation. According to the results of our study, patients who read the information leaflet, had a higher level of education, had undergone FDG PET/CT before, and were informed about the examination by the referring physician answered 'yes' with a higher percentage when asked whether they knew the questions about the radiation involvement of FDG PET/CT examination.

Schuster et al. asked 101 patients who underwent abdominopelvic CT in the emergency department and health care providers, including physicians practicing in the hospital, to compare the radiation dose of the examination with chest X-ray (12). Of the 61 patients who answered the comparison question, 14 (23%) gave the correct answer (the radiation exposure from 1 CT is approximately the same as from 100-250 chest X-rays). Patients who had discussed the radiation dose of the examination with their physician were more likely to estimate the correct radiation dose. In our study, patients who were informed by the referring physician were better aware of how long FDG affects the environment and how long FDG remains in the body in undetectable amounts than those who were not informed.

Singh et al. analysed patients' knowledge about radiation in medical imaging and its risks (13). Only 30.6% of the patients included in the study knew that PET/CT caused radiation exposure. In the same study, 48.3% of the patients reported that MRI, and 9.9% reported that US caused radiation exposure. In addition, only 34.2% of the patients knew that CT caused more radiation exposure than X-ray. Sin et al. conducted a survey study with 173 patients and measured their knowledge about radiation in medical imaging and its effects (14). 60.7% of patients did not know that MRI is a radiation-free medical imaging modality, and 32.7% did not know that US is a radiation-free modality. Only 17.8% of patients had correct information about the risk of developing fatal cancer due to CT. In our study, 81.1% of the patients knew that FDG PET/CT includes radiation. However, our study aims to measure the radiation awareness of patients undergoing FDG PET/CT. The higher rate of our patients knowing that FDG PET/CT contains radiation may be associated with 'bias.' However, in our study, the percentage of patients who thought that MRI and US contained radiation was similar to the literature (54% and 34%, respectively).

Ribeiro et al. investigated whether 50 patients undergoing bone scintigraphy and 52 patients undergoing FDG PET/CT were informed about the radiation content of these examinations and whether patient information leaflets provided sufficient information (11). Thirty-seven percent of patients reported not having sufficient knowledge about nuclear medicine. Only 6.7% of the questions about the ionizing radiation content of FDG PET/CT were answered correctly by the patients, and 66.8% were answered with 'I do not know.' Interestingly, 75.6% of the patients who received informa-

tion leaflets from the nuclear medicine department thought that these leaflets provided sufficient information. Patients who had previously undergone FDG PET/CT and patients with better educational status were more likely to answer the questions correctly. In our study, patients who had previously undergone FDG PET/CT answered question 9 as 'yes' in a higher percentage, and patients with higher educational levels answered question 9 and question 10 as 'yes' in a higher percentage.

The knowledge of the referrers about the radiation content of medical imaging methods and cancer formation due to this radiation is not sufficient. Uri et al. assessed the knowledge of patients' referrers about medical images' radiation content (15). Thirty-seven percent of the participants correctly ranked the radiation doses of radiological imaging techniques. Fifteen percent of the participants stated that US and MRI contain radiation, and 11% stated that radionuclide studies do not contain radiation. Also, in clinics working under heavy working conditions, it may not be possible to ensure that the referrers inform the patients adequately. Therefore, adequate information of the patients by the departments performing medical imaging will increase the awareness of the patients about radiation. Patient information leaflets should contain more satisfying information about the radiation content of the examinations and potential cancer formation due to this radiation. These information leaflets should be enriched with attention-grabbing content (visuals, etc.) and made more readable.

This study has some limitations. This survey-based study is a single-center study conducted in a clinic where approximately 12 patients per day undergo FDG PET/CT. Therefore, the number of patients participating in the study was limited. When analysing the results of our study, readers should be aware that the generalisability of these results to patient populations in different countries is limited. Studies involving larger centers with more PET/CT scans may be more representative of the population. The patients' responses to the questions related to radiation were evaluated based on their declarations. For example, if the patient answered 'yes' to the question 'Do you have information about what radiation is?', no further questions were asked to the patient to question the reliability of this answer. The educational status of the patients participating in the study is heterogeneous. Since the number of patients with low educational status was high in this study, their radiation awareness may be lower than the radiation awareness of patients in developed countries. However, we recommend paying attention to the difference between the radiation awareness of patients with and without low educational status when interpreting the results of our study.

According to our study's results, radiation awareness was found to be higher in patients who read the information leaflet, had a higher level of education, had previously undergone FDG PET/CT, and were informed by the physician who referred them for the examination. To increase patients' awareness of radiation exposure, it would be useful to ensure that their referring physicians adequately inform patients and that the information leaflets given to patients for examinations in diagnostic medicine departments are carefully prepared.

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None.

Author Contributions

Concept: **Ogün Bülbül,** Design: **Ogün Bülbül, Demet Nak,** Data collection and processing: **Ogün Bülbül, Demet Nak,** Analysis and interpretation: **Ogün Bülbül, Demet Nak,** Literature search: **Ogün Bülbül,** Writing: **Ogün Bülbül,** Approval: **Ogün Bülbül, Demet Nak.**

Conflicts of Interest

The authors declare no conflict of interest.

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The authors declare that no financial support received by authors for this research.

Ethical Approval

This study was approved by Ethics Committee and conducted according to the principles of the Declaration of Helsinki (Decision date: 13.06.2024, approval number: 2024/155). The ethical committee waived the requirement for informed consent.

Review Process

Extremely and externally peer-reviewed.

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ORIGINAL ARTICLE

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The Relationship Between Adaptation to Chronic Disease and Medication Adherence, Frequency of Emergency Department Visits, and Quality of Life in Individuals with Chronic Disease

Kronik Hastalığa Sahip Bireylerde Hastalığa Uyum, İlaç Uyumu, Acil Servis Ziyaret Sıklığı ve Yaşam Kalitesi Arasındaki İlişki

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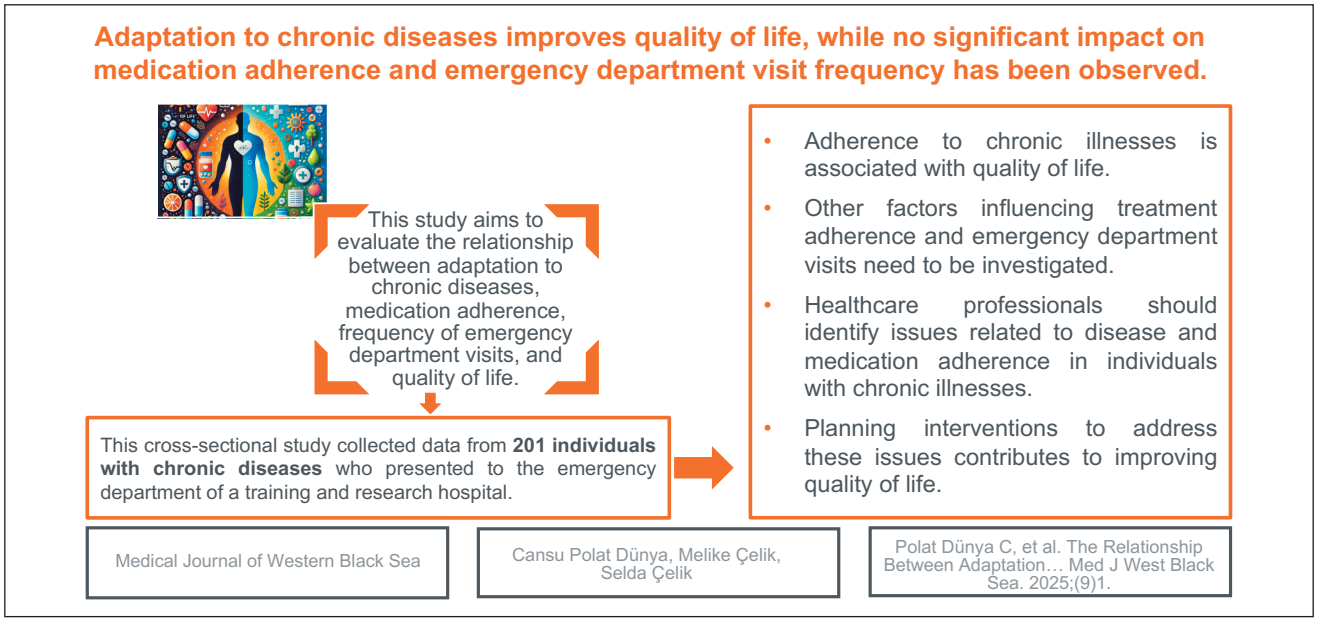
GRAPHICAL ABSTRACT



ABSTRACT

Aim: The study aimed to determine how people with chronic diseases adapt to disease and treatment and examine the relationship between the frequency of emergency department visits and quality of life.

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Material and Methods: This cross-sectional study was conducted with 201 people with chronic diseases admitted to the emergency department of a training and research hospital. Data were collected using the Patient Information Form, Adaptation to Chronic Diseases Assessment Scale, Morisky, Green, Levine Adherence Scale, and EuroQol-5D Quality of Life Scale.

Results: The mean age of the people with chronic diseases was 69.37±12.17 years. The three most common chronic diseases were hypertension 76.6%, diabetes mellitus 39.3%, and heart failure 27.9%. In the last year, 31.8% of the patients had visited the emergency department more than three times. The mean total score of adaptation to chronic diseases was 65.33±7.39, the mean medication adherence score was 1.97±0.73 and the mean quality of life score was 56.87±17.78. There was a relationship between adaptation to chronic diseases and quality of life ($p<0.001$). However, there was no relationship between adaptation to chronic diseases, medication adherence, and frequency of emergency department visits.

Conclusion: This study shows that adaptation to chronic disease is associated with quality of life and other factors affecting adherence to treatment and emergency department visits should also be investigated. Healthcare professionals' identification of problems of adaptation to disease and medication use in people with chronic diseases, and planning of interventions to address these problems, will contribute to improving quality of life.

Keywords: Adaptation, chronic disease, medication adherence, emergency department, quality of life

GRAFİKSEL ÖZET

ÖZ

Amaç: Araştırmanın amacı, kronik hastalığa sahip bireylerin hastalığa ve tedaviye uyumlarının belirlenmesi, acil servise başvuru sıklığı ve yaşam kalitesi arasındaki ilişkinin incelenmesidir..

Gereç ve Yöntemler: Kesitsel nitelikte olan bu çalışma bir eğitim araştırma hastanesinin acil servisine başvuran kronik hastalığı olan 201 birey ile gerçekleştirildi. Veriler "Hasta Tanılama Formu", "Kronik Hastalıklara Uyumu Değerlendirme Ölçeği", "Morisky, Green, Levine Uyum Ölçeği" ve "EuroQol-5D Yaşam Kalitesi Ölçeği" kullanılarak toplandı.

Bulgular: Kronik hastalığı olan bireylerin yaş ortalaması 69,37±12,17 idi. En sık görülen ilk üç kronik hastalık %76,6 hipertansiyon, %39,3 diabetes mellitus ve %27,9 kalp yetersizliği idi. Hastaların son bir yıl içinde %31,8'inin üç defadan fazla acil servise başvurmuştu. Kronik hastalıklara uyum toplam puan ortalaması 65,33±7,39, ilaç uyumu puan ortalaması 1,97±0,73 ve yaşam kalitesi puan ortalaması 56,87±17,78 idi. Kronik hastalıklara uyum ile yaşam kalitesi arasında ilişki vardı ($p<0.001$). Ancak kronik hastalığa uyum ile ilaç uyum ve acil servise başvuru sıklığı arasında ilişki bulunmadı.

Sonuç: Bu çalışma, kronik hastalığa uyumun yaşam kalitesi ile ilişkili olduğunu, tedaviye uyum ve acil servis başvurularını etkileyen diğer faktörlerin de araştırılması gerektiğini göstermektedir. Sağlık profesyonellerinin kronik hastalığı olan bireylerin hastalığa ve ilaç kullanımına uyum sorunlarını belirlemeleri ve sorunların çözümüne yönelik girişimlerini planlamaları yaşam kalitesinin artırılmasına katkı sağlayacaktır.

Anahtar Sözcükler: Uyum, kronik hastalık, ilaç uyumu, acil servis, yaşam kalitesi

INTRODUCTION

Chronic diseases are health problems that profoundly affect the quality of life of people and place a heavy burden on health systems. Diseases such as cardiovascular disease, diabetes, and respiratory disorders require long-term care and treatment. The impact of these diseases is not only limited to physical health but also significantly affects the overall well-being and quality of life of those affected (1,2). Managing chronic diseases involves a complex process that requires individuals to make substantial changes in their lives.

One of the most important factors in the successful management of chronic diseases is ensuring adaptation to the disease. Adaptation is the process of accepting changes in the internal and external environment and developing attitudes and behaviors appropriate to these changes (3). However, only a few studies have investigated adaptation to chronic disease (3-7). The adaptation process in people with chronic diseases is influenced by several factors, including cognitive and emotional status, disease severity and complications, knowledge and awareness about the disease, financial status, presence of social support, access to healthcare services, and treatment adherence (3,4). Among these factors, medication adherence plays a critical role in controlling chronic diseases. Regular and correct use of prescribed medications is a fundamental element of disease management. Poor medication adherence can lead to uncontrolled chronic diseases, resulting in acute exacerbations and disease-related complications (8,9). Furthermore, lack of access to appropriate outpatient care leads to more frequent emergency department visits, increasing the burden on emergency departments from individuals with chronic diseases (10,11). Therefore, it is of great importance to investigate the effects of disease and treatment adherence on the frequency of emergency department visits and quality of life in people with chronic diseases. A review of the literature shows that medication adherence and quality of life are often emphasized in people with chronic diseases (8,9). However, there is a limited amount of research on the relationship between chronic disease adherence to medication, frequency of emergency department visits, and quality of life (5,7,12).

The purpose of this study is to examine the relationship between adaptation to chronic diseases and medication adherence, frequency of emergency department visits, and quality of life in individuals with chronic diseases.

MATERIALS and METHODS

Research Design

The study is descriptive and cross-sectional in design. This study aimed to address the following research questions: What is the relationship between adaptation to chronic diseases and medication adherence? How does adaptation to chronic diseases affect the frequency of emergency department visits? and What is the association between adaptation to chronic diseases and quality of life?

The population of the study consisted of individuals who met the inclusion criteria and visited the emergency department of a training and research hospital in Istanbul between October 2021 and May 2022. A purposive sampling method was used to select participants. The inclusion criteria included being 18 years of age or older, having at least one chronic disease, receiving multiple drug treatments, being able to communicate verbally, and volunteering to participate in the study. Individuals with severe cognitive problems were excluded. The study was concluded with 201 individuals due to reasons such as unwillingness to participate (inability to focus on the survey due to the urgency of their situation) and incomplete survey responses (Participation rate: 82%). Following data collection, a post-hoc power analysis was conducted to ensure that the study's sample size was sufficient to detect statistically significant results with a power of 95%, a significance level of 0.05, and an effect size of 0.45.

Data Collection Tools

Patient information forms, Adaptation to Chronic Diseases Assessment Scale, Morisky, Green, Levine Adherence Scale, and EUROQOL 5D-Visual Analog Scale were administered to patients who met the study's inclusion criteria.

Patient Information Form: This form, which was prepared in line with the literature, includes questions on the socio-demographic characteristics (age, gender, income status, etc.) of individuals with chronic diseases and questions on disease diagnosis and treatment (3-7).

Adaptation to Chronic Diseases Assessment Scale: The scale was developed by Kacaroğlu and Birgili (3). The scale consists of 28 items and the responses are in triple Likert type (1=strongly agree, 2=undecided, 3=strongly disagree). The scale has four sub-dimensions: Physiological (4 items), Psychological (16 items), Social (5 items) and Spiritual (3 items). The score that can be obtained from the scale is in the range of 28-84. As the score obtained from the scale increases, the adaptation level of individuals to chronic diseases increases. In the Turkish version of the scale, the total Cronbach's alpha value was 0.83 (3). In this study, it was calculated as 0.80.

Morisky, Green, Levine Adherence Scale: This scale was developed by Morisky et al. to evaluate drug compliance (13). The status of believing in the benefit of treatment, the habit of taking medication on time, and the status of forgetting or stopping medication are questioned. The scale consists of four questions. In the evaluation of the answers given as "Yes" or "No"; in question 2, the yes answer is calculated as 1

point, and the no answer is calculated as 0 point; in the other questions, the yes answer is calculated as 0 points and no answer is calculated as 1 point. A high score indicates high medication compliance. In the Turkish adaptation study of the scale, Cronbach's alpha reliability coefficient was found to be 0.62 (14). In this study, the Cronbach's alpha reliability coefficient was found to be 0.68

EUROQOL 5D-Visual Analog Scale: It is a visual analog scale in which individuals give values between 0 and 100 about their current health status and mark it on a thermometer-like scale. A high score obtained from the scale indicates a high quality of life. In the Turkish adaptation study of the scale, Cronbach's alpha reliability coefficient was found to be 0.86 (15). In this study, the Cronbach's alpha reliability coefficient was found to be 0.83.

Data Collection

Individual patient interviews conducted face-to-face were used to gather research data. Each patient was informed before the study, and their informed consent was obtained verbally and in writing to participate in the research.

Ethical Considerations

Declaration of Helsinki principles were followed in the conduct of the study. Ethics committee permission was obtained from the Health Sciences University Hamidiye Scientific Research Ethics Committee (Date:21.09.2021 and Number:4656) Written and verbal "Informed Voluntary Consents" were obtained by explaining to the individuals who volunteered to participate in the research that the purpose of the study, all personal information would remain confidential, they could leave the research at their request and the research data would not be shared with anyone.

Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences 21.0 (IBM Corp., Armonk, NY, USA). Descriptive statistical methods (Number, Percentage, Mean, Standard deviation) were used to evaluate the data. The normal distribution of the data was analyzed by Kolmogorov-Smirnov and Shapiro-Wilk tests. Kruskal-Wallis non-parametric tests were used to compare variables between groups in the case of more than two groups. When there was a significant difference between the groups, Dunn's post hoc test was used to determine which particular groups showed significance. The relationship between the variables of the study was tested by Spearman correlation analysis. The findings were evaluated at a 95% confidence interval and 5% significance level.

RESULTS

The mean age of the people with chronic disease was 69.37±12.17 (Min-Max= 21-88) years. It was determined that 65.2% of the population was male, 69.7% had a primary school and lower education, 77.6% were married and 70.1% had moderate income (Table 1).

The most common chronic condition was hypertension, affecting 76.6% of participants, followed by diabetes mellitus (39.3%), heart failure (27.9%), arrhythmias (26.9%), COPD (9%), kidney failure (3.5%), and other diseases (9%). The mean number of chronic diseases was 1.92± 0.94 (Min-Max: 1-5). In terms of education about their disease, 67.7% had not received any training, while 32.3% had received training. When it comes to attending regular health checkups, 51.7% of participants reported attending regularly, whereas 48.3% did not. Regarding emergency department visits in the past year, 68.2% visited 1-3 times, 18.9% visited 4-6 times, and 12.9% visited 7 or more times. The primary reason for visiting the emergency department was chest pain (81.6%), followed by getting an examination (12.4%), and other reasons such as prescribing medication (6%) (Table 2).

The mean total score of adaptation to chronic diseases was found to be 65.33±7.39. It was observed that 80.6% of the patients had moderate medication adherence. The mean quality of life score was 56.87±17.75 (Table 3).

A positive and significant relationship was found between the total and subscale scores of the chronic disease adaptation assessment scale and quality of life. There is a moderate, positive, and statistically significant relationship between physiological adaptation (rho = 0.312, p = 0.014) and psychological adaptation (rho = 0.353, p <0.001) with quality of life. Social adaptation (rho = 0.246, p <0.001) and spiritual adaptation (rho = 0.139, p = 0.048) show a weak but statistically significant positive relationship with quality of life. There was no significant relationship between adherence to chronic diseases and medication adherence (Table 4).

Table 1. Distribution of sociodemographic characteristics of people with chronic diseases

Distribution of sociodemographic characteristics		Findings (n=201)
Gender, n (%)	Female	70 (34.8)
	Male	131 (65.2)
Education status, n (%)	Primary school and lower education	140 (69.7)
	High school	34 (16.9)
	University and higher education	27 (3.4)
Marital status, n (%)	Married	156 (77.6)
	Single	45 (22.4)
Income status, n (%)	Income > expenses	22 (11)
	Income = expenses	141 (70.1)
	Income < expense	38 (18.9)

The present study analyzed adaptation to chronic diseases based on various disease characteristics. There was no significant difference in adaptation levels among individuals who visited the emergency department 1-2 times (65.16±7.49), 4-6 times (66.23±6.22), or 7 or more times (64.92±8.53) within the past year (KW = 0.158, p = 0.924). However, we found a statistically significant difference when examining adaptation levels based on the reasons for emergency department visits. A post hoc Dunn's test was conducted to determine which groups differed from each other. The results showed that individuals visiting for examinations (68.64±5.80) had significantly higher adaptation levels compared to those visiting due to chest pain (64.77±7.39) ($p < 0.05$). No significant difference was found between other groups (KW = 2.789, p = 0.044).

Table 2. Distribution of disease characteristics of people with chronic diseases

Distribution of disease characteristics		Findings (n=201)
Chronic Diseases*, n (%)	Hypertension	154 (76.6)
	Diabetes mellitus	79 (39.3)
	Heart failure	56 (27.9)
	Arrhythmias	54 (26.9)
	COPD	18 (9)
	Kidney failure	7 (3.5)
	Other	18 (9)
Receiving education about the disease, n (%)	Yes	65 (32.3)
	No	136 (67.7)
Attending regular health check-ups, n (%)	Yes	104 (51.7)
	No	97 (48.3)
Number of visits to the emergency department in the last year, n (%)	1-3 times	137 (68.2)
	4-6 times	38 (18.9)
	7 ve above	26 (12.9)
Reason for visiting the emergency department in the last year, n (%)	Chest pain	164 (81.6)
	Getting examination	25 (12.4)
	Other (prescribing medication etc.)	12 (6)

* More than one option was selected; **COPD:** Chronic Obstructive Pulmonary Disease

Table 3. Mean scores of adaptation to diseases, medication adherence, and quality of life of people with chronic diseases

Scores		Values (n=201)
Adaptation to Chronic Diseases*	Total	65.33±7.39 (44-80)
	Physiological	9.79±1.79 (4-12)
	Psychological	35.60±5.04 (24-48)
	Social	12.40±2.37 (5-15)
	Spiritual	7.54±1.81 (3-9)
$EQ\text{-}5D_{VAS}$*		56.87±17.78 (10-100)
Medication adherence*	Total	1.97±0.73 (0-4)
		n (%)
	Low (0 point)	6 (3)
	Moderate (1-2 points)	162 (80.6)
	High (3-4 points)	33 (16.4)

$EQ\text{-}5D_{VAS}$: EUROQOL 5D-Visual Analog Scale, ***Min-Max:** Minimum-Maximum, **SD:** Standard Deviation

DISCUSSION

In this study, adaptation to chronic diseases was found to be associated with quality of life. However, it was observed that adaptation to chronic diseases did not make a significant difference on medication adherence and frequency of emergency department visits. In this context, our study emphasizes the importance of adaptation to chronic diseases in improving quality of life in the management of chronic diseases, but other factors affecting adherence to medication and emergency department visits should also be investigated.

Adaptation to chronic diseases has a critical importance in terms of controlling the disease, improving quality of life, preventing complications, protecting psychological and emotional health, and reducing health-related costs (3,4). For this purpose, the adaptation scale for chronic diseases developed by Kacaroglu and Birgili (3) guides in determining adaptation problems. In this study, it was found that the adjustment levels of individuals with chronic diseases were above the average (65.33±7.39). In the literature, it is supported by similar findings that the adjustment levels of individuals with different chronic diseases are above the average (5-7). These findings highlight the importance of tools for assessing patients' adaptation levels in clinical practice and provide healthcare professionals with the opportunity to develop care plans tailored to patients' needs. Strategies to enhance adaptation levels can be strengthened through initiatives such as patient education and support groups, contributing to the improvement of patient's quality of life. In this way, healthcare professionals can play a more effective role in chronic disease management and help patients cope with the challenges they face in their daily lives.

Table 4. The relationship between adaptation to diseases, medication adherence, and quality of life in people with chronic diseases

Adaptation to Chronic Diseases	Medication Adherence		$EQ\text{-}5D_{VAS}$	
	rho	p	rho	p
Physiological	-0.014	0.841	0.312	0.014
Psychological	0.027	0.706	0.353	<0.001
Social	0.077	0.276	0.246	<0.001
Spiritual	-0.022	0.761	0.139	0.048
Total	0.023	0.742	0.380	<0.001

$EQ\text{-}5D_{VAS}$: EUROQOL 5D-Visual Analog Scale, Spearman correlation, $p < 0.05$

Medication adherence in chronic diseases is a critical factor that directly affects the health outcomes of patients (8). Medication adherence requires taking medications at the right dose, at the right time, and regularly and is affected by various factors. In the literature, although adherence to chronic diseases is generally considered as medication adherence, studies frequently focus on specific diseases such as hypertension, diabetes, and renal diseases (8,16). In this study, it was found that 80.6% of individuals with different chronic diseases had moderate medication adherence. A comprehensive study by Garcia et al. found that 72.2% of patients with chronic heart disease were moderate/good adherent (17). In the literature, there are studies indicating that people with chronic disease have high medication adherence as well as studies reporting poor medication adherence (18,19). Adaptation to chronic disease covers a wide range and includes individual characteristics, level of awareness, and psychosocial and spiritual factors (3,4). In this study, no relationship was found between medication adherence and adaptation to general disease, and this may have resulted from the fact that the two types of adaptation have different components. Therefore, it is important that healthcare professionals evaluate patients in a comprehensive and individualized manner and question both disease and medication adherence in routine examinations.

Management of chronic diseases is closely related directly with the quality of life of patients (18). In people with various chronic diseases such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease, and renal failure, compliance with treatment is associated with quality of life (20-22). The positive relationship between adaptation to chronic diseases and quality of life occurs when patients improve their physical, psychological, and social lives (3-4). In this study, a significant relationship was observed between adaptation to chronic diseases and quality of life, which supports these findings. This shows that increasing adaptation to chronic diseases is an important factor in improving the quality of life of individuals. Factors such as education, motivation, and social support can contribute to the improvement of quality of life by promoting adaptation to chronic diseases. Therefore, healthcare professionals should be aware that chronic disease adaptation is associated with quality of life and reflect this awareness in health policies and programs. Developing strategies to increase adherence to chronic diseases will make significant contributions to the improvement of public health.

The management of chronic diseases is directly related to patients' quality of life (18). Studies have shown that adherence significantly improves the quality of life in chronic conditions such as hypertension, diabetes, chronic obstructive pulmonary disease, and kidney failure (20-22). Specifically, individuals who demonstrate high adherence to treatment experience positive benefits, including reduced physical symptoms, improved psychological well-being, and increased social participation. Chantzaras and Yfantopoulos (23) reported that diabetic patients who adhered to their treatment regimens showed significant improvements in both glycemic control and quality of life. Similarly, Jarab et al. (24) noted that individuals with chronic obstructive pulmonary disease who regularly took their medications and made lifestyle changes experienced reduced disease severity, thereby improving their quality of life. In this study, a significant relationship was found between adaptation to chronic diseases and quality of life, suggesting that patients can improve their quality of life by enhancing their physical, psychological, and social well-being. In this context, it is crucial to regularly assess patients' treatment adherence levels in clinical practice and develop personalized care plans. Health policies should promote the expansion of educational and counseling services tailored to the needs of individuals with chronic diseases. Additionally, strengthening support systems by forming multidisciplinary teams that include nurses, psychologists, dietitians, and social workers can offer an effective approach to enhancing patients' quality of life. Such strategies can help healthcare professionals develop more effective treatment processes and improve overall public health.

Since chronic diseases are conditions that require long-term and complex health management, different symptoms, acute changes, and various complications may be frequently observed in the health status of patients. It has been reported that approximately 40% of patients presenting to the emergency department are elderly and have chronic diseases (10,11). The reasons for presenting to the emergency department are quite diverse, including preventable presentations due to non-urgent problems (25). However, one of the surprising findings of our study was that there was no correlation between the frequency of emergency department visits and hospitalization status of individuals with chronic disease in the last year and their adaptation to chronic disease. This finding may have resulted from the lifestyle, socioeconomic status, access to the healthcare system, comorbidities (other comorbidities), and crises. These findings suggest that a more comprehensive and multifaceted approach is required in the health management of individuals with chronic diseases. Additionally, the relationship between adaptation and medication adherence can be influenced by factors such as personal motivation, psychosocial support, and disease awareness. Adaptation involves the strategies patients use to manage their illness, while medication adherence pertains to their commitment to the treatment regimen (3,8). These two processes have different components, requiring healthcare professionals to consider both when developing personalized care plans.

Our study has some limitations. Firstly, due to the cross-sectional design of the study, our sample was limited to patients in a specific region and data were collected from only one hospital, which limits the generalizability of the findings. In addition, the fact that our study was conducted in a certain period may have caused the long-term changes in the course of chronic disease and fluctuations in the level of adaptation to chronic disease to be overlooked. Adjustment to chronic illness may change over time and longer follow-up studies are needed to fully understand these dynamics. Future research needs to examine these relationships in more depth with larger and more diverse samples, longitudinal designs, and controllable variables. Recognizing these limitations is important for interpreting the findings and guiding future studies.

In conclusion, this study found that adaptation to chronic diseases is associated with quality of life, but not with medication adherence and the frequency of emergency department visits. These findings emphasize the importance of adherence to the disease in improving quality of life and suggest that other factors affecting adherence to treatment and emergency department visits should be investigated. It is anticipated that this study will raise awareness among healthcare professionals and people with chronic diseases about the importance of adaptation and guide the development of effective strategies for managing chronic diseases.

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Author Contributions

Concept: **Cansu Polat Dünya, Melike Çelik,** Design: **Cansu Polat Dünya, Melike Çelik, Selda Çelik,** Data Collection or Processing: **Cansu Polat Dünya, Melike Çelik,** Analysis or Interpretation: **Cansu Polat Dünya, Melike Çelik, Selda Çelik,** Literature search: **Cansu Polat Dünya, Melike Çelik,** Writing: **Cansu Polat Dünya, Melike Çelik,** Approval: **Selda Çelik.**

Conflicts of Interest

The authors declare no conflict of interest.

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There is no financial disclosure to declare in this study

Ethical Approval

This study was approved by the Health Sciences University Hamidiye Scientific Research Ethics Committee, with an approval number of 4656 and an approval date of 21.09.2021.

Review Process

Extremely and externally peer-reviewed.

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ORIGINAL ARTICLE

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Evaluation of Earthquake Victims Admitted to an Emergency Department in Izmir Following a Major Earthquake Occurring More Than 1000 Kilometers Away

1000 Kilometreden Daha Uzakta Gerçekleşen Büyük Bir Deprem Sonrası İzmir'de Bir Acil Servise Başvuran Depremzedelerin Değerlendirilmesi

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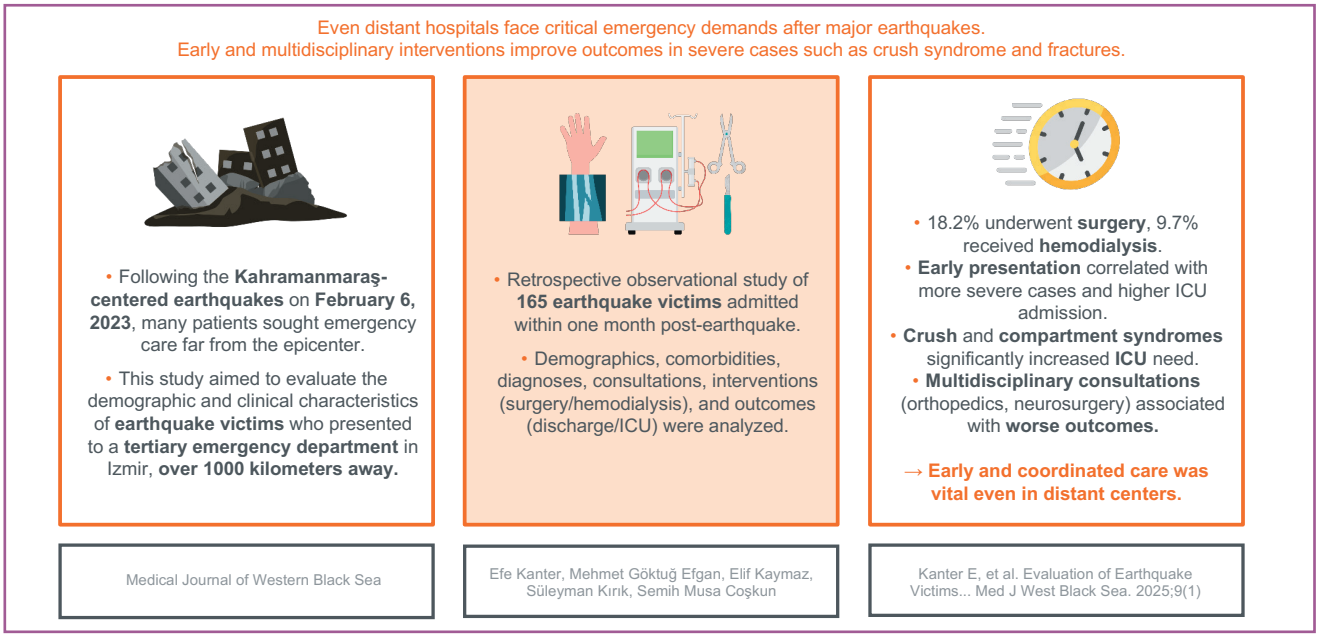
GRAPHICAL ABSTRACT



ABSTRACT

Aim: The major earthquakes centered in Kahramanmaraş on February 6, 2023, caused widespread destruction in the southern and southeastern regions of Turkey. This study evaluates how a distant earthquake affects emergency healthcare services over 1000 kilometers.

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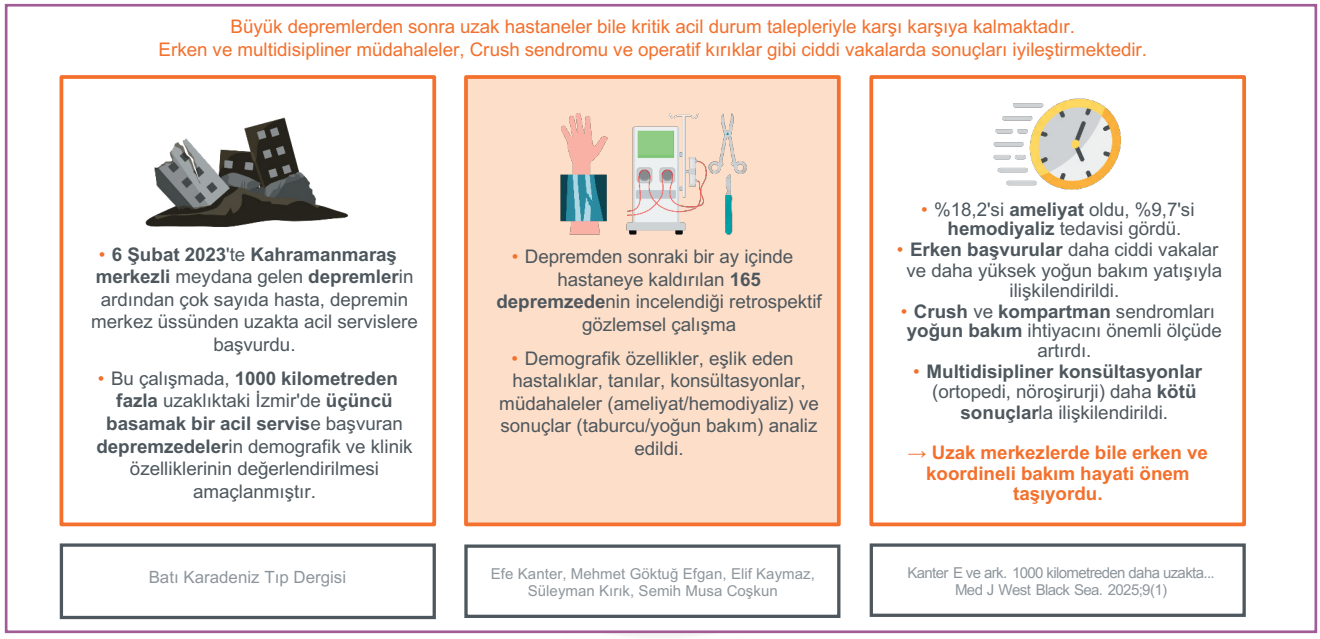
Material and Methods: This study retrospectively analyzes the demographic and clinical characteristics of 165 patients with the ICD code X34—Earthquake Victim—who presented to a tertiary emergency department in Izmir following the February 6, 2023 earthquakes. The patients' presentation times, medical histories, types of trauma, presence of Crush syndrome, and the treatments administered were examined. Additionally, the relationship between the need for hemodialysis and surgical intervention with the time of presentation was evaluated.

Results: The average age of the patients was 48 years, with 56.4% being female and 43.6% male. Hemodialysis was performed in 9.7% and surgical intervention was performed in 18.2% of the patients. These needs were found to be associated with earlier presentations. Additionally, a significant portion of these patients was diagnosed with Crush syndrome and related complications.

Conclusion: The study underscores the importance of early intervention and a multidisciplinary approach following earthquakes. Severe injuries, particularly those related to Crush syndrome, limb fractures, and emergency hemodialysis, are associated with better outcomes when managed promptly and in a coordinated manner. These findings highlight the critical importance of rapid medical response even in distant centers following major earthquakes.

Keywords: Earthquake, crush syndrome, disaster management, hemodialysis

GRAFİKSEL ÖZET



ÖZ

Amaç: 6 Şubat 2023'te Kahramanmaraş merkezli meydana gelen büyük depremler, Türkiye'nin güney ve güneydoğu bölgelerinde geniş çaplı yıkıma yol açmıştır. Bu çalışma, 1000 kilometreden daha uzak mesafedeki bir depremin acil sağlık hizmetlerini nasıl etkilediğini değerlendirmektedir.

Gereç ve Yöntemler: Bu çalışma, 6 Şubat 2023'teki depremler sonrasında İzmir'deki bir üçüncü basamak acil servise başvuran ve X34-Depremzede tanı kodu almış 165 hastanın demografik ve klinik özelliklerini retrospektif olarak analiz etmektedir. Hastaların başvuru zamanları, tıbbi geçmişleri, travma türleri, Crush sendromu varlığı ve uygulanan tedavi yöntemleri incelenmiştir. Ayrıca, bu hastaların hemodiyaliz ve cerrahi müdahale gereksinimleri ile başvuru zamanları arasındaki ilişki de değerlendirildi.

Bulgular: Hastaların ortalama yaşı 48,27±20,17 yıl olup, 93'ü kadın (%56,4) ve 72'si erkektir (%43,6). Hastaların ortalama %9,7'si hemodiyaliz uygulanmış ve %18,2'si cerrahi müdahale uygulanmıştır. Hemodiyaliz ve cerrahi müdahale gereksinimleri, daha erken başvurularla ilişkili bulunmuştur. Ayrıca, bu hastaların önemli bir kısmında Crush sendromu ve ilgili komplikasyonlar saptanmıştır.

Sonuç: Çalışma, deprem sonrası erken müdahalenin ve multidisipliner yaklaşımın önemini vurgulamaktadır. Özellikle Crush sendromu, ekstremite fraktürleri ve acil hemodiyaliz gerektiren durumlar gibi ciddi yaralanmalar, hızlı ve koordineli tıbbi müdahaleyle daha iyi sonuçlar alınabileceğini göstermektedir. Bu bulgular, büyük depremler sonrası uzaktaki merkezlerde bile hızlı tıbbi yanıtın kritik önem taşıdığını ortaya koymaktadır.

Anahtar Sözcükler: Crush sendromu, afet yönetimi, deprem, hemodiyaliz

INTRODUCTION

Earthquakes are sudden-onset natural disasters that often result in significant material damage and are associated with high mortality and morbidity rates. The consecutive major earthquakes that struck on February 6, 2023, centered in Kahramanmaraş, deeply impacted the southern and southeastern regions of Turkey, leading to widespread destruction. One of the critical medical conditions observed during such disasters is Crush syndrome, commonly seen in patients trapped under rubble. This syndrome can lead to acute kidney injury (AKI) and often necessitates interventions such as amputation, fasciotomy, and hemodialysis, which are crucial for improving the prognosis of affected patients (1,2).

Investigating the demographic and clinical characteristics of earthquake victims presenting to emergency departments is essential for evaluating the effectiveness of post-disaster healthcare services. Despite being far from the earthquake's epicenter, many patients fled to different cities due to injuries or other impacts, seeking refuge and medical care elsewhere (3).

In the immediate aftermath of the earthquake, temporary disruptions in healthcare services may have occurred in the affected regions. Healthcare workers, often facing long and exhausting shifts, demonstrated exceptional dedication to managing the crisis. Even hospitals located far from the disaster zone had to handle the increased patient load during the post-disaster period (4).

The aim of this study is to analyze the demographic and clinical characteristics of earthquake victims admitted to a tertiary emergency department in a distant region following a major earthquake, evaluating the medical needs and healthcare burden. This study provides an assessment of the impact of this significant earthquake, which occurred in a distant region, on the earthquake victims admitted to an emergency department in Izmir.

MATERIALS and METHODS

Study Design and Setting

This single-center, retrospective observational study was conducted in the emergency department of a hospital in Izmir, Turkey, where approximately 300,000 patients are treated annually. The study commenced following approval from local Clinical Research Ethics Committee. Patients who presented to our emergency department after the two major earthquakes that occurred on February 6, 2023, in Kahramanmaraş, with epicenters located 1,082 kilometers and 1,099 kilometers from our hospital, were included in the study.

Study Population

Patients who presented to Izmir Katip Çelebi University Atatürk Training and Research Hospital within one month from February 6, 2023, were included in the study. The study encompassed not only patients presenting with earthquake-related trauma symptoms but also those presenting with internal, psychiatric, and other non-traumatic conditions. Patients with incomplete data or those who were referred to another facility were excluded from the study.

Data Collection

A retrospective screening was conducted, including patients whose presenting complaints were related to the earthquake. To identify earthquake victims, data were collected from patients assigned the ICD-10 diagnosis code X34—Victim of Earthquake, as specified by the WHO. The evaluation included demographic data such as age, gender, and date of admission, as well as comorbidities. Additionally, diagnoses made in the emergency department, the specialties consulted in the emergency department, the presence of fractures, the need for surgery, the need for emergency hemodialysis, outcomes, and mortality status were recorded. Patients with incomplete records were excluded from the analysis to ensure data integrity and reliability. All data were documented in a data recording form and used for statistical analysis.

In the comparative analyses, variables included demographic data (age, gender, date of admission), comorbidities (e.g., hypertension, diabetes, heart failure), trauma-related diagnoses (e.g., crush syndrome, compartment syndrome, fractures, soft tissue injuries), non-traumatic conditions (e.g., infections, chest pain, headache, dyspnea), treatments (need for surgery, emergency ur), patient outcomes (discharge, ward/ICU admission), and consulted specialties (e.g., internal medicine, surgery, orthopedics, neurosurgery). These parameters were used to explore associations with clinical outcomes such as surgical intervention, dialysis need, and ICU admission.

Statistical Analysis

All data analyses were performed using SPSS for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive data were presented as mean ± standard deviations (SD) and median (min-max) values for continuous variables, and as frequencies (n) and percentages (%) for categorical variables. The Mann-Whitney U test was used to compare two independent groups for non-normally distributed continuous variables, while the Kruskal-Wallis test was applied for comparisons involving more than two groups. Fisher's Exact test or Chi-Square test (χ^2) was used for the comparison of categorical data, depending on sample size and expected frequencies. A p-value of <0.05 was considered statistically significant.

RESULTS

In this retrospective observational study, we analyzed the demographic and clinical characteristics of patients who presented to the emergency department following the major earthquakes on February 6, 2023. A total of 165 patients were included, with a mean age of 48.27±20.17 years (ranging from 1 to 93 years). Of these patients, 56.4% were female, and 43.6% were male. The mean time to presentation at the emergency department was 6.87±4.54 days, with a median of 5 days (Table 1).

Among the patients, the most common chronic conditions were hypertension (8.5%), diabetes mellitus (15.2%), and congestive heart failure (4.8%). Among the patients, 32.1% required an orthopedic consultation, 9.7% were evaluated by internal medicine, and 6.1% were consulted by general surgery (Table 1).

18.2% of patients presented with fractures and required surgical interventions (18.2%). The need for emergency hemodialysis was observed in 9.7% of the patients (Table 1). The mean time to presentation was significantly shorter in patients who required surgery (4.33±2.66 days) compared to those who did not (7.44±4.68 days, p<0.001) (Table 2). Similarly, patients who required emergency hemodialysis had a significantly shorter mean time to presentation (3.43±1.50 days) compared to those who did not (7.24±4.60 days, p<0.001). Moreover, patients diagnosed with crush syndrome had a mean presentation time of 3.43±1.50 days, significantly earlier than those without crush syndrome (7.24±4.60 days, p<0.001) (Table 2).

Regarding patient outcomes, 61.8% were discharged, 33.9% were admitted to the wards, and 4.2% required intensive care unit (ICU) admission. The time to presentation was significantly associated with patient outcomes; those admitted to the ICU presented earlier (mean 3.85±2.26 days) compared to those who were discharged (mean 7.97±4.67 days, p<0.001) (Table 2).

Diagnoses such as crush syndrome and compartment syndrome were strongly linked to worse outcomes, with significantly higher ICU admission rates (p<0.001 for both). Specifically, 71.4% of patients with crush syndrome and 28.6% with compartment syndrome required ICU care. Similarly, patients with extremity fractures and soft tissue injuries had higher ICU admission rates (p<0.001) (Table 3).

Consultations with certain specialties, particularly orthopedic surgery, neurosurgery, and thoracic surgery, were associated with increased ICU admissions (p<0.001, p=0.005, and p=0.003, respectively). Orthopedic consultations had the highest ICU admission rate at 71.4%. The need for multi-specialty consultations, including cardiology and general surgery, was also linked to poorer outcomes, indicating the complexity and severity of these cases (Table 4).

Table 1: General Demographic, Clinical Characteristics and Outcomes of Patients

Variables		Findings (n=165)
Gender, n (%)	Female	93 (56.4)
	Male	72 (43.6)
Age (Year±SD), median (min-max)		48.27±20.17
		49 (1-93)
Admission Date (Day±SD), median (min-max)		6.87±4.54
		5 (2-21)
Chronic Disease, n (%)	Hypertension	14 (8.5)
	Diabetes Mellitus	25 (15.2)
	Congestive Heart Failure	8 (4.8)
	Chronic Kidney Disease	4 (2.4)
	COPD	1 (0.6)
	Atrial Fibrillation	2 (1.2)
Consultation Unit, n (%)	Internal Medicine	16 (9.7)
	General Surgery	10 (6.1)
	Thoracic Surgery	10 (6.1)
	Orthopedics	53 (32.1)
	Plastic Surgery	9 (5.5)
	Cardiovascular Surgery	6 (3.6)
	Neurosurgery	18 (10.9)
	Ophthalmology	4 (2.4)
	Otorhinolaryngology	1 (0.6)
	Psychiatry	3 (1.8)
	Infectious Diseases	5 (3.0)
	Gynecology and Obstetrics	3 (1.8)
	Urology	1 (0.6)
	Cardiology	6 (3.6)
	Pulmonology	3 (1.8)
	Neurology	2 (1.2)
	Anesthesiology	13 (7.9)
Diagnosis, n (%)	Crush Syndrome	15 (9.1)
	Compartment Syndrome	10 (6.1)
	Respiratory Tract Infection	19 (11.5)
	Soft Tissue Disorder	57 (34.5)
	Extremity Fracture	18 (10.9)
	Spinal Fracture	4 (2.4)
	Thoracic Fracture	6 (3.6)
	Pelvic Fracture	5 (3.0)
	Hemopneumothorax	4 (2.4)
	Urinary Tract Infection	3 (1.8)
	Anxiety Disorder	2 (1.2)
	Chest Pain	11 (6.7)
	Dyspnea	6 (3.6)
	Headache	5 (3.0)
	Abdominal Pain	6 (3.6)
	Myalgia	8 (4.8)
	Stroke	3 (1.8)
	Abnormal Uterine Bleeding	1 (0.6)
Treatment, n (%)	Fracture Management	30 (18.2)
	Need for Surgery	30 (18.2)
	Emergency Hemodialysis	16 (9.7)
Outcome, n (%)	Discharged	102 (61.8)
	Ward Admission	56 (33.9)
	ICU Admission	7 (4.2)

COPD: Chronic obstructive pulmonary disease, **ICU:** Intensive care unit, **$\bar{x}$:** Mean, **s:** Standard deviation.

Table 2: Association of Admission Date with Clinical Interventions and Outcomes

	Need for Operation		Test Statistics	
	No	**Yes**	**z-value**	**p-value**
Admission Date				
(Day±SD), median (min-max)	7.44±4.68 6 (2-21)	4.33±2.66 3 (3-16)	4.652	<0.001
Fracture, n (%)				
No	119 (88.1)	16 (53.3)	19.999	<0.001
Yes	16 (11.9)	14 (46.7)		
	Emergency Hemodialysis		**Test Statistics**	
	No	**Yes**	**Test value**	**p-value**
Admission Date				
(Day±SD), median (min-max)	7.24±4.60 6 (2-21)	3.43±1.50 3 (3-9)	4.812	<0.001
Crush syndrome, n (%)				
No	145 (97.3)	5 (31.3)	76.306	<0.001
Yes	4 (2.7)	11 (68.8)		
	Outcome			**Test Statistics**
	Discharged	**Ward**	**ICU**	**H-value**	**p-value**
Admission Date					
$\bar{x}$±s	7.97±4.67	5.26±3.84	3.85±2.26	32.258	<0.001
median (min-max)	6 (3-21)a	4 (2-21)b	3 (3-9)b		

ICU: Intensive care unit, **$\bar{x}$:** Mean, **s:** Standard deviation. Mann-Whitney U test was used for Admission Date. and Fisher's Exact test was used for Fracture. The Kruskal-Wallis test was used for comparisons among three groups. Post-hoc pairwise comparisons were performed using Dunn's test where applicable.

Table 3: Relationship Between Diagnoses and Outcome

	Outcome (n=165)*			Test Statistics	
	Discharged	**Ward**	**ICU**	**value**	**p-value**
Crush syndrome	0 (0.0)	10 (17.9)	5 (71.4)	48.321	**<0.001**
Compartment syndrome	0 (0.0)	8 (14.3)	2 (28.6)	19.465	**<0.001**
Respiratory Tract Infection	18 (17.6)	1 (1.8)	0 (0.0)	9.878	**0.007**
Soft Tissue Disorder	46 (45.1)	11 (19.6)	0 (0.0)	14.218	**0.001**
Extremity Fracture	4 (3.9)	12 (21.4)	2 (28.6)	13.747	**0.001**
Spinal Fracture	0 (0.0)	4 (7.1)	0 (0.0)	7.979	**0.019**
Thoracic Fracture	2 (2.0)	4 (7.1)	0 (0.0)	3.046	0.218
Pelvic Fracture	1 (1.0)	2 (3.6)	2 (28.6)	17.055	**0.007**
Hemopneumothorax	0 (0.0)	3 (5.4)	1 (14.3)	8.734	**0.013**
Urinary Tract Infection	2 (2.0)	0 (0.0)	1 (14.3)	7.144	**0.028**
Anxiety Disorder	2 (2.0)	0 (0.0)	0 (0.0)	1.250	0.535
Chest Pain	7 (6.9)	4 (7.1)	0 (0.0)	0.527	0.768
Dyspnea	1 (1.0)	5 (8.9)	0 (0.0)	5.904	0.051
Headache	5 (4.9)	0 (0.0)	0 (0.0)	2.775	0.338
Abdominal Pain	6 (5.9)	0 (0.0)	0 (0.0)	3.846	0.146
Myalgia	8 (7.8)	0 (0.0)	0 (0.0)	5.193	0.075
Cerebrovascular stroke	1 (1.0)	2 (3.6)	0 (0.0)	1.495	0.474
Abnormal Uterine Bleeding	0 (0.0)	1 (1.8)	0 (0.0)	1.958	0.376

*Data were shown as n (%). **ICU:** Intensive care unit. Fisher's Exact test or Chi-Square test (χ^2) was used for the comparison of categorical variables. depending on sample size and expected frequencies.

Table 4: Relationship Between Consultation Units and Patient Outcome Status

Relationship Between Consultation Units and Patient Outcome*	Outcome			Test Statistics	
	Discharged	Ward	ICU	value	p-value
Internal Medicine	2 (2.0)	8 (14.3)	6 (85.7)	33.115	**<0.001**
General Surgery	0 (0.0)	7 (12.5)	3 (42.9)	27.307	**<0.001**
Chest surgery	2 (2.0)	6 (10.7)	2 (28.6)	11.372	**0.003**
Orthopedics	13 (12.7)	35 (62.5)	5 (71.4)	46.227	**<0.001**
Plastic Surgery	3 (2.9)	5 (8.9)	1 (14.3)	3.619	0.164
Cardiovascular Surgery	1 (1.0)	4 (7.1)	1 (14.3)	6.284	**0.043**
Neurosurgery	5 (4.9)	11 (19.6)	2 (28.6)	10.429	**0.005**
Ophthalmology	2 (2.0)	1 (1.8)	1 (14.3)	4.353	0.113
Otorhinolaryngology	1 (1.0)	0 (0.0)	0 (0.0)	0.621	0.733
Psychiatry	2 (2.0)	1 (1.8)	0 (0.0)	0.142	0.932
Infectious Diseases	2 (2.0)	3 (5.4)	0 (0.0)	1.648	0.439
Obstetric diseases	2 (2.0)	1 (1.8)	0 (0.0)	0.1442	0.932
Urology	0 (0.0)	1 (1.8)	0 (0.0)	1.958	0.376
Cardiology	3 (2.9)	3 (5.4)	0 (0.0)	0.878	0.645
Pulmonology	0 (0.0)	3 (5.4)	0 (0.0)	5.947	0.051
Neurology	0 (0.0)	2 (3.6)	0 (0.0)	3.941	0.139
Anesthesiology	0 (0.0)	6 (10.7)	7 (100.0)	48.168	**<0.001**

*Data were shown as n (%). **ICU:** Intensive care unit. Fisher's Exact test or Chi-Square test (χ^2) was used for the comparison of categorical variables. depending on sample size and expected frequencies.

DISCUSSION

The findings from our study provide crucial insights into the demographic and clinical characteristics of earthquake victims who presented to an emergency department in Izmir, Turkey, following the major earthquakes of February 6, 2023. The study underscores the importance of early and multidisciplinary intervention, particularly for patients with severe conditions such as crush syndrome, fractures, and those requiring emergency hemodialysis (5,6).

Our results revealed that patients with more severe injuries, including those requiring surgical interventions and emergency hemodialysis, tended to present earlier to the emergency department. This aligns with previous research demonstrating the critical role of rapid medical response in disaster scenarios (7,8). Early presentation has been shown to significantly impact outcomes, particularly in crush syndrome cases, where the risk of acute kidney injury (AKI) is high (9). Studies have documented that early intervention, including aggressive fluid resuscitation and timely hemodialysis, can reduce mortality and morbidity associated with AKI in crush syndrome patients (10). Similarly, prompt surgical management of fractures and compartment syndrome is crucial in improving patient outcomes (11,12).

The high rate of ICU admission among patients with crush syndrome and compartment syndrome highlights the severity of these conditions and the necessity for intensive monitoring and care (13). Our findings further indicate a significant association between the need for orthopedic, neurosurgical, and thoracic surgical consultations and higher ICU admission rates, reflecting the complexity and severity of injuries sustained by these patients (14). This is consistent with literature suggesting that patients with multi-system injuries, particularly those requiring multiple surgical interventions, are at a higher risk of complications and poor outcomes (8).

Furthermore, our study demonstrated a strong link between early presentation and better overall outcomes, including lower ICU admission rates and higher discharge rates (5). These results are supported by existing literature, which emphasizes that delays in medical care can lead to the progression of injuries and worse prognosis (7). The need for consultations from various specialties, including cardiology and general surgery, underscores the complexity of these cases and the necessity for coordinated care (11,15).

In conclusion, our findings highlight the critical importance of early, multidisciplinary intervention in improving outcomes for patients with severe earthquake-related injuries. The significant associations observed between early pres-

entation and better outcomes underscore the necessity of rapid, coordinated medical response in disaster settings (10). These findings reinforce the importance of prioritizing early intervention and multidisciplinary care to optimize patient outcomes following large-scale disasters (6,16).

Our study is limited by its retrospective design, which may introduce biases related to data accuracy and completeness. This study acknowledges the inherent bias in retrospective designs, including selection bias. To minimize this, only patients with complete records were included in the analysis. Additionally, being a single-center study, the generalizability of our findings is restricted. The small sample size, especially with only one patient outcome resulting in death, limited our ability to draw significant conclusions regarding mortality. Moreover, the reliance on patients who traveled from distant regions may have introduced variability in the timing and severity of presentations, potentially affecting the outcomes observed. However, a key strength is the detailed assessment of earthquake victims in a non-epicenter region, providing valuable insights into post-disaster healthcare needs.

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Author Contributions

Concept: **Efe Kanter, Mehmet Göktuğ Efgan,** Design: **Efe Kanter, Süleyman Kırık,** Data Collection or Processing: **Semih Musa Coşkun, Süleyman Kırık,** Analysis or Interpretation: **Elif Kaymaz, Efe Kanter,** Literature Search: **Mehmet Göktuğ Efgan,** Writing: **Efe Kanter,** Approval of Final Manuscript: **All authors.**

Conflicts of Interest

The authors declare no conflicts of interest.

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Ethical Approval

Ethical approval for the study was obtained from the Izmir Katip Celebi University Clinical Research Ethics Committee (Approval No: 0434, Date: 21.09.2023).

Review Process

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ORIGINAL ARTICLE

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Real-World Data on the Development of Relapse in Graves' Disease from a Tertiary Referral Center

Graves Hastalığı'nda Nüks Gelişimi: Üçüncü Basamak Referans Merkezin Gerçek Yaşam Verileri

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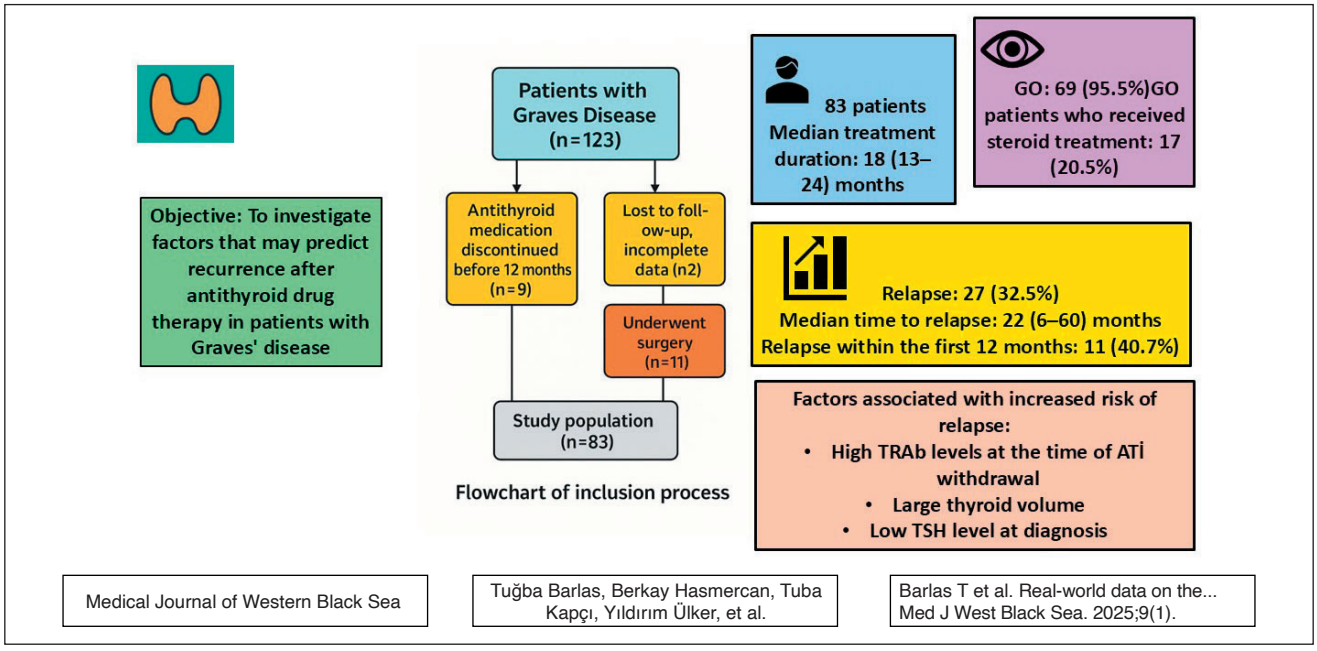
GRAPHICAL ABSTRACT



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ABSTRACT

Aim: We aimed to evaluate clinical and laboratory parameters that may predict relapse in patients who have received adequate antithyroid drug (ATD) therapy for Graves' disease (GD).

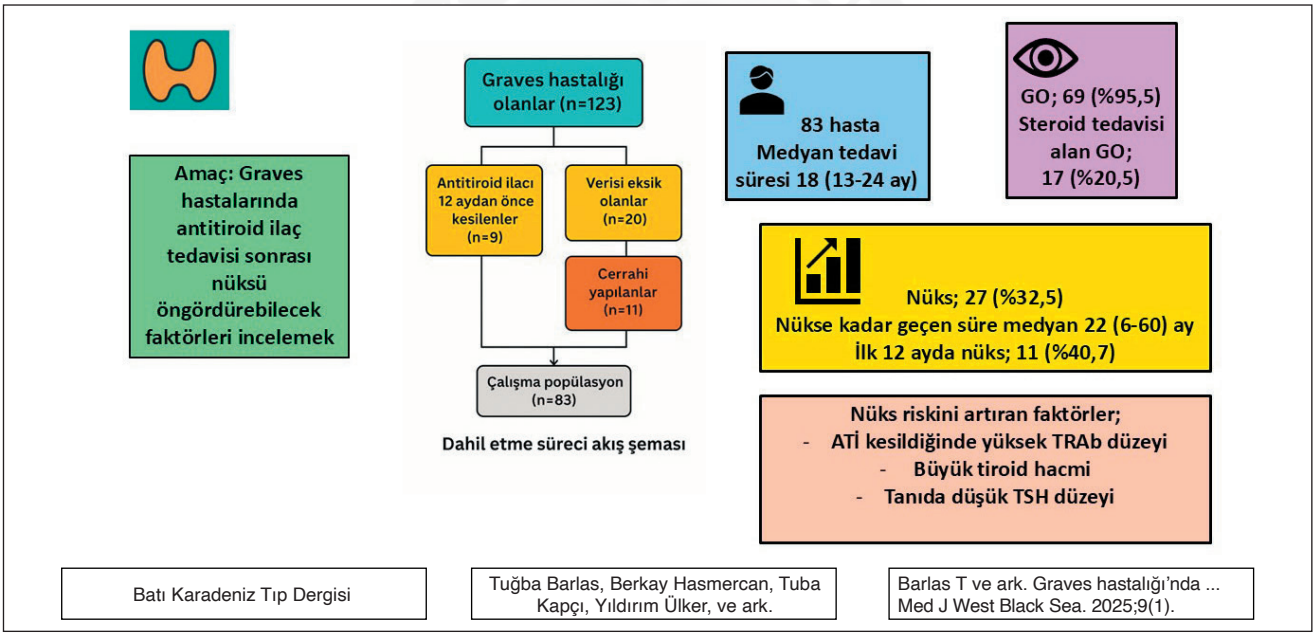
Material and Methods: We included patients with GD who received ATD therapy for at least 12 months and were followed for at least 12 months after treatment. Patients were classified into relapse and non-relapse groups, and their demographical, laboratory, imaging findings, and follow-up information were recorded retrospectively.

Results: Eighty-three patients were included, with a median treatment duration of 18 (13-24) month. Graves' orbitopathy (GO) was present in 58 (69.9%) of patients, and 17 (20.5%) received steroid therapy for GO. Relapse occurred in 27 (32.5%) of patients, with a median time to relapse of 22 (6-60) months, and 11 (40.7%) relapsed within the first 12 months. No association was found between TRAb positivity at diagnosis and relapse (p=0.542), but higher TRAb levels at ATD discontinuation (p=0.026), larger thyroid volumes (p=0.043), and lower TSH levels at diagnosis (p=0.027) were related with increased relapse risk. In the whole patient group, GH relapse was lower in those treated with corticosteroids as GO therapy (p=0.030). The regression model identified thyroid volume (p=0.044) and corticosteroid usage for GO (p=0.042) as predictors of relapse.

Conclusion: Our findings suggest that while GH relapse might be more frequent in patients with larger thyroid volumes, corticosteroid therapy administered for GO may serve as a protective factor for GH relaps. The real-world data from our tertiary referral center may contribute to studies on GD relapse development, especially when considering sociodemographical differences.

Keywords: Antithyroid drugs, corticosteroid therapy, Graves' orbitopathy, hyperthyroidism, thyrotoxicosis

GRAFİKSEL ÖZET



ÖZ

Amaç: Graves Hastalığı (GH) için yeterli antitiroid ilaç (ATİ) tedavisi almış hastalarda nüksü öngördürebilecek klinik ve laboratuvar parametrelerini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: En az 12 ay boyunca ATİ tedavisi almış ve tedavi sonrası en az 12 ay takip edilmiş GH olan hastalar çalışmaya dahil edildi. Hastalar, nüks ve nüks olmayan gruplar olarak sınıflandırıldı. Hastaların demografik, laboratuvar, görüntüleme bulguları ile takip verileri retrospektif olarak kaydedildi.

Bulgular: Toplam 83 hasta çalışmaya dahil edildi ve medyan tedavi süresi 18 (13-24) aydı. Hastaların 58 (%69,9)'inde Graves orbitopatisi (GO) mevcuttu ve 17 (%20,5)'si GO için steroid tedavisi almıştı. Hastaların 27 (%32,5)'sinde nüks gelişmişti ve nükse kadar geçen süre medyan 22 (6-60) aydı. Nüks gelişen hastaların 11 (%40,7)'sinde nüks ilk 12 ay içinde gelişmişti. Tanı sırasındaki TRAb pozitifliği ile nüks gelişimi arasında bir ilişki bulunmadı (p=0,542), ancak ATİ tedavisinin kesilmesi sırasında daha yüksek TRAb seviyeleri (p=0,026), daha büyük tiroid hacmi (p=0,043), ve tanı anında daha düşük TSH seviyeleri (p=0,027) artmış nüks riski ile ilişkili bulundu. Tüm hasta grubunda GO tedavisi olarak steroid uygulananlarda GH nüks sıklığı daha düşüktü (p=0,030). Regresyon modelinde, tiroid hacmi (p=0,044) ve GO için kortikosteroid kullanımı (p=0,042) nüks gelişimi ile ilişkili faktörler olarak saptandı.

Sonuç: Tiroid hacmi daha yüksek olanlarda GH nüksü daha fazla gözlenebilirken, GO'da uygulanan kortikosteroid tedavisi nüks gelişimi üzerinde koruyucu bir faktör olabilir. Bulgularımız, özellikle sosyodemografik farklılıklar göz önünde bulundurulduğunda, GH'de nüks gelişimi üzerine yapılan çalışmalara ek katkı sağlayabilir.

Anahtar Sözcükler: Antitiroid ilaç, Graves orbitopatisi, hipertiroidi, kortikosteroid tedavi, tirotoksikoz

INTRODUCTION

Graves' disease (GD) is an autoimmune disorder in which the thyroid gland is targeted by the immune system (1). In areas with sufficient iodine, GD is the most common cause of hyperthyroidism, with an incidence of 20–30 cases per 100,000 people each year (2). GD can lead to an increase in long-term morbidity and mortality, as well as an impairment in quality of life. The objectives of treatment are to safely and promptly restore thyroid function, prevent recurrence and adverse effects of therapy, and maintain long-term normal thyroid function, as GD has a significant impact on affected individuals (3).

The treatment options for GD include antithyroid drugs (ATD), radioactive iodine (RAI), and surgery. The choice of initial and subsequent treatments often depends on local standards and practices (4). The European Thyroid Association Guidelines recommend ATD as the initial treatment for GD, especially in younger individuals (1). The optimal duration of ATD therapy using the titration regimen is 12–18 months, with maximum remission rates of 50–55% achieved within this period (5-7). It is recommended to measure the thyroid-stimulating hormone receptor antibody (TRAb) levels before discontinuing ATD therapy, as normal levels suggest a higher likelihood of remission (6, 8). Relapse is most common within the first 6–12 months after stopping ATD but can occur years later (1). However, predicting relapse and identifying risk factors might be challenging due to the autoimmune nature of the disease. The existing literature indicates that certain factors, such as severe hyperthyroidism, large goiters, and persistently high TRAb titers, can make remission more difficult and increase relapse risk (9-11). Furthermore, there are studies aiming to predict relapse risk using models that combine clinical and genetic markers (12-14). However, the efficacy of numerous clinical and laboratory parameters in predicting the risk of relapse in clinical practice remains controversial. In this study, we aim to evaluate clinical and laboratory parameters that may predict relapse in patients who have received adequate ATD therapy for GD.

MATERIALS and METHODS

Study Design and Participants

The study was conducted retrospectively from January 2016 to June 2024 at an outpatient clinic of the Endocrinology and Metabolism Department of a tertiary center. It was approved by the Ethical Committee of Gazi University. The study included patients who were diagnosed with GD, underwent at least 12 months of ATD therapy, and were monitored for at least 12 months after ATD cessation. The patients were grouped into relapse and nonrelapse. The exclusion criteria were as follows: (i) patients with an uncertain diagnosis of GD; (ii) patients who discontinued their ATD treatment before 12 months; (iii) patients who were followed up for less than 12 months after discontinuing ATD; (iv) patients who underwent surgery or RAI as their initial treatment for hyperthyroidism; and (v) patients with a hyperthyroidism etiology other than GD; (vi) pregnancy, major illness, or medical treatment influencing thyroid function. The flowchart of inclusion process was provided in Figure 1.

Data Collection and Definitions

Patients' demographical features, past medical histories, laboratory and imaging findings, and follow-up data were obtained from medical records. The diagnosis of GD was established based on the following criteria: serum thyroid-stimulating hormone (TSH) levels below the lower normal limit, accompanied by elevated free thyroxine (fT4) and/or free triiodothyronine (fT3) levels, along with increased serum TRAb levels and/or increased radioactive iodine uptake. Additionally, appropriate clinical features such as symptoms of hyperthyroidism, a diffuse goiter (as defined by ultrasonography), or Graves orbitopathy (GO) were considered. Relapse was defined as the occurrence of hyperthyroidism, indicated by fT4 or fT3 levels above the upper normal limit and TSH levels below the lower normal limit, at any point during the follow-up period (1).

Laboratory parameters such as neutrophil, lymphocyte, alanine aminotransferase (ALT), aspartate aminotransferase (AST), low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride, and vitamin D levels at the time of the initial diagnosis were recorded. TRAb level was recorded as negative, 1-2 times higher or higher than 2 times of upper limit normal (ULN). Thyroid volume was calculated using the formula 0.479 × length (cm) × width (cm) × height (cm) (15).

Statistical Analysis

Statistical analyses were conducted using SPSS version 22.0. The Shapiro-Wilk test assessed the normality of con-

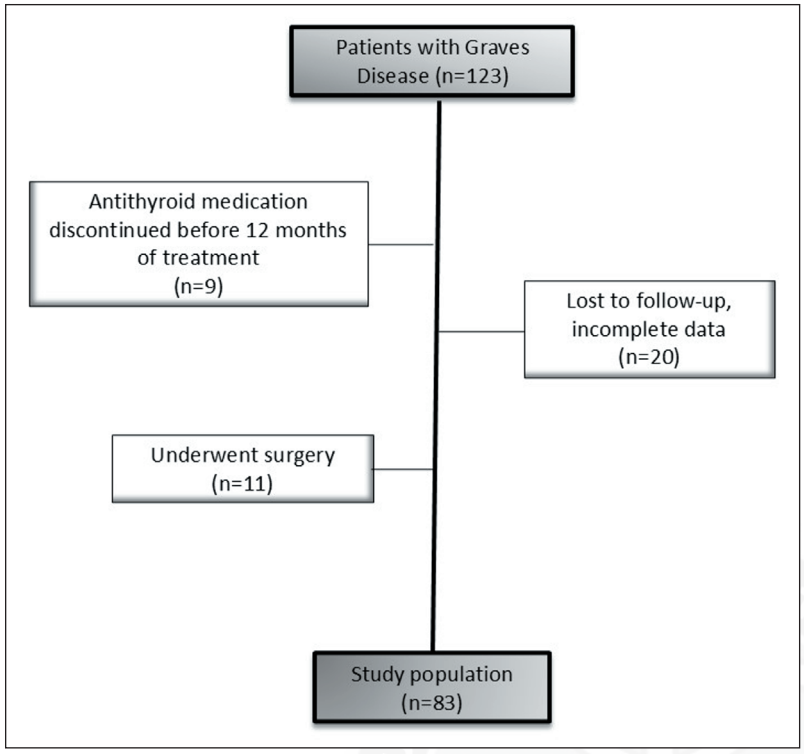


Figure 1: Flowchart of inclusion process

tinuous data. We reported normally distributed continuous variables as mean and standard deviation, and presented non-normally distributed variables as median and interquartile range. The Mann-Whitney U, independent sample t test compared continuous variables. The $\chi 2$ (chi-squared) and Fisher's exact tests compared categorical variables. A multivariate logistic regression analysis was conducted to determine the factors that affect the relapse of GD. The threshold for statistical significance was established at $p < 0.05$.

RESULTS

After applying exclusion criteria, a total of 83 patients were included in the study. The mean age of the patients was 46.5±12.5 years, and 62 (74.7%) patients were female. The median treatment duration was 18 (13-24) months. A total of 38 patients (45.8%) were smokers. GO was present in 58 patients (69.9%), and 17 patients (20.5%) had received steroid therapy for GO.

In our study, relapse occurred in a total of 27 patients (32.5%). Among these cases, relapse occurred within the first 12 months in 11 patients (40.7%). The median time to relapse was 22 (6-60) months. The median follow-up duration for the group without relapse was 39 (30-56) months. The characteristics of patients with and without relapse are summarized in Table 1. No association was found between TRAb positivity at the time of diagnosis and relapse. However, an increased relapse rate was observed in patients with higher TRAb levels at the time of ATD discontinuation. Furthermore, patients with larger thyroid volumes and lower TSH levels at diagnosis exhibited a higher incidence of relapse. In the whole patient group, GH relapse was lower in those treated with corticosteroids as GO therapy. In the regression model developed to predict relapse risk, it was found that thyroid volume and the administration of steroids for GO treatment were associated with relapse (Table 2).

DISCUSSION

In our study, the relapse rate of GD was found to be 32.5%. While varying results have been reported in the literature, a meta-analysis including 3,242 patients found relapse rates as high as 51.9% (11). Since the risk of relapse is significantly increased and it also affects the choice of treatment, certain factors in predicting the risk of relapse were investigated. Moreover, some scoring systems have been developed to assess relapse risk of GD (13). Factors such as younger age, large goiter, smoking, male sex, higher TRAb levels, longer therapy duration, and elevated thyroid hormone levels have been considered to have an impact for relapse (11, 13, 16, 17). However, the combined influence of various genetic, developmental, immunological, and environmental factors can lead to different outcomes (18). In our study, higher thyroid volume was found to be related with the development of relapse. Supporting our findings, Liu et al. (9) demonstrated that, in addition to larger goiter size, higher TRAb levels, and lower TSH levels at the time

Table 1. Characteristics of the patients with Graves disease

	Patients with relapse, n=27	Patients without relapse, n=56	p value
Age, years	48.4 ± 12.7	45.6 ± 12.4	0.344
Gender, Female, n (%)	21 (77.8)	41 (73.2)	0.654
Smoking, n (%)	9 (33.3)	29 (51.8)	0.143
GO, n (%)	16 (59.3)	42 (75.0)	0.143
Steroid therapy for GO, n (%)	2 (7.4)	15 (26.8)	**0.030**
ATD duration, months	18 (12-26)	18 (14-22)	0.883
TRAb positivity at diagnosis, n (%)	24 (88.9)	52 (92.9)	0.542
TPO positivity at diagnosis, n (%)	19 (70.4)	34 (60.7)	0.699
TRAb, at the end of the ATD therapy, n (%)			**0.026**
Negative	14 (51.9)	36 (54.3)	
Positive (1-2x)	7 (25.9)	3 (5.4)	
Positive (>2x)	6 (22.2)	17 (30.4)	
TSH at diagnosis, mIU/mL	0.01 (0.01-0.03)	0.01 (0.01-0.89)	**0.027**
sT3 at diagnosis, pg/mL	4.89 (3.86-11.90)	4.40 (3.51-11.18)	0.232
sT4 at diagnosis, ng/dL	2.31 (1.23-3.82)	1.40 (0.97-2.93)	0.072
NLR at diagnosis	1.8 (1.2-2.7)	1.7 (1.2-2.1)	0.292
ALT at diagnosis, U/L	21.9 ± 10.0	22.8 ± 11.9	0.928
AST at diagnosis, U/L	20.8 ± 6.5	21.0 ± 5.1	0.767
LDL at diagnosis, mg/dL	113.7 ± 32.8	111.4 ± 42.3	0.639
Thyroid volume, ml	22.3 (16.2-36.6)	14.7 (11.4-27.8)	**0.043**
ATD, n (%)			0.542
MMI	24 (88.9)	52 (92.9)	
PTU	3 (11.1)	4 (7.1)	

GO: Graves orbitopathy, **ATD:** Anti-thyroid drug, **TRAb:** Thyrotropin receptor antibodies, **TPO:** Thyroid peroxidase antibodies, **TSH:** Thyroid-stimulating hormone, **sT3:** Free triiodothyronine, **sT4:** Free thyroxine, **NLR:** Neutrophil-to-lymphocyte ratio, **ALT:** Alanine aminotransferase, **AST:** Aspartate aminotransferase, **LDL:** Low-density lipoprotein, **MMI:** Methimazole, **PTU:** Propylthiouracil

Table 2. The logistic regression model to predict relapse development

	Exp (B)	95% CI	p value
TSH at diagnosis, mIU/mL	2.40	0.54-10.64	0.250
Thyroid volume, ml	1.06	0.93-0.99	**0.044**
Steroid therapy for orbitopathy	0.10	0.11-0.92	**0.042**
TRAb, at the end of the ATD therapy	0.12	0.01-1.01	0.051
sT3 at diagnosis, pg/mL	1.03	0.93-1.15	0.524

TSH: Thyroid-stimulating hormone, **TRAb:** Thyrotropin receptor antibodies, **ATD:** Anti-thyroid drug, **sT3:** Free triiodothyronine
Nagelkerke R^2 value of the model was 0.332.

of GD diagnosis also play a role in the development of relapse. In the study by Tun et al. (19), the risk of relapse was found to be 58% in patients with TRAb levels <0.9 IU/L at the time of treatment cessation, whereas it was 82% in those with TRAb levels >1.5 IU/L. On the other hand, despite our study demonstrating a higher relapse rate in patients with lower initial TSH and higher TRAb level at the time of ATD discontinuation, the regression analysis did not reveal the influence of TSH and TRAb levels. This may be due to the fact that TSH levels at diagnosis were often too low to be measured in some patients as well as categorical analysis of TRAb levels.

Interestingly, in our study, patients who received corticosteroid therapy for the treatment of GO had a lower relapse frequency in whole patient group. Similarly, a study by Moli et al. (20) also reported a reduced relapse rate in patients treated with pulse steroid therapy for GO, with this effect being more pronounced in younger patients. The autoimmune nature of GD and the immunosuppressive effect of corticosteroid therapy could potentially explain this finding (1, 21). Furthermore, our study revealed a higher incidence of GO than previously reported in the literature, potentially due to our center's role as a tertiary referral center for GO management (22, 23).

Recent publications have emphasized that long-term low-dose ATD therapy may reduce the risk of relapse (16, 24,

25). We found no significant difference in ATD duration between patients who experienced relapse and those who did not. However, due to the retrospective design of our study, we did not include long-term low-dose treatment regimens, which can last up to approximately 14 years, as mentioned in a review by Azizi and Malboosbaf (24). This recommendation, which stands out among the modifiable risk factors for relapse, may potentially influence the general approach to the treatment of GD if further studies support it (26).

Additionally, while relapse in GD is generally reported to occur within the first 12 months, in our study, relapse was observed at a median of 22 months (22). This may be related to our center being a tertiary referral center for GO patients, the higher number of patients receiving immunosuppressive therapy for GO, as well as the fact that patients are closely monitored and followed up for longer periods without interruption.

Our study has certain limitations. Firstly, it is designed as a retrospective study and includes a limited number of patients. The results are difficult to generalize to the broader population because they were administered in a single center. However, it provides valuable insights into real-world data from a tertiary center. Additionally, due to changes in the reference range of TRAb levels over the years, numerical analysis could not be performed.

Our findings suggest that thyroid volume and corticosteroid treatment for GO might be associated with the development of relapse in GD. Various genetic and environmental factors are known to influence relapse in GD. We believe that investigating the factors contributing to relapse development in our study, based on real-world data from different populations and even individual centers, could provide valuable insights into relapse outcomes.

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None

Author Contributions

All authors contributed to the study conception and design. The first draft of the manuscript was written by **Tuğba Barlas, Füsun Baloş Törüner** and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no conflict of interest in relation with the present study.

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The study was approved by Gazi University Ethical Committee.

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Does Tumor Laterality Influence Response to Neoadjuvant Chemotherapy in HER2-Positive Breast Cancer?

Tümör Lateralitesi, HER2-pozitif Meme Kanserinde Neoadjuvan Kemoterapiye Yanıtı Etkiler mi?

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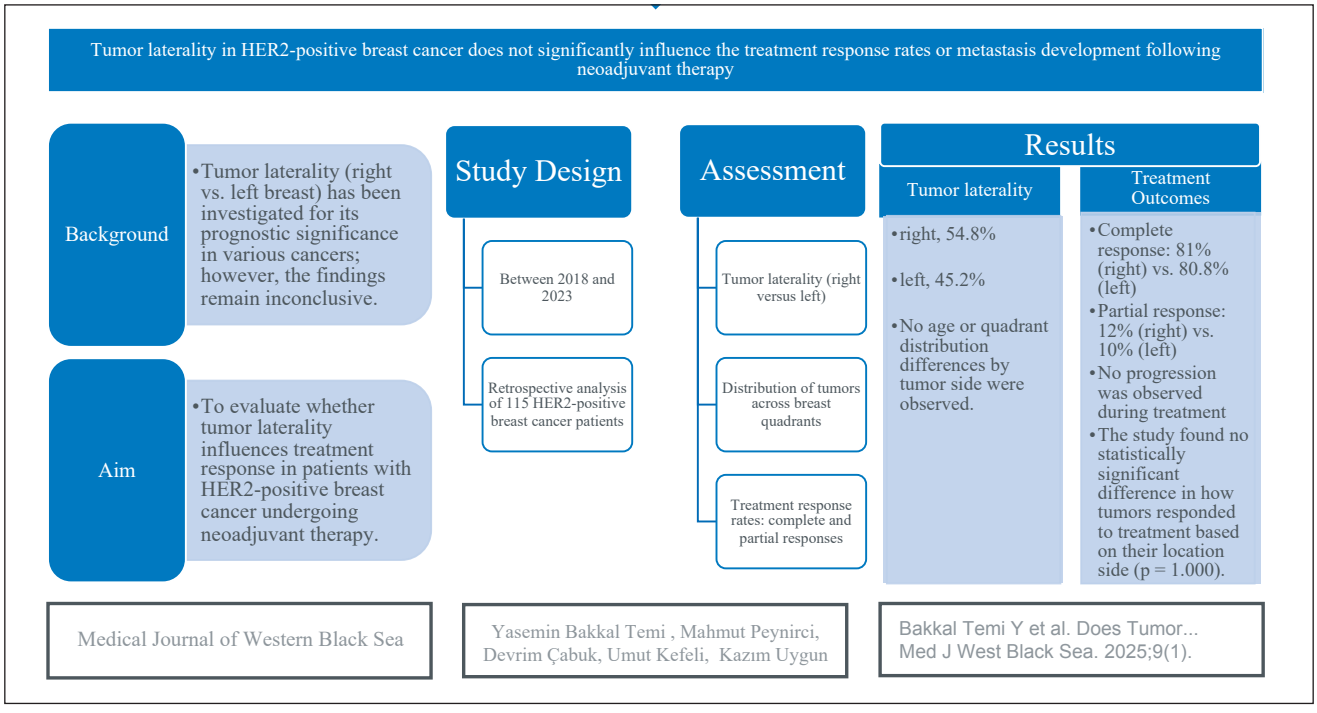
GRAPHICAL ABSTRACT



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ABSTRACT

Aim: The prognostic significance of tumor laterality has been explored in various solid malignancies, with varying findings across different cancer types. This study investigated the potential for predicting treatment response rates based on cancer laterality in patients with HER2-positive breast cancer undergoing neoadjuvant therapy.

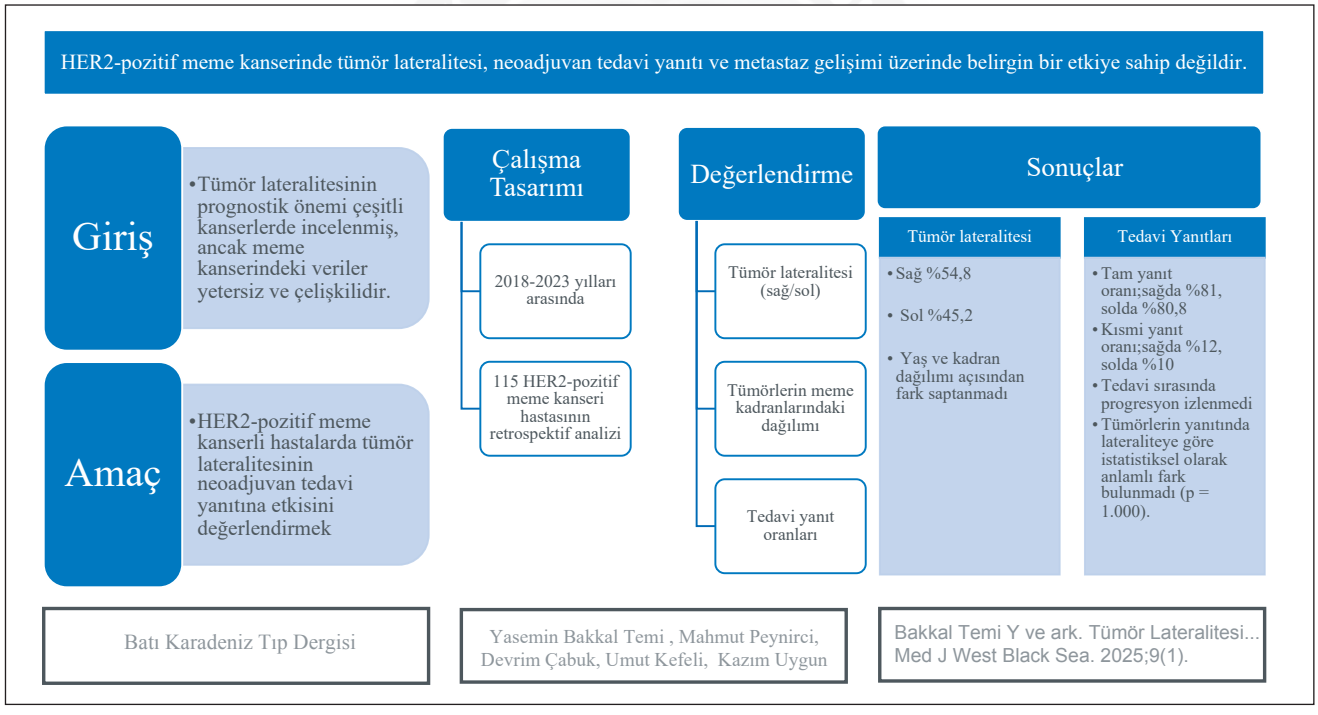
Material and Methods: A retrospective analysis was conducted on 115 patients diagnosed with HER2-positive breast cancer who underwent neoadjuvant therapy at the Department of Medical Oncology, Kocaeli University Hospital between January 2018 and March 2023.

Results: The median age of the patients was 49 years (range 41–59 years), with no significant difference in age distribution between the right and left breast tumors (p = 0.704). The study group was composed of 54.8% right breast tumor sand 45.2% left breast tumors. The distribution of primary tumors across quadrants in both breasts did not show a significant difference (p = 0.659). When examining the response to neoadjuvant therapy, no patient exhibited progression during treatment. Complete response rates were 81% and 80.8% for right-sided and left-sided breast tumors, respectively, and partial response rates were 12% and 10%, respectively. There was no statistical significance observed in treatment responses based on tumor location side (p = 1.000). During follow-up, 9.6% of patients developed metastasis.

Conclusion: This study highlights the lack of significant differences in treatment response rates and metastasis development based on tumor laterality in HER2-positive breast cancer patients receiving neoadjuvant therapy. Further research is needed to identify potential predictive factors for treatment response in this patient population.

Keywords: Breastcancer, HER2-positive, neoadjuvant therapy, laterality

GRAFİKSEL ÖZET



ÖZ

Amaç: Tümör lateralitesinin prognostik önemi, çeşitli solid malignitelerde farklı sonuçlar ortaya koymuştur. Bu çalışmada, neoadjuvan tedavi uygulanan HER2-pozitif meme kanseri hastalarında tümörün yerleşim tarafının tedavi yanıt oranlarını ön görmedeki rolü araştırılmıştır.

Gereç ve Yöntemler: Ocak 2018 ile Mart 2023 tarihleri arasında Kocaeli Üniversitesi Hastanesi Tıbbi Onkoloji Bölümü'nde neoadjuvan tedavi almış HER2-pozitif meme kanseri tanılı 115 hasta retrospektif olarak incelenmiştir.

Bulgular: Hastaların medyan yaşı 49 (41-59) idi ve sağ ve sol meme tümörleri arasında yaş dağılımında anlamlı bir fark bulunmadı (p=0,704). Çalışmaya dahil edilen hastaların %54,8'inde sağ, %45,2'sinde ise sol meme tümörleri saptandı. Her iki memede de primer tümörlerin kadranlara göre dağılımında anlamlı bir fark görülmedi (p = 0,659). Neoadjuvan tedavi sırasında hiçbir hastada progresyon izlenmezken, sağ meme tümörlerinde tam yanıt oranı %81, sol meme tümörlerinde ise %80,8 olarak bulundu; kısmi yanıt oranları sırasıyla %12 ve %10 idi. Tümörün yerleşim tarafına göre tedavi yanıtlarında istatistiksel olarak anlamlı bir fark bulunmadı (p = 1.000). Takip sürecinde hastaların %9,6'sında metastaz gelişti.

Sonuç: Neoadjuvan tedavi almış HER2-pozitif meme kanseri hastalarında tümörün lateralitesi, tedavi yanıt oranları ve metastaz gelişimi üzerinde belirleyici bir faktör olarak görülmemiştir. Bu hasta grubunda tedavi yanıtını öngörebilecek diğer potansiyel faktörlerin belirlenmesi için daha kapsamlı araştırmalara ihtiyaç duyulmaktadır.

Anahtar Sözcükler: Meme kanseri, HER2- pozitif, neoadjuvan tedavi, lateralite

INTRODUCTION

Breast cancer (BC) is the most frequently diagnosed malignancy in women and remains one of the leading causes of cancer-related mortality worldwide (1). Over the past three decades, mortality rates have consistently declined (2). This decline is primarily attributed to advancements in early detection through widespread mammography screening, increased public awareness, and significant progress in therapeutic strategies. BC is a heterogeneous disease. It is classified into four subtypes with distinct clinical characteristics: luminal A, luminal B, Human epidermal growth factor receptor 2 (HER2) positive (non-luminal) and basal tumours (3). HER2-positive breast cancer has attracted a lot of attention among these subtypes because of its unique molecular characteristics and potential therapeutic applications.

HER2 is a glycoprotein on the cell membrane that possesses intrinsic tyrosine kinase activity. It belongs to the epidermal growth factor receptor (EGFR) family. Approximately 15% of primary invasive breast cancers exhibit amplified or overexpressed HER2 oncogenes (4). HER2-positive tumors are associated with increased aggressiveness, higher recurrence rates, and reduced survival (5). Theuse of HER2-targeted therapies has resulted in improved survival outcomes in patients with the HER2-positive breast cancer subtype (6-9). In patients with HER2-positive breast cancer, neoadjuvant doublet anti-HER2 therapies have been administered to enhance the rate of pathological complete response (pCR) and improve over all survival outcomes (10-12). It is essential to recognize that patients receiving anti-HER2 therapy do not always exhibit a uniform response rate. The disparity in response rates can be ascribed to several factors, such as the unique biology of individual tumors and the specific clinical characteristics of patients.

Cancer laterality refers to the side of the body where a tumor develops, specifically in paired organs like breasts. In breast cancer, laterality distinguishes between left and right breast tumors. This concept has gained attention due to potential differences in prognosis and treatment outcomes based on tumor location (13,14). The role of breast cancer laterality in treatment decisions remains unclear, as factors like tumor stage, grade, and molecular subtype are generally considered more critical in determining treatment approaches and prognosis.

This study explored the potential for predicting treatment response rates based on cancer laterality in patients with HER2-positive breast cancer undergoing neoadjuvant therapy. Our analysis focused on the differences in breast cancer laterality and associated clinical and pathological features while also comparing our findings with those of previous studies.

MATERIALS and METHODS

This study included 115 individuals diagnosed with HER2-positive breast cancer. All participants were diagnosed and treated between January 2018 and March 2023. The following criteria were established for inclusion: primary, unilateral, non-metastatic invasive breast cancer, and trastuzumab-pertuzumab plus neoadjuvant chemotherapy (NACT). This study included patients whose neoadjuvant chemotherapy protocol adhered to the recommendations of the National Comprehensive Cancer Network (NCCN) Guidelines (Version 3. 2024) for HER2-positive breast cancer (15). Patients with invasive HER2-positive breast cancer confirmed through core needle biopsy were included in the study. HER2 status was evaluated using immunohistochemistry (IHC) in accordance with the guidelines of the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines (16). Specimens with an IHC score of 2+ underwent further evaluation using silver in situ hybridization (SISH) to confirm HER2 gene amplification. Biopsy samples were processed and analyzed at the Kocaeli University Hospital Pathology Laboratory in accordance with standardized protocols.

The patients received NACT before under going surgical intervention and completed the neoadjuvant therapy regimen before either lumpectomy or mastectomy. The study population did not include patients with phyllodes tumors, male sex, bilateral disease, ductal carcinoma in situ (DCIS), stage IV cancer, or those lacking stage data.Patients with bilateral disease and DCIS were excluded because of their significant differences in clinical management and prognosis compared with those with unilateral invasive breast cancer (17). Patients with stage IV cancer were excluded because neoadjuvant therapy is not the standard treatment for metastatic breast cancer and does not align with the study's objectives (15). Patients with missing stage data were excluded to ensure accuracy of the analysis and consistency in treatment evaluation.

Patient demographic and clinical data were retrieved from the medical records. The variables included age, body mass index (BMI), tumor localization, lymph node status,

stage at diagnosis, response to neoadjuvant therapy, metastasis, and mortality. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²) and categorized according to the WHO classifications (18). Tumor localization was documented using laterality (right or left breast) and quadrant (upper outer, upper inner, lower outer, lower inner, or central). Lymph node status was determined through histopathological evaluation and staging was performed according to the 8th edition of the AJCC TNM classification and prognostic stage criteria (19). Response to neoadjuvant therapy was categorized as complete (ypT0/is N0), partial (tumor size reduction or decreased lymphnode involvement), or progressive (tumor growth). Distant metastases during follow-up and patient mortality, including the date and cause of death, were documented to evaluate disease progression, treatment efficacy, and overall survival.

Statistical Analysis

Statistical analyses were performed using SPSS version 20.0 (SPSS, Chicago, IL, USA) and MedCalcversion 14 (MedCalc Software, Ostend, Belgium).Categorical variables are presented as frequencies and percentages, whereas continuous variables are reported as mean ± standard deviation or as median swith minimum–maximum values for non-normally distributed data. Descriptive statistics appropriate for each variable type were used to summarize patient demographics and clinical characteristics by side (left versus right). Comparisons between groups were performed using Mann–Whitney U tests for continuous variables and Pearson'schi-squaretests for categorical variables. To assess how the side influences different demographic and clinical subgroups, separate Cox regression models were customized, incorporating side, subgroup variables, and their interaction as predictive factors. Statistical significance was established at $p < 0.05$.

RESULTS

The study included 115 patients with a median age of 49 years (range 41–59 years). Patients with right-sided breast tumors had a median age of 49 years (range: 41–59 years), whereas those with left-sided tumors had a median age of 50 years (range: 42–59 years), showing no significant age difference (p = 0.704). Right breast tumors were present in 54.8% of the participants and left breast tumors were present in 45.2%. The tumor distribution across the breast quadrants was not significantly different (p = 0.659). The detailed cancer characteristics are provided in Table 1.

Table 1: Clinicopathological features of left and right breast cancer

Characteristic	Total (n= 115)	Right-Sided Breast (n=63)	Left-Sided Breast (n= 52)	p
Age (years)[a]	49 (41-59)	49 (41-59)	50 (42-59)	0.704
Age under 50 (years)[b]	59 (51.3)	34 (57.6)	25 (42.4)	0.577
BMI (kg/m)[a]	27.6 (24.6-32.0)	27.7 (24.6-32.3)	27 (24.6-31.4)	0.467
Tumor Location Side[b]	115	63 (54.8)	52 (45.2)	
Tumor Quadrant Localization[b]				
Upper outer	52 (45.2)	26 (41.3)	26 (50.0)	
Upper inner	14 (12.2)	7 (11.1)	7 (13.5)	0.659
Lower outer	17 (14.8)	9 (14.3)	8 (15.4)	
Lower inner	11 (9.6)	8 (12.7)	3 (5.8)	
Periareolar	21 (18.3)	13 (20.6)	8 (15.4)	
Lymph Node Status[b]				
cN0	61 (53.0)	36 (57.1)	25 (48.1)	
cN1	35 (30.4)	17 (27.0)	18 (34.6)	0.595
cN2	19 (16.5)	10 (15.9)	9 (17.3)	
Stage at Diagnosis[b]				
Stage 2	59 (51.3)	32 (50.8)	27 (51.9)	1.000
Stage 3	56 (48.7)	31 (49.2)	25 (48.1)	
Neoadjuvant Response[b]				
Complete	93 (80.9)	51 (81)	42 (80.8)	1.000
Partial	22 (19.1)	12 (19)	10 (19.2)	
Metastasis [b]				
Yes	11 (9.6)	7 (11.1)	4 (7.7)	0.752
Mortality[b]				
Death	3 (2.6)	2 (3.1)	1 (1.9)	

BMI: Body Mass Index, **a:** Median (IQR), **b:** n (%).

None of the patients with either right- or left-sided breast tumors exhibited disease progression during neoadjuvant therapy. Complete response was achieved in 51 (81%) patients with right-sided tumors and 42 (80.8%) with left-sided tumors. Partial responses were observed in 12% of right-sided tumors and 10% of left-sided tumors. The treatment response did not differ significantly based on the tumor location (p = 1.000).

During the follow-up period, 11 patients (9.6%) developed metastasis. Of these, seven (63.6%) had right breast tumors and four (36.4%) had left breast tumors (p = 0.752). Regarding neoadjuvant therapy, of the 93 patients with a complete response, 8 (8.6%) developed metastasis, whereas among the 22 patients with a partial response, 3 (16.6%) developed metastasis (p = 0.438). Among the 7 right breast metastasis cases, 71.4% involved bone metastasis, whereas none of the 4 left breast cases involved bone metastasis (p = 0.061). There were no statistically significant differences in the diagnostic stages or number of pathological lymph-nodes between the groups (Table 1).

The distribution of HER2 status among the patients, including the observed immunohistochemical and molecular subtypes, is presented in detail in Table 2. Regarding treatment response, 76 of 90 patients (84.4%) with HER2 3+ achieved a complete response, compared with 17 of 25 (68.0%) with HER2 IHC 2+/SISH+ (p = 0.085). Metastasis occurred in seven of the 90 HER2 3+ patients and in four of the 25 HER2 IHC 2+/SISH+ patients (p = 0.251). Tumor analysis based on pathological patterns, using data from 44 patients because of technical limitations, showed no significant differences in lymphovascular invasion (LVI) or perineural invasion (PNI). However, a significant association was found between DCIS (p = 0.016). Table 2 summarizes the tumor characteristics according to the pathological patterns for right- and left-sided tumors.

Table 2: Tumor Characteristics Based on Pathological Patterns for Right and Left Tumors

Characteristics*	Total (n=115)	Right-sided Breast (n=63)	Left-sided Breast (n=52)	P
ER %				
ER >50%	38 (33.0)	23 (36.5)	15 (28.8)	
ER 10-50%	15 (13.0)	6 (9.5)	9 (17.3)	
ER < 10%	8 (7.0)	6 (9.5)	2 (3.8)	
ER negative	54 (47.0)	28 (44.4)	26 (50)	0.354
PR %				
PR > 50%	16 (13.9)	63 (54.8)	8 (15.4)	
PR 10-50%	20 (17.4)	12 (19.0)	8 (15.4)	0.854
PR < 10%	16 (13.9)	10 (15.9)	6 (11.5)	
PR negative	63 (54.8)	33 (52.4)	30 (57.7)	
HER2				
3+	90 (78.3)	50 (79.4)	40 (76.9)	0.929
2+/ SISH +	25 (21.7)	13 (20.6)	12 (23.1)	
Grade				
Grade 1	8 (7.0)	5 (8.1)	3 (5.8)	
Grade 2	65 (56.5)	40 (64.5)	25 (48.1)	0.110
Grade 3	41 (35.7)	17 (27.4)	24 (46.2)	
Ki-67				
Ki-67 > 20%	64 (55.7)	32(69.6)	32 (72.7)	
Ki-67 10-20%	20 (17.4)	9 (19.6)	11 (25)	0.284
Ki-67 < 10%	6 (5.2)	5 (10.9)	1 (2.3)	
Not available	25 (21.0)	17 (26.9)	8 (15.3)	
LVI				
Negative	31 (70.5)	20 (76.9)	11 (61.1)	
Positive	13 (29.5)	6 (23.1)	7 (38.9)	0.427
Not available	71 (61.7)	37 (58.7)	34 (65.3)	
DCIS				
Negative	11 (25.0)	10 (38.5)	1 (5.6)	
Positive	33 (28.7)	16 (61.5)	17 (94.4)	0.016
Not available	71 (61.7)	37 (58.7)	34 (65.3)	

*Data were shown as n (%). **ER:** Estrogen receptor, **PR:** Progesterone receptor, **HER2:** Human Epidermal Growth Factor Receptor 2, **SISH:** Single-cell sequencing, **Ki-67:** Proliferation index, **LVI:** Lymphovascular invasion, **DCIS:** Ductal carcinoma in situ.

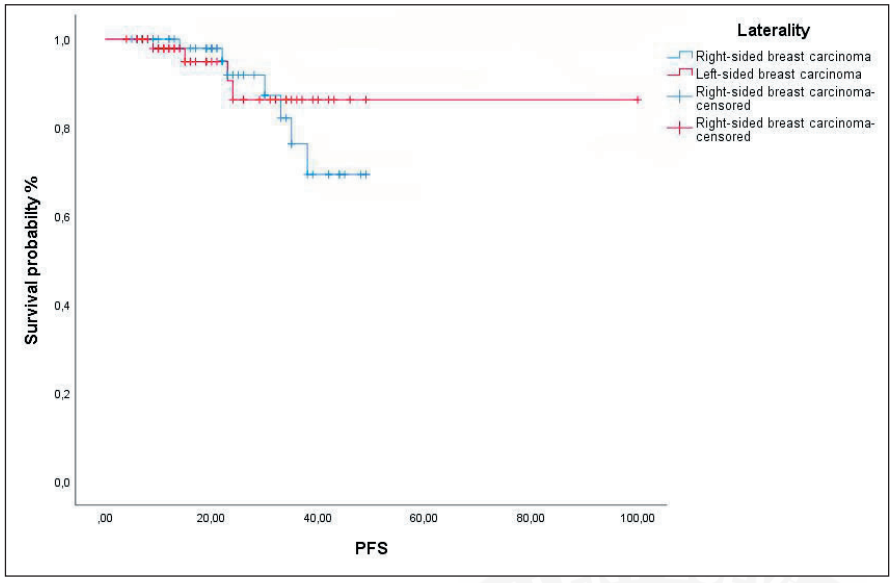


Figure 1: Kaplan-Meier curves of patients based on laterality

In our study, the median observation period was 22 months (IQR 12-34 months). According to the Kaplan–Meier analysis, the progression-free survival in right breast tumors was 43.3 ± 1.83 months, whereas it was 88.9 ± 5.2 months in left breast tumors (Figure 1). However, this observed disparity failed to attain statistical significance, yielding a p-value of 0.687.

DISCUSSION

In breast cancer characterized by over expression of the HER2 gene, patients who achieve pathological complete response after neoadjuvant therapy end to have beter overall survival rates than those who do not achieve it (20). The effectiveness of neoadjuvant therapy is influenced by a variety of histological, genetic, and molecular factors, which has led to the question of whether tumor location can serve as a simpler and quicker prognostic indicator. In the present study, we discovered that there was no detectable variation in the response to neoadjuvant therapy based on the laterality of the tumor, regardless of whether it was on the left or right side, among patients with HER2-positive breast cancer. Our results indicate that there was no difference in the incidence of metastasis between patients with breast cancers on the left or right side.

In contrast to the results of our study, Abdou et al. observed that left-sided tumors exhibited lower pCR than right-sided tumors (21). This difference may be due to various factors such as tumor characteristics, patient demographics, or treatment received. This disparity highlights the intricate nature of the factors that influence the response to neoadjuvant therapy in patients with HER2-positive breast cancer and under scores the necessity for further research to elucidate the underlying mechanisms driving tumor response based on tumor laterality.

Unlike the outcomes of an extensive investigation, which indicated a higher incidence of left-sided breast tumors, our research revealed a noticeable numerical predominance of right-sided tumors among the patient population (21,22). Several studies have indicated a minor deterioration in breast cancer-related death rates in the lower left iner quadrant; nonetheless, our research did not reveal any notable connection between laterality and the primary tumorsite (23,24). Consistent with our study, most previous studies have shown no disparity in survival outcomes based on breast cancer laterality (25,26).

After analyzing tumor characteristics based on the pathological patterns of right and left tumors, we found a notably higher incidence of DCIS in left-sided tumors. However, despite this observation, our data showed no disparity in neoadjuvant therapy response rates between tumors on the right and left sides. This finding contrasts with previous research, which has consistently shown that tumors with adjacent DCIS exhibit less aggressive behavior and enjoy significantly beter overall survival rates than those without DCIS (5-year OS, 89.3% vs. 85.5%, p<0.001)(27). Furthermore, patients achieving pCR, regardless of the presence or absence of DCIS, demonstrated significantly improved overall survival and disease-free survival compared with those with residual invasive cancer (28). No differences were observed in neoadjuvant treatment responsesbased on the HER2-positive subtype (HER2 IHC 3+ / IHC 2+/SISH+); no differences were noted between the right and left sides. Despite studies indicating that the overexpression of the HER2 protein could assist in predicting treatment response, our data did not reveal any differences in responses (29).

This study had certain limitations, primarily due to its retrospective design. Unfortunately, we failed to obtain patholog-

ical pattern data for all patients. Consequently, we could not definitively establish the influence of the higher incidence of DCIS in the left breast than in the right breast on neoadjuvant response rates. Instead, we could only identify these associations.

In conclusion, our findings indicate that there is no significant difference in the response to neoadjuvant chemotherapy between the right and left breast tumors. In addition, no disparity in metastasis development was observed during the follow-up period. Therefore, laterality is not considered a prognostic factor for breast cancer.

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None.

Author Contributions

Yasemin Bakkal Temi: Project development, desing, literature research, data analysis, manuscript writing. **Mahmut Peynirci:** Data collection, data analysis. **Devrim Çabuk:** Project development, management, manuscript editing. **Umut Kefeli:** Project development, manuscript editing. **Kazım Uygun:** Manuscript editing.

Conflicts of Interest

The authors declare that they have no competing interests relevant to the content of this article. We confirm that neither the manuscript nor any parts of its content are currently under consideration or published in another journal. Furthermore, the manuscript has not been presented at any conference.

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Ethical Approval

The Institutional Review Board of Kocaeli University approved the study and adhered to the principles of the Declaration of Helsinki. (Ethics Approval Code: KOÜ GOKAEK-2023/08.37, Project Identifier: 2023/131). Informed consent was not require dowing to the retrospective design of the study.

Review Process

Extremely and externally peer-reviewed.

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ORIGINAL ARTICLE

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Efficacy of Intra-Arterial vs. Intravenous tPA Monotherapy in Acute Ischemic Stroke Treatment

Akut İskemik İnme Tedavisinde Sadece İntra-Arteriyel tPA ile Sadece İntravenöz tPA'nın Karşılaştırılması

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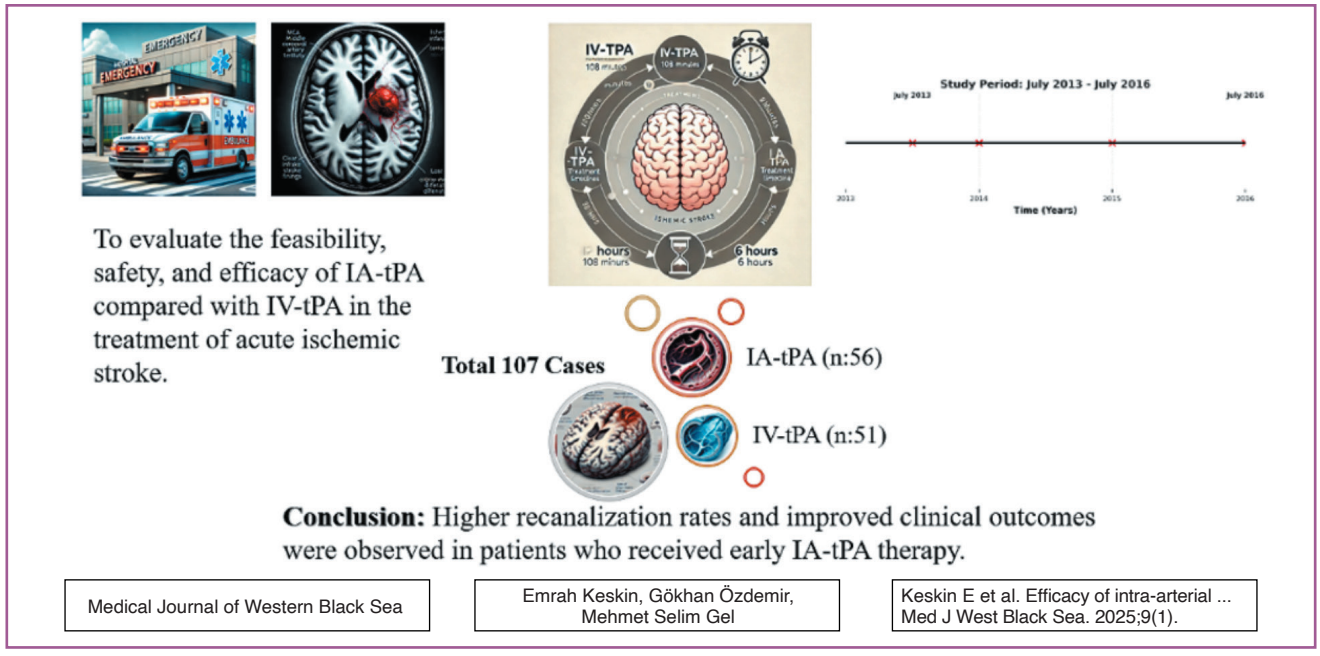
GRAPHICAL ABSTRACT



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ABSTRACT

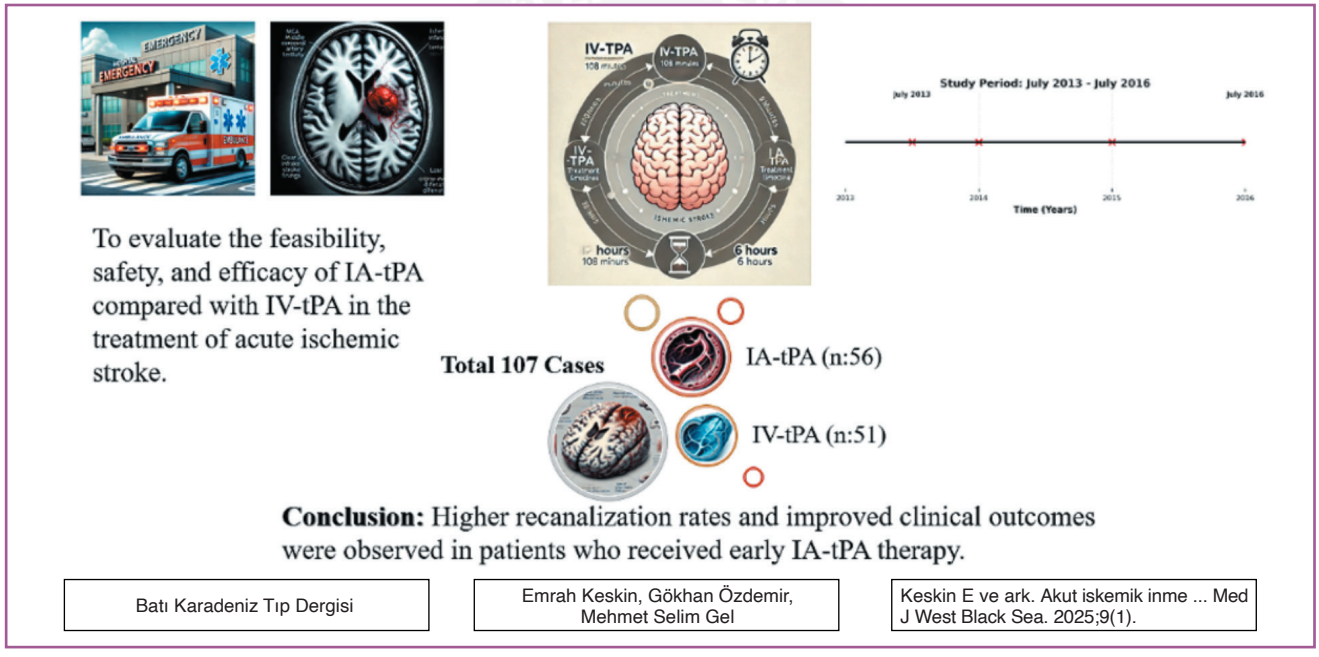
Aim: The method and timing of administration of tissue plasminogen activator (tPA) in the treatment of acute ischemic stroke (AIS) remain unclear. In our study, we aimed to compare the effectiveness of intra-arterial (IA)-tPA compared to intra-venous (IV)-tPA in AIS.

Material and Methods: Patients with AIS received IV-tPA within one hundred and eight minutes or IA-tPA within the first six hours. Before both treatments, their conditions were evaluated and treatments were performed. AIS patients were divided into those receiving IV alteplase (maximum 0.90 mg/kg) and those receiving IA alteplase (maximum 0.30 mg/kg). Demographic characteristics, systemic diseases and clinical outcomes were evaluated in both groups.

Results: It was observed that the clinical findings of the patients in the IA group were worse at the time of admission, but were better than those in the IV group after the procedure. While the ICH rate was similar in both groups (p>0.817); the recanalization rate was higher in the IA group compared to the IV group (p<0.001). Patients receiving IA treatment with alteplase doses of 20 mg or less had better clinical improvement (p = 0.020). In the IA group, the relationship between recanalization rate and the time of the onset of early treatment was statistically significant (p = 0.007).

Conclusion: According to the findings of our study, IA administration of tPA in the treatment of AIS is a more effective and applicable treatment option than IV administration. In addition, since higher recanalization rates and better clinical outcomes are observed in patients who receive IA-tPA treatment in the early period, more effective results can be obtained, especially in patients with large vessel occlusion.

GRAFİKSEL ÖZET



ÖZ

Amaç: Akut iskemik inme (Aİİ) tedavisinde doku plazminojen aktivatörünün (tPA) uygulanma yöntemi ve zamanlaması hala belirsizliğini korumaktadır. Çalışmamızda, Aİİ'de intra-arteriyel (İA)-tPA'nın intra-venöz (İV)-tPA ile etkinliğini karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Aİİ'li hastalara yüz sekiz dakika içinde İV-tPA veya ilk altı saat içinde İA-tPA verildi. Her iki tedaviden önce durumları değerlendirildi ve tedaviler uygulandı. Aİİ hastaları İV alteplaz (maksimum 0,90 mg/kg) alanlar ve İA alteplaz (maksimum 0,30 mg/kg) alanlar olarak ayrıldı. Her iki grupta da demografik özellikler, sistemik hastalıklar ve klinik sonuçlar değerlendirildi.

Bulgular: İA grubunun çalışmanın başlangıç noktasında İV grubuna göre daha yüksek Ulusal Sağlık Enstitüleri İnme Ölçeği (NIHSS) ve modifiye Rankin skorları (mRS) olmasına rağmen, iyi klinik sonuçlar İA grubunda daha iyiydi. Her iki gruptaki intrakranial kanama oranı benzer iken (p >0,817); rekanalizasyon oranı İA grubunda İV gruba kıyasla daha yüksekti (p<0,001). İA grubunda, rekanalizasyon oranı ile erken tedavinin başlama zamanı arasındaki ilişki istatistiksel olarak anlamlıydı (p = 0,007).

Sonuç: Çalışmamızın bulgularına göre Aİİ tedavisinde tPA'nın İA uygulanması, İV uygulanmasına göre daha etkili ve uygulanabilir bir tedavi seçeneğidir. Ayrıca erken dönemde İA-tPA tedavisi uygulanan hastalarda daha yüksek rekanalizasyon oranları ve daha iyi klinik sonuçlar gözlendiğinden, özellikle büyük damar tıkanıklığı olan hastalarda daha etkili sonuçlar elde edilebilir.

Anahtar Sözcükler: İntra-arteriyel, intra-venöz, tPA, akut, iskemik İnme

INTRODUCTION

The first hours are critical in the treatment of acute ischemic stroke (AIS). Many studies show that tissue plasminogen activator (tPA) administered up to 4.5 hours after the onset of the first symptoms in AIS can improve clinical outcomes (1-3). On the other hand, IV alteplase is considerably less successful at restoring blood flow in the proximal segments of the principal intracranial arteries (middle cerebral artery (MCA), basilar artery) (4). The additional impact of intra-arterial (IA) tPA may vary depending on whether the initial treatment is IV-tPA or a conventional therapy. Given the treatment's extended time window, a localized IA thrombolytic infusion could prove beneficial for stroke patients presenting later. In patients who cannot receive IV tPA, IA tPA is recommended for strokes caused by blockage of a large vessel such as the MCA artery. The time required to administer IA tPA may be the first six hours from the onset of symptoms (5-7).

Intra-arterial thrombolysis (IAT) provides several benefits compared to IV thrombolysis (IVT). For instance, angiographic planning enables a tailored treatment strategy; targeted injections deliver a high local concentration of the drug while minimizing the overall dose, and mechanical devices can either accelerate recanalization or enable it when drugs alone are insufficient (8). In contrast to IVT, IA treatment is a lengthier and more invasive process. It also relies on costly technologies that are typically accessible only at specialized centers equipped with neuro-interventional teams (9). Successful vessel recanalization is linked to superior clinical outcomes (10). Although overall mortality rates are the same, the clinical consequences of intracranial hemorrhage (ICH) are higher. (11).

This study compared the clinical outcomes of both treatment approaches while controlling for factors like age, chronic conditions, and smoking habits. Ultimately, we aimed to evaluate the superiority of using only IA-tPA compared to using only IV-tPA in treating AIS.

MATERIALS and METHODS

Study Design

The main objective of this study was to determine if stroke patients undergoing IAT in the experimental group were more likely to achieve functional independence at 90 days than those receiving IVT in the control group. Patients with a modified Rankin scale (mRS) score of 0 at the third month of treatment were considered cured. The study also aimed to compare both groups regarding neurological impairment—assessed by National Institutes of Health Stroke Scale [NIHSS] scores on days 0, 1, and 7—and treatment safety, evaluated through the rates of symptomatic ICH, fatal and nonfatal strokes, overall mortality, and any neurological decline within the first week. In addition, patients' ages, chronic diseases (diabetes mellitus (DM), hypertension (HT), atrial fibrillation (AF), hypercholesterolemia), current cigarette smoking, survival times were compared between the two groups by examining their files.

Study Population

All patients diagnosed with AIS based on computed tomography (CT) and/or magnetic resonance imaging (MRI) findings who were consecutively admitted to our stroke center were enrolled in this study. The patients were 16 years of age or older (there was no upper age limit in the IA-tPA group, but the age limit was 80 years old in the IV-tPA group) and had AIS caused by an intracranial occlusion. The patients were recruited from July 2013 through July 2016. The included study randomized 107 patients (IA-tPA n =56, IV-tPA n = 51). Patients were admitted to hospitals by air or road, and all patients received IA-tPA within a six-hour window and IV-tPA within a 4.5-hour window, per NINDS criteria. All patients or their family members consented to thrombolytic treatment. Patients presenting with ICH or significant cerebral edema detected on CT scans were excluded from the study. Additional exclusion criteria included prior significant disability (mRS >2), severe comorbid conditions, and contraindications for thrombolytic therapy (Table 1) (12). The baseline assessment involved neurological and physical examinations, stroke severity scoring via the NIHSS and mRS scales, routine blood tests, electrocardiography and CT/MRI. Before the intervention, digital subtraction angiography (DSA) was conducted on candidates for IA-tPA to evaluate their vascular condition.

Following thrombolytic therapy, all patients had a follow-up CT scan within 24 hours. On the seventh day, additional imaging studies, including MRI, magnetic resonance angiography, and duplex ultrasonography, were performed to evaluate vascular and neurological recovery.

IV-tPA administration involved alteplase (50 mg, Boehringer Ingelheim, Rhein, Germany) at a dose of 0.9 mg/kg (maximum 90 mg), with an initial 10% bolus followed by a continuous infusion over 60 minutes. IA-tPA was delivered locally with a maximum of 30 mg in the carotid system and 20 mg in the vertebrobasilar system. Patients in the IA group were treated within 45 minutes of arriving at the hospital, and DSA was used post-procedure to assess recanalization success. IV heparin (25000 IU/ml, Pharmada, Istanbul, Türkiye) was initiated with a 3000-10000 U bolus during procedures in which IA-tPA was performed. General anesthesia was not administered (only two patients were given sedation). The IA-tPA patients were treated within 45 minutes (from the emergency to the intervention). Using a steerable microguidewire, an infusion microcatheter featuring a single distal opening was navigated into the thrombus's core. Sometimes the catheter may not be placed in the thrombus

Table 1. Major inclusion and exclusion criteria (12).

Inclusion criteria
- Sudden focal neurological deficit attributable to a stroke.
- Start within the first 4.5 hours for IV treatment; start within the first 6 hours for IA treatment
- Age between 16 and 80 years in IV-tPA (no upper age limit in IA-tPA).
CT/MRI exclusion criteria
- ICT except for small lesions
- Brain hemorrhage regardless of size
- Acute infarction or edema
Other exclusion criteria
- Poor level of consciousness at the time of first presentation (coma)
- Severe stroke as assessed clinically (eg, NIHSS score .25)
-Patients with rapid improvement in neurological status and minor symptoms
-Any major surgery or trauma within the last four weeks
- Baseline INR greater than 1.3, aPTT more than 1.5 times normal
- Platelet count less than 100 000 per cubic millimeter
- Blood glucose concentrations below 60 mg/dl or above 400 mg/dl
-Blood pressure ≥185 mm Hg systolic or ≥110 mm Hg diastolic on at least 3 consecutive measurements or uncontrolled hypertension that does not respond to treatment
- Situations in which the administration of thrombolytic drug is contraindicated

IV: İntra-venous, **IA:** intra-arterial, **CT:** computed tomography, **MRI:** Magnetic resonance imaging, **ICT:** intra-cranial tumor, **aPTT:** activated partial thromboplastin time, **INR:** international normalized ratio, **NIHSS:** National Institutes of Health Stroke Scale, **mRS:** modified Rankin Scale.

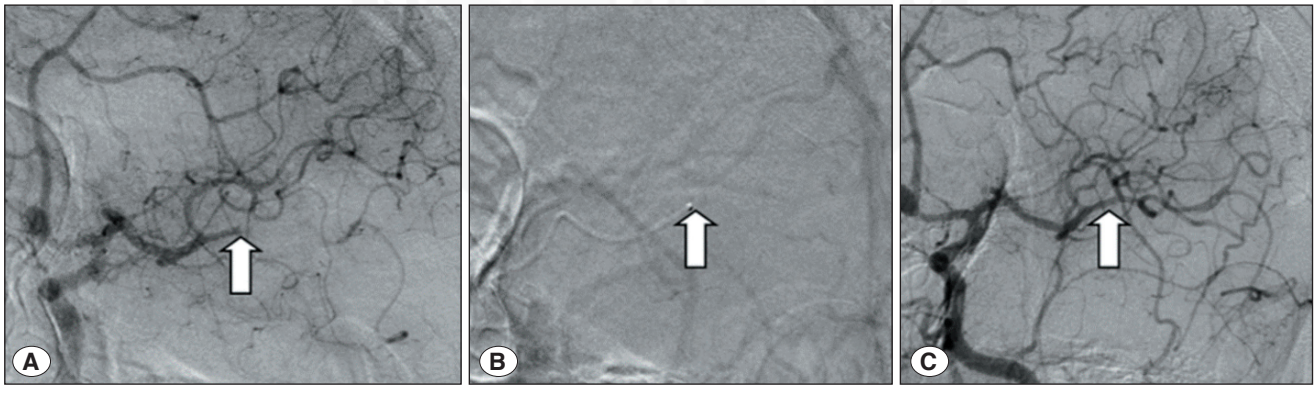


Figure 1: Obstruction is observed in the narrowing of the middle cerebral artery **(A)**, and after advancing the microcatheter **(B)** to the distal part of the obstruction, recanalization **(C)** was achieved by removing the clot with the help of aspiration and a retriever stent.

area. In this case, the catheter was parked as proximal to the thrombus as possible. At this stage, a superselective angiogram was performed to see the relationship between the catheter and the thrombus (Figure 1). This treatment procedure was performed in accordance with the European Stroke Organization guidelines (13).

All patients in both treatment groups were kept under observation in the stroke intensive care unit due to the importance of close monitoring of the process. In addition, control cranial CT scans were performed on the patients 24 hours after treatment. Antiplatelet therapy and low-dose subcutaneous heparin (25000 IU/5 ml, Pharmada, Istanbul, Türkiye) were started in all patients without bleeding on CT scan.

Patient records were scanned from the archives and risk factors were assessed. These were age, sex, HT, diabetes mellitus (DM), smoking status, hypercholesterolaemia, heart disease, AF (Table 2). We also examined patients already taking antiplatelets to determine the drugs' effects on ICH and the effectiveness of the treatment.

Statistical Methods

Statistical evaluation was performed using SPSS 18.0. The minimum and maximum values of the descriptive statistics, numbers, percentages of categorical variables, average of numeric variables, standard deviation, hydrangea, percentile 25 (Q1), and percentile 75 (Q3) were presented. The normal distribution of variables was examined using visual (histogram and probability graphics) and analytical (Kolmogorov-Smirnov and Shapiro-Wilk tests) methods. The Mann-Whitney U Test was used in two independent group comparisons in which no normal distribution condition was provided for numerical variables. The Students'-test was performed when the normal distribution was provided. For independent multiple-group comparisons, an analysis of variance (ANOVA) was applied when the assumption of normal distribution was met, whereas the Kruskal-Wallis test was utilized when this assumption was not satisfied. In the post hoc analyses, the Mann-Whitney Test was performed using the Bonferroni correction. The chi-squared test was performed for binary and multiple comparisons of the categorical variables, the Fisher's Exact Test was performed for binary comparisons not provided by the chi-squared condition, and the Multi-Eyed Fisher's Extermination Test was used for multiple comparisons. For correlations that did not meet the normal distribution condition, Spearman's coefficient test statistic was used in relation to the numerical values. P values less than 0.05 were considered significant.

RESULTS

The patients' mRS scores on day 90 and NIHSS scores on days 1-7 were evaluated. The incidences of recanalization and ICH are presented in the Table 3. Although in the IA group had NIHSS and mRS scores that were higher than the scores of the IV group at the starting point, the improved results were better in the IA group. The recanalization rate was higher in the IA group (p<0.001, Table 3). The rate of ICH complications was similar in both groups. Although survival times were similar for both groups, they were better in the IA group (Figure 2).

In the IA group, the highest glucose values were found in those with ICH and in those who had recanalization (p = 0.018 and p = 0.004, respectively, Table 4). In the IA group, the improved NIHSS and mRS scores were correlated with low glucose values (p = 0.002 and p = 0.001, respectively, Table 4).

Table 2. Demographics and Vascular Risk Factors of Patients Treated With Intravenous and Intraarterial t-PA.

Characteristics	Intravenous (n=51)	Intra-arterial (n=56)	p
Mean age (Year±SD)	67.5±11.6	70.2±9.7	0.674
Hypertension, n (%)	37 (71.2)	41 (73.2)	0.291
Diabetes mellitus, n (%)	18 (34.6)	15 (26.8)	0.167
Hypercholesterolemia, n (%)	20 (38.5)	12 (21.4)	0.678
Current smokers, n (%)	10 (19.2)	15 (26.8)	0.259
Atrial fibrillation, n%	14 (26.9)	19 (33.9)	0.229
Heart disease, n (%)	26 (50.0)	41 (73.2)	0.141

SD: standard deviation, Mann Whitney Test

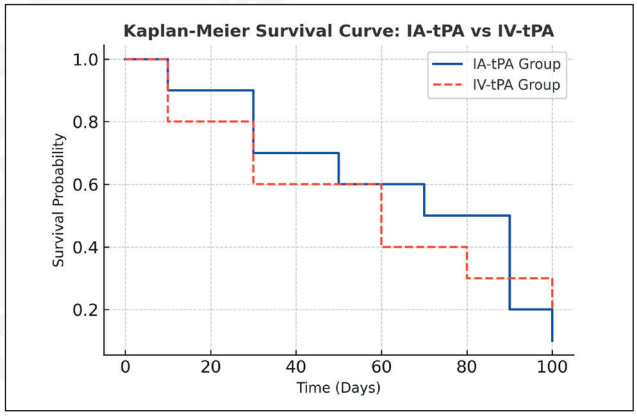


Figure 2: Results of Intra-arterial tPA and Intravenous tPA groups according to Kapla-Meier curve.

Table 3. Data on primary outcomes (scores on mRS at day 90 and NIHSS on days 1-7) and incidences of recanalization and ICH.

		IA Group (n=56)	IV Group (n=51)	p
NIHSS, (score±SD)	Start	17.2±5.62	15.86±2.27	0.106[A]
	Day one	14 (8.5-18)	12 (8-15)	0.049[C]
	Day seven	6 (4-12)	8 (6-12)	0.103[C]
mRS, (Q1-Q3)	Start	5 (4-5)	3 (3-4)	<0.001[C]
	Three months	1 (0-3)	2 (1-3)	0.051[C]
Recanalization	After treatment	41 (73.2%)	20 (39.2%)	<0.001[F]
Hemorrhage	After treatment	10 (17.9%)	10 (19.6%)	0.817[F]

ICH: intracranial hemorrhage, **IA:** intra-arterial, **IV:** intra-venosus, **NIHSS:** National Institutes of Health Stroke Scale, **mRS:** modified Rankin Scale, [A] Student T Test, [B] Anova, [C] Mann Whitney Test, [D] Kruskal Wallis Test, [E] Fisher's Extermination Test, [F] chi-square Test, [G] Multi-Eyed Fisher's Extermination Test, [H] Spearman Test

Table 4. In the IA treatment group; the relationship between hemorrhage, re-canalization, re-occlusion, NIHSS and mRS treatment results and glucose values.

IA Group Glucose Levels		Findings (n=56, Mean±SD)	p
Hemorrhage	Nope	124.78±24.98	0.018[A]
	Yes	146.2±25.93	
Re-canalization	Nope	145.07±18.2	0.004[A]
	Yes	122.59±26.32	
Post-recanalization	Nope	128.47±26.85	-*
	Yes	131±14	
Re-occlusion	Nope	128.35±24.69	0.819[A]
	Yes	131.2±42.97	
NIHSS Treatment Result	Nope	154.88±14.46	0.002[A]
	Yes	124.23±25.27	
mRS Treatment Result	Nope	154±13.77	0.001[A]
	Yes	123.74±25.31	

IA: intra-arterial, **SD:** standard deviation, **NIHSS:** National Institutes of Health Stroke Scale, **mRS:** modified Rankin Scale, [A] Student T Test, * Analysis could not be performed because the number of patients was not sufficient.

The patients in the IA treatment group who were given an alteplase dose of 20 mg or less had the most improved scores on the first day, at the end of the first week, and at the end of the third month of the study (p = 0.011, p = 0.020, and p = 0.007, respectively, Table 5). The decreased rate of ICH was found to be statistically significant in the IA patients who received alteplase doses of 20 mg or less (p = 0.032, Table 5).

DISCUSSION

Many studies have emphasized the importance of IA-thrombolysis for the treatment of AIS. This study showed that patients with AIS at various locations who received only IAT treatment had better functional outcomes than those who received only IVT treatment. In addition, this study showed that symptomatic ICH did not differ significantly between the treatment groups.

The IV administration of thrombolytic, or IVT, is one of the most well proven beneficial treatments for the emergency management of ischemic stroke (5). A local IA infusion of thrombolytic, or IAT, might also be beneficial for ischemic stroke patients. For patients who are not eligible for IVT, IAT is advised if initiated within six hours of a stroke onset caused by a blockage in the MCA (6, 7). Nonetheless, comparative studies evaluating the effectiveness of IAT versus IVT are currently limited.

Ciccone and Valvassori evaluated the clinical outcomes of 362 patients who were randomly treated with IVT or IAT.

Table 5. Relationship of alteplase dose with hemorrhage, re-canalization, re-occlusion, NIHSS and mRS treatment outcomes in the IA treatment group.

	IA-Alteplase Dosage Group		
	20 and under, (n=24)	20 and above, (n=32)	p
NIHSS	15.54±5.94	18.44±5.1	0.055[A]
NIHSS Treatment Result	11.5 (8-15.5)	17 (11-20.5)	0.011[B]
mRS Treatment Result	5 (3-8)	8 (4-18)	0.020[B]
	4 (3.5-5)	5 (4-5)	0.042[B]
Hemorrhage	23 (95.8)	24 (75)	
	23 (95.8)	23 (71.9)	0.032[C]
Re-canalization	1 (4.2)	9 (28.1)	
	22 (91.7)	29 (90.6)	1.000[C]
	2 (8.3)	3 (9.4)	
Post-recanalization	4 (16.7)	11 (34.4)	0.139[D]
	20 (83.3)	21 (65.6)	
Re-occlusion	22 (91.7)	31 (96.9)	-*
	2 (8.3)	1 (3.1)	

IA: intra-arterial; **NIHSS:** National Institutes of Health Stroke Scale; **mRS:** modified Rankin Scale, [A] Student T Test, [B] Mann Whitney Test, [C] Fisher's Extermination Test, [D] chi-square Test, * Analysis could not be performed because the number of patients was not sufficient.

The distribution of patients in both treatment groups was equal. In this study, they evaluated the disability-free survival rates of the patients. The 90-day survival rates were similar in both groups at 30%. In conclusion, they showed that IAT was not superior to standard therapy (14). Similarly, in the two randomized studies by Ducrocq et al. (15) and Ciccone et al. (9), a significant difference in favorable outcomes between IAT or IVT in conjunction with therapy was not found. In contrast, four studies with different numbers of subjects found more favorable outcomes with IAT than with IVT in patients with AIS (16-19).

In the present study, the IA group had more favorable NIHSS scores than the IV group. In this study, by the end of the three-month period, the IA group dropped from 17 points to 6 points, and the IV group dropped from 15 points to 8 points. In addition, over the three-month period, the mRS scores in the IA group dropped from 5 points to 1 point, and the IV group dropped 3 points to 2 points.

Saver et al. (20) emphasized the importance of administering speedy endovascular therapy with thrombectomy in patients who have achieved reperfusion. In the present study, such patients were taken into treatment with in 45 minutes (from the emergency department to groin puncture) in the IA-tPA group. This study showed that IA treatments applied

sooner after a stroke resulted in higher recanalization rates than IA treatments applied later after a stroke ($p<0.05$). However, there was no relationship between recanalization and treatment time in the IV group. The precise process by which bridging therapy enhances functional recovery has not yet been elucidated (21). Although the present study showed that the recanalization rates in the IA group were very high and were associated with improved NIHSS and mRS scores, these rates did not correlate with the improved scores. This study has highlighted that improved reperfusion was not a guarantee of clinical efficacy.

The primary objective in managing AIS is to restore circulation by reopening vessels that have been blocked (22). Recanalization can be attained by IV or IAT. Among patients receiving IVT, the overall rate of vessel reopening is around 46%; however, success drops significantly when the blockage involves a major artery (23-26). In the present study's IV group, the overall recanalization rate was 39.2%. Some studies have indicated that IAT tends to result in more effective vessel reopening compared to IVT (10, 18, 27). This study revealed that the IA group achieved significantly greater recanalization rates than the IV group ($p = 0.001$).

Recent studies on IAT have reported rates of ICH ranging from 0% to 33% (17, 28). Multiple studies have demonstrated that the incidence of symptomatic hemorrhage does not significantly differ between the treatment options (9, 14, 15). In this study, the IAT group experienced an ICH rate of 17.9%, yet no symptomatic hemorrhages were observed. The decreased rate of ICH was found to be statistically significantly in IA patients who received alteplase doses of 20 mg or less ($p = 0.032$). In addition, the patients who received the IA treatment and who were given alteplase doses of 20 mg or less had the most improved scores.

Different studies have observed differences between functional outcomes and risk factors in AIS patients. Ping Yu's research indicated that patients with better functional outcomes tended to be older, had a lower proportion of males, and showed a higher prevalence of AF, coronary heart disease, and DM. In addition to the different functional outcomes, clinical characteristics and smoking status of the patients also differed. These patients also had irregularities in terms of medication use (29). According to Tziomalos et al., factors such as older age, previous ischemic stroke and admission NIHSS score predicted poor outcomes at discharge as independent factors, while previous statin therapy was linked to more favorable outcomes (30-33). Individuals with stress-induced hyperglycemia experienced strokes that were more severe compared to those without this condition (32). In the IA group in the present study, the highest glucose value was found in those with the ICH and in those who had recanalization (respectively, $p = 0.018$ and $p = 0.004$, Table 4). In the IA group, the most improved NIHSS and mRS scores were correlated with lower glucose values (respectively, $p = 0.002$ and $p = 0.001$, Table 4).

This study's limitation was that the number of participants was restricted by the single-center nature of the study.

In conclusion, the use of immediate IAT as sole treatment for AIS patients is not only safer but also more effective than IVT alone in restoring blood flow, significantly reducing disability and increasing the percentage of individuals achieving functional independence three months after stroke.

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None.

Author Contributions

Conception, design, data collection, literature search, writting, approval: **Gökhan Özdemir,** Conception, design, literature search, writting, approval: **Gökhan Özdemir, Emrah Keskin,** Analysis and interpretation of data, writting, approval: **Emrah Keskin.** All co-authors have had the opportunity to review the final manuscript and have provided their permission to publish the manuscript.

Conflicts of Interest

There is no conflict of interest among the authors. Written consent for medical treatment was obtained from the families of cases under 18 years of age.

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Ethical Approval

The research was approved by the Research Ethics Committee at Selcuk University (certificate number 2018-5/80). Informed consent was obtained from all patients in the study.

Review Process

Extremey and externally peer-reviewed.

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ÖZGÜN ARAŞTIRMA

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Fazio Lateralite Envanteri'nin Türkçe Geçerlilik ve Güvenilirlik Analizi

Validity and Reliability Analysis of the Turkish Version of the Fazio Laterality Inventory

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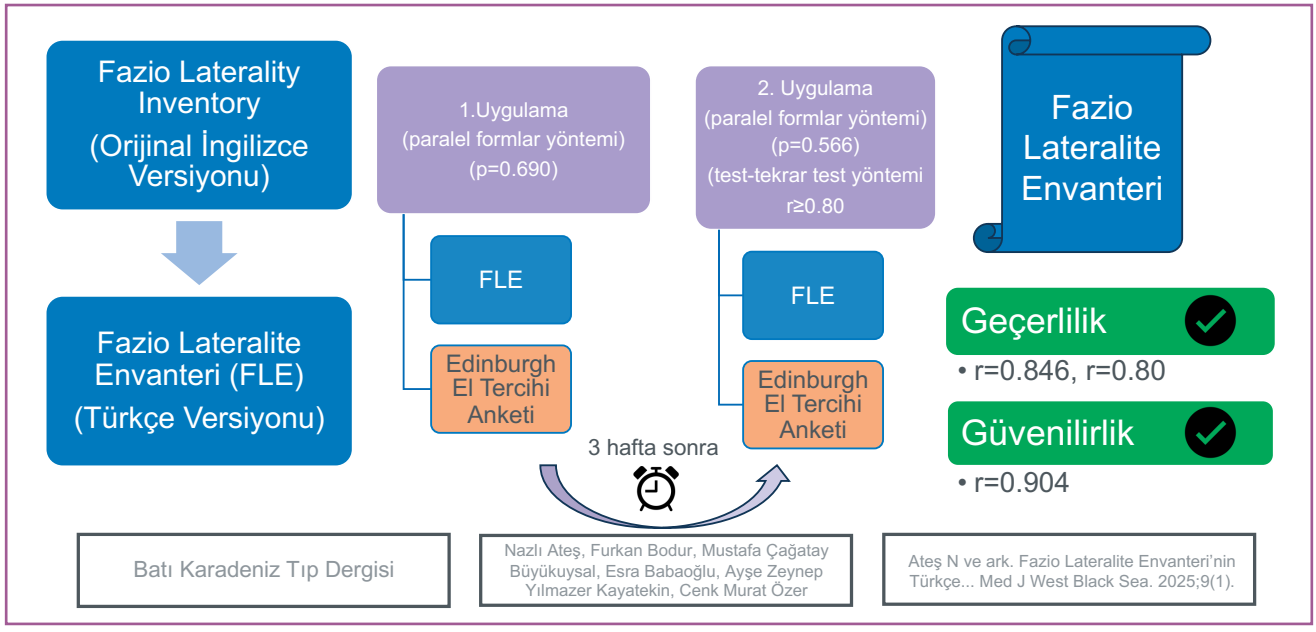
GRAFİKSEL ÖZET



ÖZ

Amaç: El tercihinin belirlenmesi amacıyla en sık uygulanan anketlerden biri Edinburgh El Tercihi Anketi (EETA)'dir. Bu anketin güncelliğini yitirmiş maddeler içerdiği düşünüldüğü için Fazio Lateralite Envanteri (FLE) gibi modernize alternatifler oluşturulmuştur. Çalışmamızın amacı FLE'nin Türkçe güvenilirlik ve geçerlilik analizini yaparak ülkemizde de uygulanabilirliğini ölçmektir.

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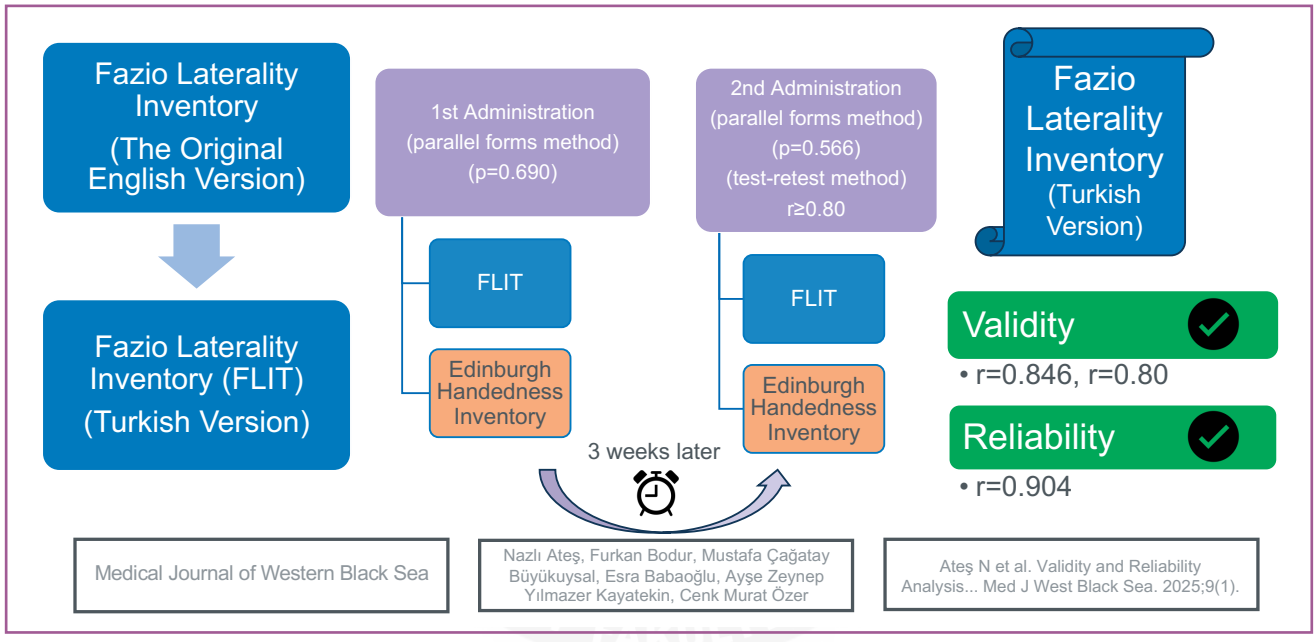
Gereç ve Yöntemler: FLE'nin orijinal versiyonunun Türkçe çevirisi Beaton prosedürüne göre gerçekleştirildi. Yaşları 18-34 arasında değişen 255 üniversite öğrencisine eş değer (paralel) formlar yöntemi ile Türkçe versiyonu bulunan EETA ve FLE uygulandı. İlk test uygulamasından 3 hafta sonra test-tekrar test yöntemi ile her iki test tekrar edildi. Anketlerin sonuçları EETA için lateralite katsayısı (LQ skoru), FLE için Lateralite İndeksi (Lİ) kullanılarak hesaplandı. Anket sonuçlarına göre katılımcılar sağ el baskın, sol el baskın ve ambidekstroz olarak gruplandırıldı.

Bulgular: Paralel formlar yöntemine göre ilk ve ikinci uygulamalarda FLE ve EETA formlarının paralel (eş değer) oldukları görülmüştür (p=0.690 ve 0.566). Test-tekrar test yöntemine göre Lİ1, Lİ2 ve LQ1, LQ2 değerlerinin yüksek derecede ilişkili olduğu belirlendi (r≥0.80). Çalışmamızda FLE için güvenirlik katsayısı 0.904, EETA için 0.947 olarak saptandı. Birinci uygulamada FLE'nin kapsam geçerliliği 0.846, ikinci uygulamada ise 0.800 olarak bulundu. Katılımcıların gruplandırılmasında FLE ve EETA arasında yaklaşık %90 uyum olduğu saptandı.

Sonuç: Çalışmamızda elde edilen veriler, FLE'nin Türkçe versiyonunun geçerli ve güvenilir bir yöntem olduğunu göstermektedir. Bundan sonra yapılacak klinik araştırmalarda el tercihinin belirlenmesinde FLE'nin de kullanılabileceğini önermekteyiz.

Anahtar Sözcükler: Edinburgh el tercihi anketi, fazio lateralite envanteri, geçerlilik, güvenilirlik, lateralite

GRAPHICAL ABSTRACT



ABSTRACT

Aim: The Edinburgh Handedness Inventory (EHI) is the most widely used tool for determining handedness. However, due to its potentially outdated items, modern alternatives like the Fazio Laterality Inventory (FLI) have emerged. This study aimed to evaluate the reliability and validity of the FLI in Turkish and explore its applicability in Türkiye.

Material and Methods: The FLI was translated into Turkish following the Beaton procedure. Both the Turkish versions of the EHI and FLI were administered to 255 university students aged 18-34 years using the parallel forms method. After three weeks, the tests were repeated for test-retest method. Handedness was determined by calculating the laterality quotient (LQ) for EHI and the laterality index (LI) for FLI, classifying participants as right-handed, left-handed, or ambidextrous.

Results: According to the parallel forms method, it was observed that the FLI and EHI forms were parallel in the first and second applications (p=0.690 and 0.566). According to the test-retest method, it was determined that LI1, LI2 and LQ1, LQ2 values were highly correlated (r≥0.80). The reliability coefficient was 0.904 for the FLI and 0.947 for EHI. The content validity of the FLI was 0.846 for the first administration and 0.800 for the second. Approximately 90% agreement was found between the FLI and EHI in the grouping of participants.

Conclusion: The data obtained in our study show that the Turkish version of the FLI is a valid and reliable method. So we suggest that the FLI can be used to determine hand preference in future studies.

Keywords: Edinburgh handedness inventory, fazio laterality inventory, laterality, reliability, validity

GİRİŞ

El tercihi kişinin belirli bir işi yaparken bir eli yerine diğer elini kullanma yönündeki doğal eğilimi olarak tanımlanır (1, 2). El tercihinin beyindeki dominant dil bölgesiyle ilişkili olduğu, sağ elini kullanan bireylerin beyinlerindeki dil bölgesinin bulunduğu dominant hemisferin sol hemisfer, sol el baskın kişilerinse dominant dil hemisferinin sağ hemisfer olduğu saptanmıştır (3). Beyindeki bellek işleme süreçlerinde de el tercihiyle ilişkili olarak beyinde fonksiyonel asimetri olduğunu gösteren çalışmalar vardır (4). El tercihinin beyindeki fonksiyonel asimetriyle ilişkisi olmasının yanı sıra genetik ve çevresel faktörlerle de ilişkili olabileceği ileri sürülmüştür (5-7). Bu tip araştırmalarda dominant hemisferin belirlenmesi amacıyla kişilerin dominant el tercihini belirlemek için, kişilere hangi el baskın olduğunun sorulmasının yanı sıra, kişileri belli eylemleri yaparken gözlemlemek veya katılımcılara anket uygulamaları yapmak gibi yöntemler uygulanmaktadır (1, 8). Uygulama kolaylığı, hızlı uygulanabilmesi ve düşük maliyetli olması sebebiyle en sık kullanılan yöntem anket uygulamalarıdır (9).

Edinburgh el tercihi anketi, el tercihinin belirlenmesinde en sık kullanılan anketlerden biridir (10). Belirli eylemler için hangi elin tercih edildiğinin sorgulandığı Edinburgh El Tercihi Anketi'nde el tercihiyle ilgili 10 soruya ek olarak dominant ayağın belirlenmesi için bir soru ve dominant göz kullanımının belirlenmesi için bir soru yer alır (11). Edinburgh El Tercihi Anketi'nde günümüzde sık kullanılmayan "süpürge kullanımı", "kibrit yakma" gibi güncelliğini yitirmiş maddeler olduğu, eğitim seviyesi düşük bireyler tarafından anlaşılabilirliğinin zor olabileceği ve cevaplama şekli olarak kişilere aşırı uçlu cevaplama seçenekleri ("her zaman sağ el", "her zaman sol el" gibi) sunması bakımından eksiklikleri olabileceği düşüncesiyle Fazio ve ark. tarafından modernize bir alternatif anket olarak Fazio Lateralite Envanteri geliştirilmiştir (12). Çalışmamızın amacı, Fazio Lateralite Envanteri'nin Türkçe geçerlilik ve güvenilirlik analizini yaparak ülkemizde de uygulanabilirliğini test etmektir.

GEREÇ ve YÖNTEMLER

Çalışmamız için Zonguldak Bülent Ecevit Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan onay alınmıştır (Karar No: 2024/04). Anketin orijinal versiyonunu geliştiren yazar Rachel Fazio ile iletişime geçilerek anketin Türkçe'ye çevrilerek geçerlilik ve güvenilirlik analizinin yapılacağı çalışmamız için onay alınmıştır.

Çalışmamızda, çeviri işlemi Beaton prosedürüne göre gerçekleştirilmiştir (13). Fazio Lateralite Envanteri'nin orijinal İngilizce versiyonu ana dili Türkçe olan bilingual iki araştırmacı ve ana dili İngilizce olan bilingual bir araştırmacı tarafından Türkçe'ye çevrilmiştir. Sonraki adımda, Türkçe'ye çevrilen anket, ana dili İngilizce olan iki bilingual araştırmacı tarafından tekrar İngilizce'ye çevrilmiştir. Bu çeviriler karşılaştırılarak anketin nihai versiyonu oluşturulmuştur. Bu anket 30 kişiye uygulanarak maddelerin anlaşılırlığı test edilmiş, bu ilk uygulama çalışmadaki istatistiksel analizlerin dışında bırakılmıştır.

Çalışmamıza yaşları 18-34 arasında değişen (ortalama yaş: 20.27), herhangi bir üst ekstremite patolojisi olmayan 255 üniversite öğrencisi dahil edilmiştir. İlk uygulamada tüm katılımcılara aynı anda bilgilendirilmiş gönüllü onam formu, demografik bilgilerin kaydedildiği bir form, Türkçe versiyonu bulunan Edinburgh El Tercihi Anketi (14) ve çalışmamızda çevirisi yapılmış Fazio Lateralite Envanteri (EK-1) dağıtılmış, paralel formlar yöntemiyle katılımcılardan eş zamanlı olarak bu formları doldurmaları istenmiştir. İlk uygulamadan 3 hafta sonra test-tekrar test metodu ile aynı katılımcılara dört form tekrar dağıtılmış, katılımcılardan anketleri tekrar doldurmaları istenmiştir.

Anketlerin Değerlendirilmesi

Orijinal Edinburgh El Tercihi Anketi el tercihinin sorgulandığı 10 maddeden oluşan bir ankettir (11). Katılımcılardan her bir eylem için sorunun karşısında bulunan sol ve sağ sütununa + işareti koymaları istenir. Kişinin eğer o eylem için güçlü bir sağ el tercihi varsa sağ el sütununa ++, zayıf tercihi varsa +, güçlü bir sol el tercihi varsa sol el sütununa ++, zayıf bir sol el tercihi varsa +, eğer belirgin bir tercihi yoksa her iki sütuna birer + koyması istenir (11). Ankette bulunan iki sütundaki artılar toplanarak R ve L değerleri elde edilir. (R-L)/(R+L)x100 formülü ile Lateralite Katsayısı (LQ skoru) olarak bilinen bir değer hesaplanır. LQ skoru -100 ila +100 arasında değişir (11). Çalışmamızda Edinburgh El Tercihi Anketi'nin beşli Likert tipi cevaplama seçenekleri bulunan versiyonu kullanılmıştır (14). Bu ankette "her zaman sağ el" kutucuğuna işaret koyan katılımcı sağ sütuna ++ koymuş, "genellikle sağ el" kutucuğuna işaret koyan katılımcı sağ sütuna +, "her iki taraf eşit kullanım" kutucuğuna işaret koyan katılımcı sağ ve sol sütuna birer + koymuş gibi değerlendirilerek LQ skoru hesaplaması çalışmamızda da uygulanmıştır. Kişinin sağ el baskın, sol el baskın ya da ambidekstroz olduğunun belirlenmesi için literatürde LQ skoru'nda değişik cut-off değerleri kullanılmıştır (9, 15, 16). Ancak güvenilir aralığın 50-70 olduğu belirlenmiştir (17). Çalışmamızda cut-off değeri olarak 60 alınmış, LQ skoru -100 ile -61 olanlar solak, -60 ile +60 arası ambidekstroz ve 61-100 arası değerleri olanlar sağ el baskın olarak gruplandırılmıştır (9). Edinburgh El Tercihi Anketi için Geschwind Skoru olarak isimlendirilen başka bir skorlama sistemi daha bulunmaktadır. Bu skorlama sisteminde "her zaman sol el" kutucuğuna işaret koyan kullanıcı -10, "genellikle sol el" kutucuğu -5, "her iki el eşit kullanım" kutucuğu 0, "genellikle sağ el" kutucuğu +5, "her zaman sağ el" kutucuğu +10 olarak puanlanır. Her bir soru için alınan puanlar toplandığında, Geschwind skoru elde edilir, Geschwind Skoru -100 ile +100 arasında değişir. Çalışmamızda katılımcıların Geschwind skorları da

hesaplanmıştır. Geschwind skoru 20 ile 100 arası olanlar sağ el baskın, -15 ile 15 arasında olanlar ambidekstroz ve -20 ile -100 arasında olanlar sol el baskın olarak gruplandırılmıştır (18, 19).

Fazio Lateralite Envanteri 10 maddeden oluşan ve 10 maddedeki her bir eylem için kişinin sağ el kullanma yüzdesinin yazmasını istendiği bir ankettir (12). Örneğin katılımcı yazı yazmak için her zaman sağ elini kullanıyorsa anketteki maddenin karşısına %100, her zaman sol elini kullanıyorsa %0 yazmalıdır. Anketteki 10 maddenin karşısına yazılan yüzde değerlerinin aritmetik ortalaması Lateralite İndeksi (Lİ) değerini verir. Lateralite İndeksi'ne göre katılımcıların sağ el baskın, sol el baskın ve ambidekstroz olarak gruplandırılması için Fazio ve ark.'nın çalışmalarında önerdikleri cut-off değerleri çalışmamızda da kullanılmış, çalışmamızda Lateralite İndeksi değerleri %0-%48 olanlar sol el baskın, %49-%59 olanlar ambidekstroz, %60-%100 olanlar sağ el baskın olarak gruplandırılmıştır (12).

İstatistiksel Analiz

Çalışmanın istatistiksel analizleri JAMOVI 2.3.28 paket programı ile yapılmıştır. Çalışmada nicel değişkenlerin normal dağılıma uygunluğu Shapiro Wilk testi ile incelenmiştir. Değişkenlerin bağımlı 2 grup karşılaştırmalarında normal dağılım gösterip göstermemesine göre bağımlı örneklem t testi veya Wilcoxon testi kullanılmıştır. Nicel değişkenler arası ilişkiler Spearman ve Pearson korelasyon katsayısı ile değerlendirilmiştir. Ölçek güvenirlikleri test-tekrar test, paralel formlar yöntemleri ile değerlendirilmiştir. Aynı zamanda Fazio Lateralite Envanteri için Cronbach alfa güvenilirlik katsayısı hesaplanmıştır. Fazio Lateralite Envanteri ile Edinburgh El Tercihi Anketi'nin karşılaştırılması ağırlıklı Kappa katsayısı hesaplanarak değerlendirilmiştir (zayıf uyuşma <0.20, kabul edilebilir uyuşma 0.20-0.40, orta derecede uyuşma 0.40-0.60, iyi uyuşma 0.60-0.80, çok iyi uyuşma 0.80-1.00) (20). Çalışmadaki tüm istatistiksel analizlerde p değeri 0.05'in altındaki sonuçlar istatistiksel olarak anlamlı kabul edilmiştir.

BULGULAR

Çalışmamızda paralel formlar yöntemine göre ilk ve ikinci uygulamalarda Fazio Lateralite Envanteri ve Edinburgh El Tercihi Anketi formlarının paralel (eş değer) oldukları görülmüştür (p=0.690 ve 0.566). Test-tekrar test yöntemine göre, ilk ve ikinci uygulamadan elde edilen Lateralite İndeksi (Lİ) ve LQ Skoru değerleri yüksek derecede ilişkiliydi (r≥0.80) (Tablo 1). Çalışmamızda Fazio Lateralite Envanteri için güvenilirlik katsayısı 0.904, ilk uygulamada Cronbach alfa katsayısı 0.927, ikinci uygulamada ise 0.923 olarak saptanmıştır. Edinburgh El Tercihi Anketi'nde LQ skoru için 0.947, Geschwind skoru için 0.930 olarak bulunmuştur. İlk uygulamada Fazio Lateralite Envanteri için kapsam geçerliliği 0.846, ikinci uygulamada 0.80 olarak saptanmıştır. Katılımcılar belirlenen cut-off değerlerine göre gruplandırıldığında, ilk uygulamada Lateralite İndeksi ve LQ skoru arasında %92.1 uyum (ağırlıklı Kappa katsayısı=0.854) (Tablo 2),

Tablo 1: Fazio Lateralite Envanteri'ndeki Lateralite İndeksi (Lİ), Edinburgh El Tercihi Anketi'ndeki Lateralite Katsayısı (LQ Skoru) ve Geschwind Skoru Değerlerinin İlişkisi

	Lİ-1	Lİ-2	LQ-1	LQ-2	Geschwind-1	Geschwind-2
Lİ-1	1					
Lİ-2	0.904*	1				
LQ-1	0.846*	0.820*	1			
LQ-2	0.817*	0.800*	0.947*	1		
Geschwind-1	0.850*	0.828*	0.971*	0.928*	1	
Geschwind-2	0.824*	0.820*	0.913*	0.965*	0.930*	1

*p<0.01

Tablo 2: İlk ölçümde Lateralite İndeksi ve LQ skoru'na göre grupların dağılımı

			Edinburgh El Tercihi Anketi LQ Skoru (İlk Ölçüm)			
			Sol el baskın	Ambidekstroz	Sağ el baskın	Toplam
Fazio Lateralite Envanteri Lateralite İndeksi (İlk Ölçüm)	Sol el baskın	n (%)	19 (7.5)	3 (1.2)	0 (0)	22 (8.6)
	Ambidekstroz	n (%)	0 (0)	3 (1.2)	3 (1.2)	6 (2.4)
	Sağ el baskın	n (%)	0 (0)	14 (5.5)	213 (83.5)	227 (89)
	Toplam	n (%)	19 (7.5)	20 (7.9)	216 (84.7)	255 (100)
Ağırlıklı Kappa Katsayısı: 0.854						

Tablo 3: İkinci ölçümde Lateralite İndeksi ve LQ Skoru'na göre grupların dağılımı

			Edinburgh El Tercihi Anketi LQ Skoru (İkinci Ölçüm)			
			Sol el baskın	**Ambidekstroz**	**Sağ el baskın**	**Total**
Fazio Lateralite Envanteri Lateralite İndeksi (İkinci Ölçüm)	Sol el baskın	n (%)	18 (7.1)	4 (1.6)	1 (0.4)	23 (9)
	Ambidekstroz	n (%)	0 (0)	5 (2)	3 (1.2)	8 (3.1)
	Sağ el baskın	n (%)	1 (0.4)	17 (6.7)	206 (80.8)	224 (87.8)
	Toplam	n (%)	19 (7.5)	26 (10.2)	210 (82.4)	255 (100)
Ağırlıklı Kappa Katsayısı: 0.729						

Tablo 4: İlk ölçümde Lateralite İndeksi ve Geschwind Skoru'na göre grupların dağılımı

			Edinburgh El Tercihi Anketi Geschwind Skoru (İlk Ölçüm)			
			Sol El Baskın	**Ambidekstroz**	**Sağ El Baskın**	**Toplam**
Fazio Lateralite Envanteri Lateralite İndeksi (İlk Ölçüm)	Sol el baskın	n (%)	20 (7.8)	1 (0.4)	1 (0.4)	22 (8.6)
	Ambidekstroz	n (%)	0 (0)	0 (0)	6 (2.4)	6 (2.4)
	Sağ el baskın	n (%)	1 (0.4)	1 (0.4)	225 (88.3)	227 (89)
	Toplam	n (%)	21 (8.2)	2 (0.8)	232 (90.9)	255 (100)
Ağırlıklı Kappa Katsayısı: 0.859						

Tablo 5: İkinci ölçümde Lateralite İndeksi ve Geschwind Skoru'na göre grupların dağılımı

			Edinburgh El Tercihi Anketi Geschwind Skoru (İkinci Ölçüm)			
			Sol El Baskın	**Ambidekstroz**	**Sağ El Baskın**	**Toplam**
Fazio Lateralite Envanteri Lateralite İndeksi (İkinci Ölçüm)	Sol el baskın	n (%)	20 (7.9)	2 (0.8)	1 (0.4)	23 (9)
	Ambidekstroz	n (%)	0 (0)	1 (0.4)	7 (2.7)	8 (3.1)
	Sağ el baskın	n (%)	2 (0.8)	1 (0.4)	221 (86.7)	224 (87.8)
	Toplam	n (%)	22 (8.7)	4 (1.6)	229 (89.9)	255 (100)
Ağırlıklı Kappa Katsayısı: 0.825						

ikinci uygulamada ise %89.8 uyum (ağırlıklı Kappa katsayısı=0.729) (Tablo 3) gözlenmiştir. Katılımcılar Lateralite İndeksi ve Gescwhind Skoru'na göre gruplandırıldığında ilk uygulamada iki gruplandırma arasında %96.1 uyum (ağırlıklı Kappa katsayısı=0.859) (Tablo 4), ikinci uygulamada %94.9 uyum (ağırlıklı Kappa katsayısı=0.825) (Tablo 5) olduğu görülmüştür.

TARTIŞMA

Çalışmamızda 10 maddeden oluşan Fazio Lateralite Envanteri'nin Türkçe çevirisinin paralel formlar yöntemi ve test-tekrar test yöntemiyle geçerlilik ve güvenilirlik analizi yapılmıştır.

Fazio Lateralite Envanteri'nde katılımcılara sorulan soruların cevaplarının yüzde olarak istenmesinin, katılımcılara ikili ya da beşli Likert tipi cevaplama seçeneği sunan anketlere göre esneklik sağlayarak daha geniş bir aralıkta cevap verme olanağı sunduğu söylenebilir. Örneğin çalışmamızda Fazio Lateralite Envanteri'nin ilk uygulamasında verilen cevaplarda katılımcıların 0-100 arasında bulunan 101 sayıdan 49'unu kullanmış olduğu saptandı. Bu sayı, katılımcıların daha fazla seçenek sunulduğunda esnek cevap verdiklerini doğrulamaktadır.

Çalışmamızda Fazio Lateralite Envanteri'nin güvenirliğini ölçmek için paralel formlar yöntemi ve test-tekrar test yöntemi kullanılmıştır (21). Test-tekrar test yönteminde iki ölçek uygulaması arası süre yapılan çalışmalarda 2-4 hafta olarak önerilmiş, çalışmamızda da 3 hafta sonra aynı ölçekler ikinci kez uygulanmıştır (21). Çalışmamızda Fazio Lateralite Envanteri'nin güvenirlik katsayısı 0.904 olarak saptanmış olup ilk uygulamada Cronbach alfa katsayısı 0.927, ikinci uygulamada ise 0.923 olarak saptanmıştır. Fazio ve ark., çalışmalarında geliştirdikleri anketin iç tutarlılığını değerlendirmişler, Cronbach alfa katsayısını 0.943 olarak saptamış-

lardır (12). Dragan ve ark.'nın Fazio Lateralite Envanteri'nin Lehçe çevirisinin güvenilirlik analizini yaptığı bir çalışmada ise, anketin yine iç tutarlılığı değerlendirilerek Cronbach alfa katsayısı 0.947 olarak saptanmıştır (22). Bu değerler çalışmamızda elde edilen katsayıya yakın olup benzer şekilde yüksektir.

Geçerlilik analizi için Dragan ve ark. Fazio Lateralite Envanteri'nin Lehçe çevirisini yaptıkları çalışmada, LQ skoru ile Lateralite İndeksi değerleri arasındaki korelasyon değeri 0.757 bulunmuştur (22). Fazio ve ark. çalışmalarındaysa bu değer 0.517 olarak saptanmıştır (12). Çalışmamızda LQ skoru ve Lateralite İndeksi değerleri arasındaki korelasyon ilk uygulamada 0.846, ikinci uygulamada ise 0.80 bulunmuştur. Bu değer önceki çalışmalardan yüksek olup örneklemimizin demografik özelliklerine, farklı bir dilde, farklı popülasyonda uygulanmış olmasına bağlı olabilir.

Fazio Lateralite Envanteri ve Edinburgh El Tercihi Anketi'ne göre yapılan gruplandırmalar arasındaki yüksek uyum (%90) her iki anketin de el tercihini belirlemede başarılı olduğunu göstermektedir. Bu karşılaştırmalarda birinci ve ikinci ölçümlerde ağırlıklı Kappa değeri 0.70 üzerinde saptanmış olup iki anket iyi derecede uyum göstermiştir.

Yapılan çalışmalar insanların yaklaşık %90'ının sağ el baskın olduğunu göstermektedir (1, 23). Çalışmamızda ilk uygulamada Edinburgh El Tercihi Anketi'nde LQ skoruna göre yapılan gruplandırmada %84.7, ikinci uygulamada %82.4; Geschwind skoruna göre yapılan gruplandırmada ilk ölçümde %90.9, ikinci ölçümde %89.9 olarak benzer değerler bulunmuştur. LQ skoruna göre yapılan gruplandırmada daha düşük yüzde bulunması çalışmamızda alınan cut-off değerine bağlı olabilir. Fazio Lateralite Envanteri'ne göre yapılan gruplandırmada da sağ el baskın kişi sayısı, ilk ölçümde %89, ikinci ölçümde %87.8 olarak saptanmıştır. Bu değerler önceki çalışmalarla uyumludur (1, 22).

Çalışmamızda ambidekstroz kişi sayısı Edinburgh El Tercihi Anketi'ndeki LQ skorlamasına göre ilk ölçümde 20 (%7.9), ikinci ölçümde 26 (%10.2) saptanmıştır. Geschwind skorlamasına göre ise ilk ölçümde 2 (%0.8), ikinci ölçümde ise 4 kişi (%1.6) ambidekstroz olarak gruplandırılmıştır. Fazio Lateralite Envanteri'nde ise bu değer 6 (%2.4) ve 8 (%3.1) olarak bulunmuştur. Geshwind skorlamasında ve Lateralite İndeksi'ne göre ambidekstroz kişi gruplandırılmasında LQ skoru'na göre daha dar bir aralık kullanılmıştır. Fazio Lateralite Envanteri'ne göre daha düşük sayıda ambidekstroz kişi saptanması buna bağlı olabilir. Barut ve ark. 633 kişide yaptıkları bir çalışmada el tercihi için Edinburgh El Tercihi Anketi'ni uygulamışlar, Geschwind Skorlamasına göre değerlendirerek ambidekstroz kişi sayısını 33 (%5.21) olarak saptamışlardır (24). Bu farklılık çalışmamızdaki katılımcı sayısının daha düşük olmasına ve örneklem seçiminin farklılığına bağlı olabilir.

Kişilerin el tercihi; nöral asimetri, genetik gibi biyolojik faktörlerin yanı sıra sosyokültürel faktörlerden de etkilenebilmektedir (5, 7, 15). Çalışmamızda uygulanan Edinburgh El Tercihi Anketi'nde sorulan, "Size belirli aktiviteler için belli bir eli kullanmaya yönelik özel eğitim veya teşvik verildi mi?" sorusuna 255 katılımcıdan 15'i sağ el kullanımı yönünde aile teşviği aldığını belirtmiştir. El tercihiyle ilgili daha önce yapılmış çalışmalarda, kişilerin özellikle yazı yazma eylemi için; sosyal baskı, hastalık, amputasyon, kişilerin bireysel motivasyonları gibi çeşitli sebeplerle el tercihinin değişebildiği saptanmış olup bu değişimlerin nöral yapılar dahil birçok faktörle ilişkisine dair çalışmalar günümüzde de devam etmektedir (6, 7). Bu çalışmalarda kişilere direkt olarak hangi elini kullandığı sorulması dışında belirli aktiviteler için hangi elini kullandığının gözlenmesi ya da sık olarak kullanılan anket yöntemleri uygulanmaktadır (1, 8, 9). Bizim çalışmamızda da bu anketlerden Fazio Lateralite Envanteri'nin Türkçe çevirisinin geçerlilik ve güvenilirlik analizi yapılmıştır. Bu çalışmayla, diğer anketlere bir alternatif sunarak Türkçe literatüre katkı yaptığımızı düşünmekteyiz.

Çalışmamızda Fazio Lateralite Envanteri ortalama yaşı 20.27 olan 255 üniversite öğrencisinde uygulanmıştır. Anketin çeşitli yaş gruplarını ve çeşitli eğitim düzeylerini içeren bir örneklemde uygulanmamış olması çalışmamızın limitasyonu olarak değerlendirilebilir.

Sonuç olarak, çalışmamızda Türkçe'ye çevrilen Fazio Lateralite Envanteri'nin Türkçe versiyonunun geçerli ve güvenilir bir yöntem olduğu saptanmıştır. Bundan sonra yapılacak çalışmalarda el tercihinin belirlenmesinde diğer anketlere alternatif olarak Fazio Lateralite Envanteri'nin de kullanılabileceğini önermekteyiz.

Teşekkür

Yok.

Yazar Katkı Beyanı

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Hakemlik Süreci

Kör hakemlik süreci sonrası yayınlanmaya uygun bulunmuştur.

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EK-1

FAZIO LATERALİTE ENVANTERİ

YÖNERGELER

Eylem	**%**
Yazı yazmak	
Resim çizmek	
Merhaba ya da güle güle derken el sallamak	
TV kumandası kullanmak	
Parmak şıklatmak	
Kaşınan burnu kaşımak	
Uzaktaki bir şeyi işaret etmek	
Bir nesne fırlatmak	
Bir nesneyi almak için uzanmak	
Çekiç kullanmak	

Lütfen aşağıdaki eylemler için **SAĞ** elinizi kullandığınız sürenin yüzdesini (%0 ila %100) belirtiniz. Lütfen her soruyu cevaplayınız; ancak, bir nesne veya eylemle ilgili deneyiminiz yoksa boş bırakınız. Örneğin, bir top atmak için **neredeyse her zaman** sağ elinizi kullanıyorsanız, boşluğa **"98"** yazınız. Ancak, bu eylem için her zaman **sol elinizi** kullanıyorsanız, o zaman boşluğa **"0"** yazınız.

Kendimin … olduğuna inanıyorum:

☐ Sağ el baskın

☐ Sol el baskın

☐ Ambidekstroz (her iki elini de eşit şekilde kullanan)

Yanıtlarınız omzunuzdaki, kolunuzdaki veya elinizdeki bir sağlık sorunundan (örn. amputasyon, yaralanma, artrit, paralizi, felç, vb.) etkileniyor mu?

☐ Evet ☐ Hayır

ORIGINAL ARTICLE

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2025;9(1): 115-122
DOI: 10.29058/mjwbs.1618148

Relationship Between Endometrial Biopsy Results and Risk Factors in Women with Postmenopausal Bleeding

Postmenopozal Kanama İle Başvuran Kadınların Endometrial Biyopsi Sonuçları ve Risk Faktörleri İlişkisi

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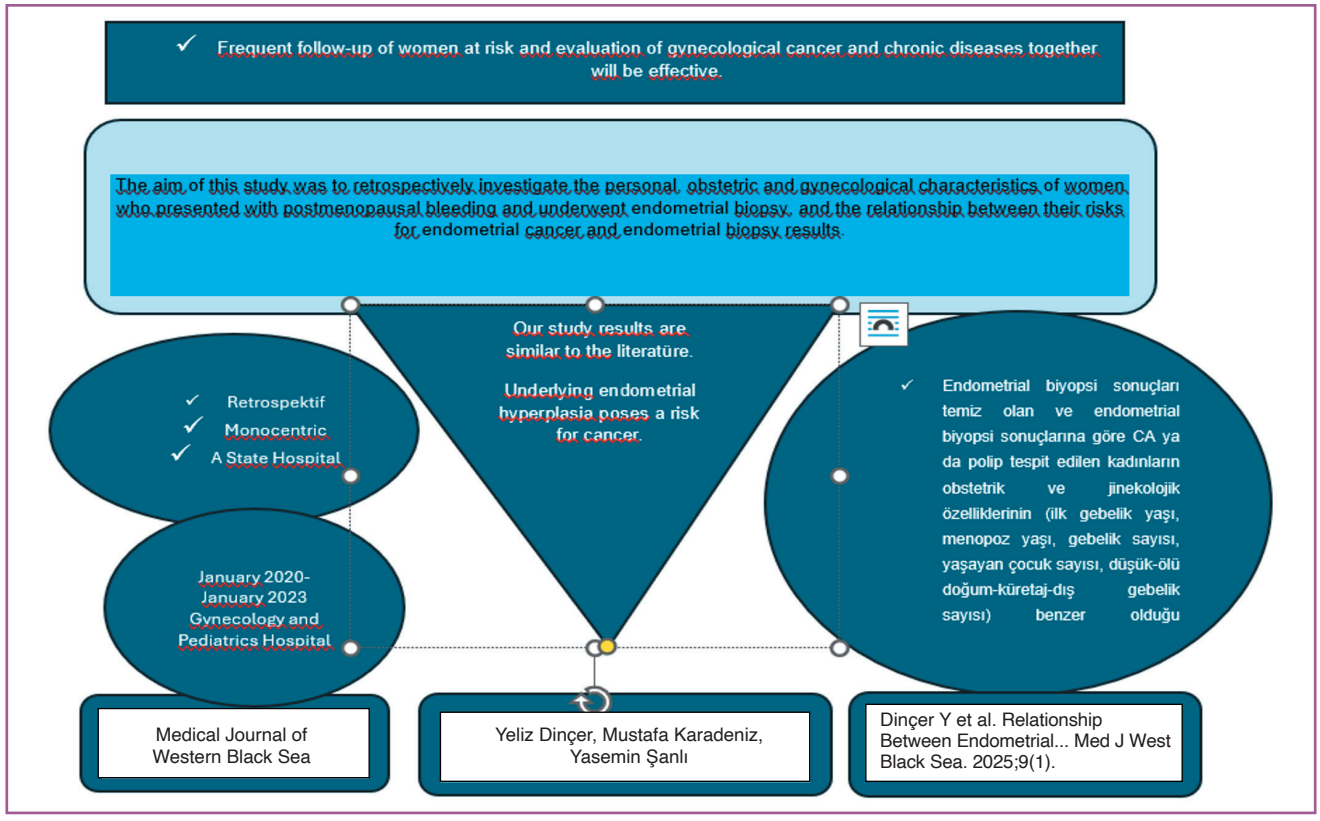
GRAPHICAL ABSTRACT



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ABSTRACT

Aim: This study aims to examine the relationship between the personal, obstetric, and gynecological characteristics of postmenopausal women who have undergone endometrial biopsy and their risks for endometrial cancer, along with their biopsy results.

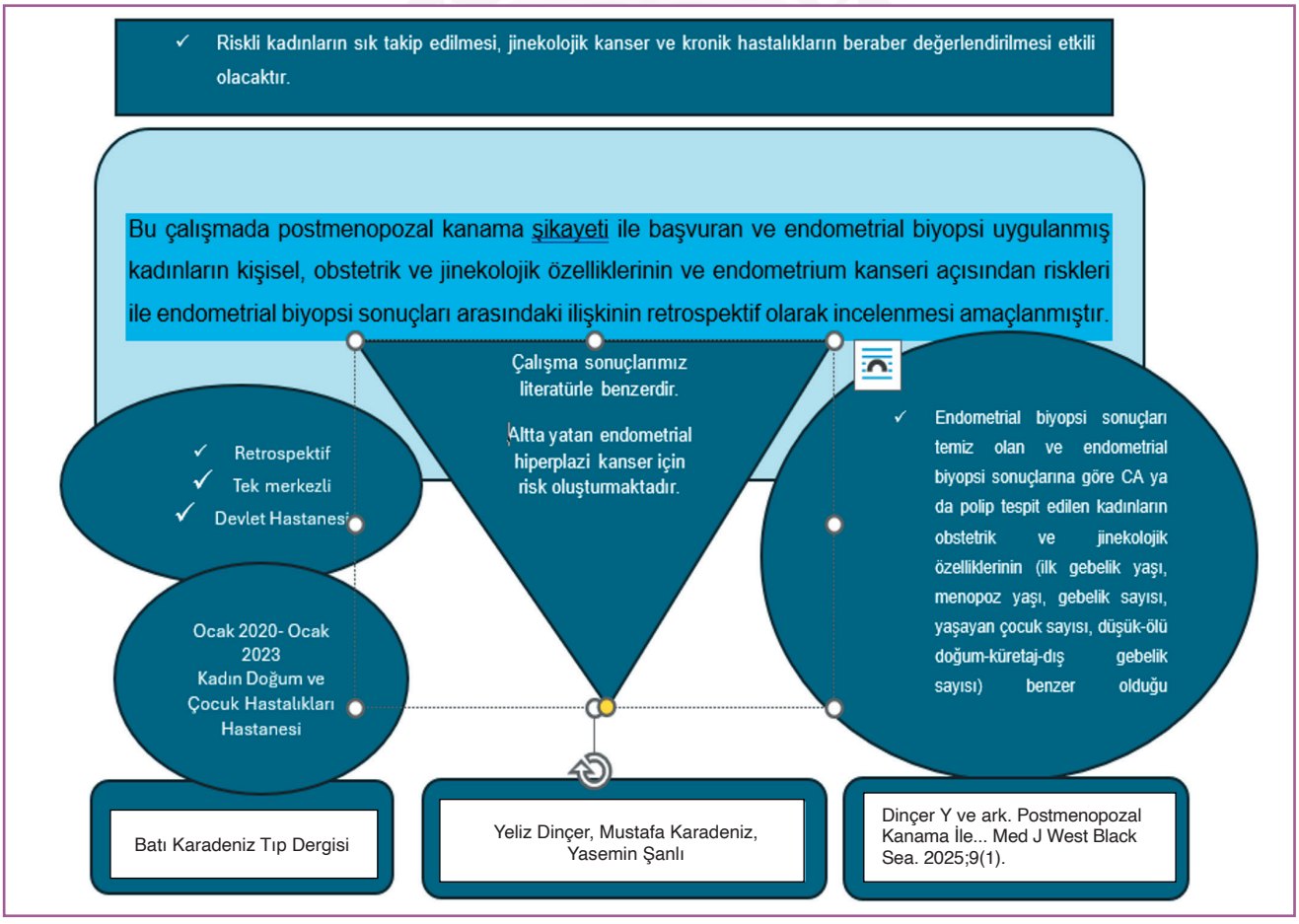
Material and Methods: This study was conducted by retrospectively analyzing the sociodemographic, obstetric, and gynecological characteristics, endometrial cancer risk factors, existing medical conditions, clinical presentations, and biopsy results of 66 women who met the study criteria. According to the study criteria, the data of these women (who applied to the hospital with postmenopausal bleeding and underwent endometrial biopsy in the last three years [January 2020 - January 2023]) were accessed through the hospital's documentation system between February and June 2023.

Results: The mean age of the women included in the study was 54.50±7.99 years, with 63.6% having completed primary education. The most common medical conditions identified were hypertension (19.7%), thyroid disease (12.1%), and diabetes mellitus (9.1%). Endometrial biopsy results indicated that 92.4% of the women had benign findings. Women diagnosed with cancer or polyps were found to have similar characteristics to those with benign outcomes but lower rates of tamoxifen use, alcohol consumption, and smoking.

Conclusion: According to the results of this study, the identified risk factors for endometrial cancer in women included obesity, endometrial hyperplasia, smoking, alcohol consumption, and tamoxifen use. Health professionals working in women's health should develop educational, activity, and awareness programs to promote healthy lifestyle behaviors. Frequent monitoring of high-risk women and the joint evaluation of gynecological cancers and chronic diseases will be effective strategies for managing these patients.

Keywords: Postmenopausal period, women, endometrial biopsy, endometrial cancer

GRAFİKSEL ÖZET



ÖZ

Amaç: Bu çalışmanın amacı, endometrial biyopsi uygulanan postmenopozal kadınların kişisel, obstetrik ve jinekolojik özellikleri ile endometrial kanser riskleri ve biyopsi sonuçları arasındaki ilişkiyi incelemektir.

Gereç ve Yöntemler: Bu çalışma, çalışma kriterlerini karşılayan 66 kadının sosyodemografik, obstetrik ve jinekolojik özelliklerini, endometrial kanser risk faktörlerini, mevcut tıbbi durumlarını, klinik sunumlarını ve biyopsi sonuçlarını retrospektif olarak analiz ederek yürütülmüştür. Çalışma kriterlerine göre bu kadınların (son üç yılda [Ocak 2020 - Ocak 2023] postmenopozal kanama ile hastaneye başvurmuş ve endometrial biyopsi yapılmış olan) verilerine hastanenin dökümantasyon sistemi üzerinden Şubat ve Haziran 2023 tarihleri arasında ulaşılmıştır.

Bulgular: Çalışmaya dahil edilen kadınların ortalama yaşı 54,50±7,99 yıl olup, %63,6'sı ilköğretimi tamamlamıştır. Tanımlanan en yaygın tıbbi durumlar hipertansiyon (%19,7), tiroid hastalığı (%12,1) ve diabetes mellitus (%9,1) idi. Endometrial biyopsi sonuçları kadınların %92,4'ünün iyi huylu bulgulara sahip olduğunu gösterdi. Kanser veya polip teşhisi konulan kadınların iyi huylu sonuçları olanlara benzer özelliklere sahip olduğu ancak daha düşük tamoksifen kullanım oranları, alkol tüketimi ve sigara içme oranlarına sahip olduğu bulunmuştur.

Sonuç: Bu çalışmanın sonuçlarına göre, kadınlarda endometrial kanser için belirlenen risk faktörleri arasında obezite, endometrial hiperplazi, sigara içme, alkol tüketimi ve tamoksifen kullanımı yer aldı. Kadın sağlığı alanında çalışan sağlık profesyonelleri, sağlıklı yaşam tarzı davranışlarını teşvik etmek için eğitim, aktivite ve farkındalık programları geliştirmelidir. Yüksek riskli kadınların sık sık izlenmesi ve jinekolojik kanserler ile kronik hastalıkların ortak değerlendirilmesi, bu hastaların yönetimi için etkili stratejiler olacaktır.

Anahtar Sözcükler: Postmenopozal dönem, kadın, endometrial biyopsi, endometrial kanser

INTRODUCTION

Abnormal uterine bleeding (AUB) is a prevalent and complex issue in women's health, encompassing bleeding outside of the menstrual cycle, excessive menstrual bleeding, or postmenopausal bleeding (1,2). Postmenopausal bleeding (PMB) refers to bleeding that occurs one year after the cessation of menstruation, with the perception of abnormality often being subjective (3,4). Although PMB is frequently attributed to atrophic endometrium, the possibility of malignancy, which accounts for approximately 10% of cases, necessitates thorough evaluation (4-7). Endometrial biopsy is the most commonly used, reliable, and effective method for obtaining histopathological diagnosis during endometrial assessments (5-8). While hyperplasias in women are observed in 1-6% of cases during the premenopausal period, this rate rises to 15% in the postmenopausal period, with bleeding being the primary symptom (8-10).

Globally, the most common cancers in women are breast, cervical, thyroid, and liver cancers, whereas in Turkey, the five most common cancers are breast, thyroid, colorectal, corpus, and lung cancers (11). Endometrial cancer, which originates from the endometrium and is also referred to as corpus or uterine cancer, is the most common gynecological cancer, accounting for 11.1% of cases, particularly among postmenopausal women, both in developed countries and in Turkey (2,5,10-12).

Several risk factors have been identified for endometrial cancer, including nulliparity, early menarche, late menopause, obesity, diabetes mellitus (DM), hormone replacement therapy (HRT), tamoxifen use, familial predisposition, and polycystic ovary syndrome. Estrogen plays a clear role in the development of the disease. Vaginal bleeding is the most frequent clinical presentation (8,12).

Raising awareness among women regarding the factors associated with endometrial cancer and encouraging them to seek medical attention promptly in response to abnormal bodily changes is crucial, as early diagnosis and treatment improve outcomes.

This study aims to retrospectively examine the relationship between the personal, obstetric, and gynecological characteristics of women presenting with postmenopausal bleeding and their risks for endometrial cancer, along with their endometrial biopsy results, over the past three years (January 2020–January 2023).

MATERIALS and METHODS

This study was conducted at Zonguldak Maternity and Child Diseases Hospital between February and June 2023. Permission has been obtained from the director of the institution where this research will be conducted and from the Provincial Health Directorate to which it is affiliated (03.06.2023), and there is ethics committee approval from the ethics committee of Zonguldak Bülent Ecevit Unv Non-Interventional Clinical Research Ethics Board (Number: 2023-02, Date: 25.01.2023). The study population consisted of all women who presented with postmenopausal bleeding and underwent endometrial biopsy at the hospital within the last three years (January 2020–January 2023). The sample included 66 women who met the inclusion criteria and whose data were accessible through the hospital's written records. The sociodemographic information (age, education), obstetric and gynecological history (parity, age at first pregnancy, age at menopause, breastfeeding status), endometrial cancer risk factors [family history, Body Mass Index (BMI), smoking and alcohol use, tamoxifen use, Hormone Replacement Therapy (HRT)], existing medical conditions, clinical presentations, and biopsy results were retrospectively reviewed from the hospital records.

Inclusion Criteria: Women in the postmenopausal period who presented with bleeding and underwent endometrial biopsy and who did not have any mental disabilities or diseases requiring intensive psychiatric treatment.

Exclusion Criteria: Women not in the postmenopausal period, those whose bleeding was of cervical origin, those with insufficient biopsy samples, and women with mental retardation or diseases requiring intensive psychiatric treatment.

Dependent Variables: Risk factors for endometrial cancer in postmenopausal women.

Independent Variables: Endometrial biopsy results of postmenopausal women.

Statistical Analysis

The data obtained in the study were analyzed using SPSS 22 (Statistical Package for the Social Sciences for Windows 22). Descriptive statistics are given with mean and standard deviation or frequency and percent. The conformity of quantitative data to normal distribution was tested with Shapiro-Wilk test and graphical examinations. Independent groups t test was used in comparisons between two groups of quantitative variables showing normal distribution. Statistical significance was accepted as $p<0.05$.

RESULTS

The demographic and clinical characteristics of the women in the study revealed that the mean age was 54.50±7.99 years, with 63.6% having completed primary education. The most commonly diagnosed conditions were hypertension (19.7%), thyroid disease (12.1%), and diabetes mellitus (9.1%). Among postmenopausal women presenting with endometrial bleeding, 60.7% reported no other complaints, while 25.8% were found to have endometrial thickening. Additionally, 92.4% of the women had benign biopsy results (Table 1). The mean Body Mass Index (BMI) of the women was 30.33 ±5.11kg/m^2.

The average age at first pregnancy for women with benign endometrial biopsy results was 20.20±5.92 years, while their average age at menopause was 50.03±3.74 years. The average number of pregnancies was 2.73±1.52, with an average of 2.45±1.53 living children. The average number of miscarriages was 0.28±0.66, stillbirths 0.03±0.18, and ectopic pregnancies 0.03±0.25.

When examining the endometrial cancer risk factors in women with benign biopsy results, one had a history of breast cancer, and another had a history of bladder cancer. Neither of these women had a family history of endometrial cancer. Among the six women with a family history of endometrial cancer, five had mothers, and one had a sibling diagnosed with this condition. Regarding other reasons for hospital visits or biopsies aside from bleeding, the most common reason was endometrial thickening, observed in 16 women (26.7%). In terms of Body Mass Index (BMI), half of the group was classified as obese (BMI ≥30, n=31). Among these, three women were classified as third-degree obese, six as second-degree obese, and 22 as first-degree obese (Table 2).

According to the endometrial biopsy results, women diagnosed with cancer (CA) or polyps had an average age at first pregnancy of 22.66±4.08 years and an average age at menopause of 50.50±2.88 years. The average number of pregnancies was 2.66±0.81, and the average number of living children was 2.33±1.03. The average number of miscarriages was 1.00±1.67.

Table 1: Distribution of Women According to Some Demographic and Disease Characteristics

Findings (n=66)		
Sociodemographic Data		
Age (Year± SD)54.5±7.99		
BMI (kg/m^2±SD)30.33 ±5.11		
Education Level	**n**	**(%)**
Primary School	42	(63.6)
High School	13	(19.7)
No Schooling	6	(9.1)
University and Above	5	(7.6)
Biopsy Results	**n**	**(%)**
Benign	61	(92.4)
CA	4	(6.1)
Polyp	1	(1.5)
Reason for Hospital Visit/Biopsy (Other than Bleeding)	**n**	**(%)**
No Other Complaint	40	(60.7)
Endometrial Thickening	17	(25.8)
Follow-up	3	(4.5)
Myoma	3	(4.5)
Other	3	(4.5)
Existing Conditions*	**n**	**(%)**
Hypertension	13	(19.7)
Thyroid Disease	8	(12.1)
Diabetes Mellitus (DM)	6	(9.1)
Heart Disease	3	(4.5)
Cholesterol	1	(1.5)
Breast Cancer	1	(1.5)
Bladder Cancer	1	(1.5)
Iron Deficiency	1	(1.5)
Rheumatic Disease	1	(1.5)
Psychiatric Disease	1	(1.5)

* Multiple responses were provided.

Table 2: Distribution of Women Characteristics

Women Characteristics	Clear Biopsy Results (n=60)		Diagnosed with CA or Polyps According to Endometrial Biopsy Results (n=6)		P
Obstetric and Gynecological History					
Age at First Pregnancy (year± SD)	20.20±5.92		22.66±4.08		p=0.325*
Age at Menopause (year± SD)	50.03±3.74		50.50±2.88		p=0.768*
Number of Pregnancies (number ± SD)	2.73±1.52		2.66±0.81		p=0.917*
Number of Living Children (number ± SD)	2.45±1.53		2.33± 1.03		p=0.857*
Number of Miscarriages (number ± SD)	0.28±0.66		1.00±1.67		p=0.344*
Number of Stillbirths (number ± SD)	0.03±0.18		-		p=0.656*
Curettage	-		-		
Number of Ectopic Pregnancies (number ± SD)	0.03±0.25		-		p=0.755*
Risk Factors for Endometrial Cancer	**n**	**(%)**	**n**	**(%)**	
Tamoxifen Use	3	(5)	1	(16.7)	p=0.253*
History of HRT Use	3	(5)	0	(0)	p=0.575*
Smoking	6	(10)	1	(16.7)	p=0.613*
Alcohol	6	(10)	1	(16.7)	p=0.613*
Family History	6	(10)	0	(0)	p=0.417*
BMI (kg/m^2±SD)	30.55±5.18		29.47±4.12		p=0.686*
Reason for Hospital Visit/Biopsy (Other than Bleeding)	**n**	**(%)**	**n**	**(%)**	
No Other Complaint	36	(60)	5	(83.3)	
Endometrial Thickening	16	(26.7)	1	(16.7)	
Follow-up	3	(5)	0	(0)	
Myoma	3	(5)	0	(0)	
Other	3	(5)	0	(0)	

Independent Sample T-test*
* Participants may have met more than one criteria.

When examining the endometrial cancer risk factors in women with biopsy-confirmed CA or polyps, it was noted that 20% (1 woman) used tamoxifen, 16.7% (1 woman) smoked, and 16.7% (1 woman) consumed alcohol. These three risk factors were more prevalent in this group than in women with benign biopsy results. None of these women had a family history of endometrial cancer. Among other reasons for hospital visits or biopsies, the most common was endometrial hyperplasia, identified in 16.7% (1 woman) of the cases. Half of the women in this group were classified as obese (n=3). Among the obese women, two were classified as first-degree obese and one as second-degree obese (Table 2).

According to the findings of the study, when women with clean biopsy results were compared with women diagnosed with cancer or polyps, no statistically significant difference was found in terms of both obstetric and gynecological characteristics and endometrial cancer risk factors. ($p<0.05$). (Table 2).

DISCUSSION

In this study, data from 66 patients who presented with postmenopausal bleeding and underwent endometrial biopsy within the last three years (2020–2023) were evaluated in terms of endometrial cancer risk factors. The reasons for performing biopsies were identified as complaints of bleeding in 60.7% of the women and endometrial thickening in 25.8%. The biopsy results showed that 92.4% of the women had benign findings, while 6.1% were diagnosed with endometrial cancer. The average age of the patients was 54, and their average BMI was 30. In addition, it was determined that the obstetric and gynecological characteristics (age at first pregnancy, age at menopause, number of pregnancies, number of living children, number of miscarriages, number of stillbirths and ectopic pregnancies) of women with benign biopsy results were similar to those of women with diagnosed CA or polyps, and there was no statistically significant difference between them.

In Zhao et al.'s retrospective study, patients with endometrial hyperplasia were found to have a higher risk of developing endometrial cancer, especially among women over the age of 50, those with a BMI ≥25 kg/m², diabetes, hypertension, and advanced hyperplasia. The study emphasized the importance of early diagnosis and treatment in high-risk patients (9). The incidence of endometrial cancer increases with age, peaking in the postmenopausal period (60–70 years). The American College of Obstetricians and Gynecologists (ACOG) has set the age of 45 as the threshold for endometrial cancer screening (13). Our study results align with the literature.

The BMI of all women included in the study who presented with postmenopausal bleeding fell within the obese range, and the BMI characteristics of women with benign and malignant results were similar. Studies have shown that obesity and diabetes are significant risk factors for endometrial cancer (14-16). For every 5 kg/m² increase in BMI, the risk of endometrial cancer increases by 1.6 times (9). Raffone et al. and Garzon et al. demonstrated that obesity increases the risk of death associated with endometrial cancer (17,18). This increased risk is due to adipose tissue being a source of estrogen in the body, leading to the effects of excessive endogenous estrogen on the endometrium, which in turn causes endometrial hyperplasia and cancer (9,17,18). Studies have also found that when insulin resistance is high, the relative risks of endometrial hyperplasia and cancer increase, and when BMI is ≥25 kg/m², progesterone treatment becomes less effective and more prone to recurrence (19,20). Therefore, weight control is essential during treatment and follow-up. While simple hypertension does not increase the risk of endometrial cancer, it often leads to complications with obesity and diabetes. Controlling weight, blood sugar and blood pressure early on is crucial, particularly for improving the prognosis of patients (21,22). Although diabetes mellitus (DM) is known to be a risk factor for endometrial cancer, none of the women diagnosed with cancer or polyps in this study had diabetes. However, consistent with the literature, half of the women diagnosed with endometrial cancer were obese and had endometrial hyperplasia.

When examining the risk factors for women diagnosed with endometrial cancer, it was found that 16.7% (1 woman) used tamoxifen, 16.7% (1 woman) smoked, and 16.7% (1 woman) consumed alcohol. These three risk factors were found to be more prevalent among women with endometrial cancer than among women with benign results, but no statistically significant difference was found between them. Several risk factors for endometrial cancer have been identified in epidemiological and retrospective studies, including nulliparity, late menopause, obesity, smoking, alcohol consumption, diabetes mellitus, unopposed estrogen therapy, tamoxifen use, and polycystic ovary syndrome. Underlying hyperplasia also poses a risk for progression to cancer (8,16,23-25). Our study findings are consistent with the literature.

One of this study's primary limitations is its relatively small sample size due to its retrospective design. Additionally, the data are limited to those obtained from a single state hospital. The information on family history was based solely on patients' self-reported disclosures of endometrial cancer in their families during medical consultations, which may lead to missing data in the system. Furthermore, retrospective data on breastfeeding status were not available, and therefore, no statistical calculations could be made regarding this variable.

The findings of this study indicate that obesity, endometrial hyperplasia, smoking, alcohol consumption, and tamoxifen use are risk factors associated with endometrial cancer in women. Endometrial cancer, similar to trends in developed countries, is the most common gynecological cancer. Women with endometrial cancer typically present with bleeding, which allows for early diagnosis and, consequently, a better prognosis. However, the incidence and mortality rates associated with this disease are rising. Factors contributing to the increasing prevalence of endometrial cancer include rising obesity rates, the absence of an effective screening test, longer life expectancies, late menopause, infrequent routine gynecological exams in asymptomatic women, and the increasing use of tamoxifen, estrogen, smoking, alcohol, and the prevalence of diseases such as diabetes and hypertension.

Identifying these risk factors is crucial for preventing the disease, especially in high-risk women. Accordingly, healthcare professionals working in women's health should develop educational, activity-based, and awareness-raising programs to promote healthy lifestyle behaviors. Frequent monitoring of at-risk women and joint evaluation of gynecological cancers and chronic diseases will also be effective in improving outcomes.

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Author Contributions

Concept: **Yeliz Dinçer, Mustafa Karadeniz, Yasemin Şanlı,** Design: **Yeliz Dinçer, Mustafa Karadeniz,Yasemin Şanlı,** Data Collection or Processing: **Yeliz Dinçer, Mustafa Karadeniz,** Analysis or Interpretation: **Yeliz Dinçer, Yasemin Şanlı,** Literature Search: **Yeliz Dinçer, Yasemin Şanlı,** Writing: **Yeliz Dinçer,** Approval: **Yeliz Dinçer.**

Conflicts of Interest

The authors declare no conflict of interest.

Financial Support

The authors declare that they did not receive any financial support during this manuscript's research or writing process.

Ethical Approval

Ethics Committee Approval: This study was conducted following the ethical principles outlined in the Helsinki Declaration. Written approval was obtained from the Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Board (25.01.2023; 2023-02) and the Provincial Health Directorate (03.06.2023).

Informed Consent Statement

Since this study is a retrospective analysis, patient consent was not obtained.

Data Availability Statement

Data are available for research purposes upon reasonable request to the corresponding author.

Review Process

Externally peer-reviewed.

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CASE REPORT

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

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A Rare Clinic Related to Paclitaxel Use: Type 2 Kounis Syndrome

Paklitaksel Kullanımı ile İlgili Nadir Bir Klinik: Tip 2 Kounis Sendromu

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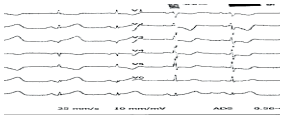
GRAPHICAL ABSTRACT

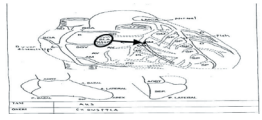
We recommend that chest pain should be questioned when allergy, anaphylaxis and angioedema develop in patients receiving chemotherapeutic drugs and that they should be alert for Kounis Syndrome

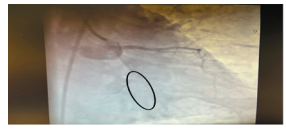
Kounis Syndrome is an acute coronary condition that arises during allergic or anaphylactic reactions. In this report, we present a case of anaphylaxis while receiving paclitaxel treatment for lung malignancy in the chemotherapy unit and the diagnosis of Type 2 Kounis Syndrome was established in the emergency department.



Patients with Kounis Syndrome typically present to the emergency department with cardiac symptoms associated with either acute or chronic allergic reactions. If left untreated, Kounis Syndrome can result in cardiorespiratory arrest or sudden death. Our case represents Type 2 Kounis Syndrome because of ST segment elevation in inferior leads and occlusion in coronary angiography. Previously reported cases in the literature were Type 1 Kounis Syndrome and our case is Type 2 Kounis Syndrome. Therefore, this case report is a rare case report. Our case is a rare case report because the culprit vessel of inferior wall ST segment elevation was not the right coronary artery (RCA) but the circumflex artery (CX).

From the perspective of public health and patient benefit, cardiac toxicity, cardiovascular hypersensitivity, and Kounis Syndrome are three critical conditions in cardio-oncology that every general practitioner and specialist should be aware of.





Medical Journal of Western Black Sea

Baycan Kuş, Mehmet Uzun, Necmi Baykan, Harun Çifci, Merve İrem Atıcı

Kuş B et al. A Rare Clinic Related to Paclitaxel Use… Med J West Black Sea 2025;9(1).

ABSTRACT

Paclitaxel is a member of the taxane class of chemotherapy medications and is utilized in the treatment of ovarian, breast, advanced non-small cell lung cancer, and Kaposi's Sarcoma associated with AIDS. Hypersensitivity reactions are relatively common and may range from mild clinical manifestations to severe, treatment-resistant, and even fatal outcomes. Approximately 30% of patients receiving taxane-based chemotherapeutic agents experience such reactions. Proposed pathophysiological mechanisms include IgE-mediated anaphylaxis—characterized by elevated serum tryptase levels—direct activation of mast cells and/or basophils, and the involvement of the complement cascade. Kounis syndrome is an acute coronary condition that arises during allergic or anaphylactic reactions. In the pathogenesis of Kounis syndrome, a variety of inflammatory mediators are thought to be involved, including proteases, tryptase, arachidonic acid metabolites, platelet-activating factor, as well as various cytokines and chemokines released during mast cell activation. The incidence in patients un-

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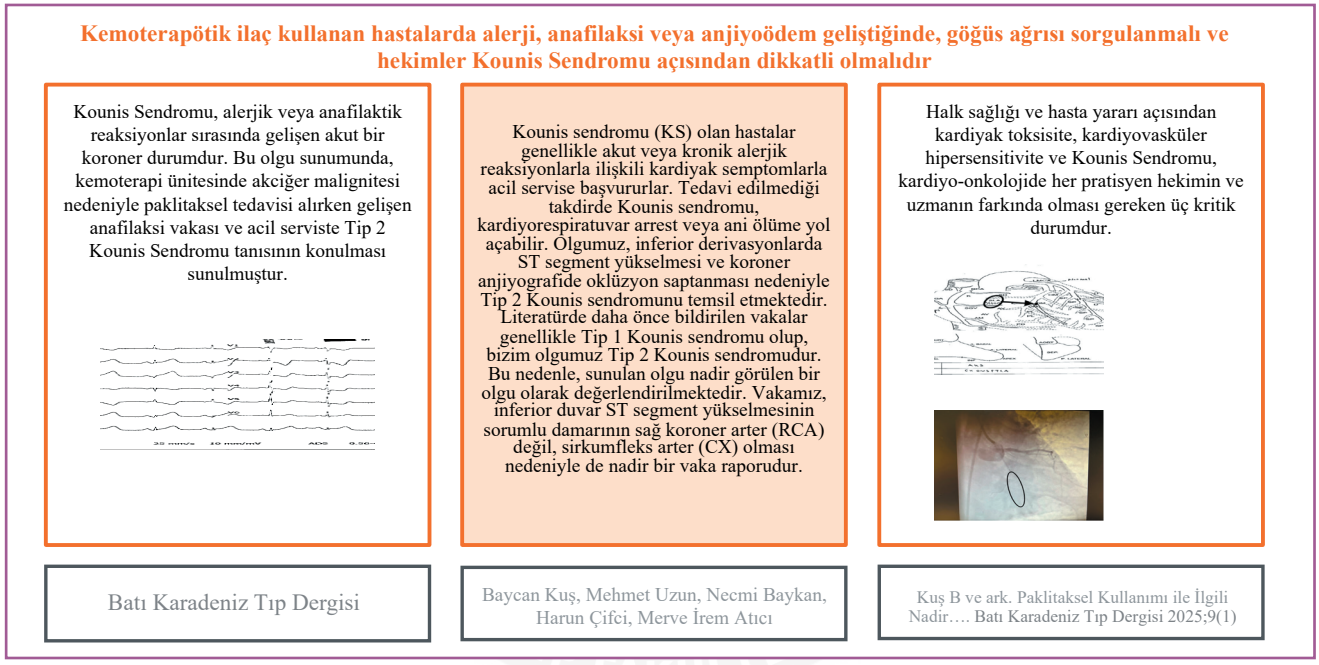
dergoing an allergic, hypersensitive, anaphylactic, or anaphylactoid reaction ranges from 1.1% to 3.4%. The most common heart complaint during application is chest pain (incidence: 86.6%). Diagnosing Kounis syndrome in the emergency department can be challenging due to the variety of clinical symptoms. It should rely on the presence of cardiovascular, allergic, or anaphylactic symptoms and signs, along with supporting evidence from laboratory tests, electrocardiograms, echocardiograms, and angiograms. In this report, we present a case of anaphylaxis while receiving paclitaxel treatment for lung malignancy in the chemotherapy unit and the diagnosis of Type 2 Kounis syndrome was established in the emergency department. Our case represents Type 2 Kounis syndrome because of ST segment elevation in inferior leads and occlusion in coronary angiography. Previously reported cases in the literature were Type 1 Kounis syndrome and our case is Type 2 Kounis syndrome. Therefore, this is a rare case report.

Our case is a rare case report because the culprit vessel of inferior wall ST segment elevation was not the right coronary artery but the circumflex artery.

Keywords: Anaphylaxis, Kounis Syndrome, lung adenocarcinoma, paclitaxel

GRAFİKSEL ÖZET



ÖZ

Paklitaksel, taksan sınıfı kemoterapi ilaçlarının bir üyesidir ve over, meme, ileri evre küçük hücreli dışı akciğer kanseri ile AIDS'e bağlı Kaposi Sarkomu'nun tedavisinde kullanılmaktadır. Aşırı duyarlılık reaksiyonları nispeten yaygındır ve hafif klinik bulgulardan şiddetli, tedaviye dirençli ve hatta fatal sonuçlara kadar geniş bir spektrumda gözlemlenebilir. Taksan bazlı kemoterapötik ajanlar alan hastaların yaklaşık %30'unda bu tür reaksiyonlar meydana gelmektedir. Öne sürülen patofizyolojik mekanizmalar arasında IgE aracılı anafilaksi, serum triptaz düzeylerinin artışı ile karakterize mast hücreleri ve/veya bazofillerin doğrudan aktivasyonu ve kompleman sisteminin devreye girmesi yer almaktadır. Kounis Sendromu, alerjik veya anafilaktik reaksiyonlar sırasında gelişen akut bir koroner durumdur. Kounis Sendromu'nun patogenezinde, mast hücresi aktivasyonu sırasında salınan proteazlar, triptaz, araşidonik asit türevleri, trombosit aktive edici faktör, çeşitli sitokinler ve kemokinler gibi farklı inflamatuvar mediatörlerin rol oynadığı düşünülmektedir. Alerjik, hipersensitif, anafilaktik veya anafilaktoid reaksiyon geçiren hastalarda insidans %1,1 ile %3,4 arasında değişmektedir. Uygulama sırasında en sık görülen kalp şikayeti göğüs ağrısıdır (insidans: %86,6). Acil serviste Kounis Sendromu'nun tanısı, çeşitli klinik semptomlar nedeniyle zorlu olabilir. Tanı, kardiyovasküler, alerjik veya anafilaktik semptomların ve bulguların varlığına ve laboratuvar testleri, elektrokardiyogram, ekokardiyogram ve anjiyogramdan elde edilen destekleyici kanıtlara dayanmalıdır. Bu raporda, kemoterapi ünitesinde akciğer malignitesi nedeniyle paklitaksel tedavisi alırken gelişen anafilaksi vakası ve acil serviste Tip 2 Kounis Sendromu tanısının konulması sunulmuştur. Vakamız, inferior derivasyonlarda ST segment yükselmesi ve koroner anjiyografide tıkanıklık olması nedeniyle Tip 2 Kounis Sendromu'nu temsil etmektedir. Literatürde daha önce bildirilen vakalar Tip 1 Kounis Sendromu iken, vakamız Tip 2 Kounis Sendromu'dur. Bu nedenle, bu nadir bir olgu sunumudur.

Vakamız, inferior duvar ST segment yükselmesinin sorumlu damarının sağ koroner arter değil, sirkumfleks arter olması nedeniyle de nadir bir vaka raporudur.

Anahtar Sözcükler: Akciğer adenokarsinomu, anaflaksi, Kounis Sendromu, paklitaksel

INTRODUCTION

Anaphylaxis is a severe, life-threatening systemic allergic reaction that manifests with various clinical symptoms such as urticaria, respiratory distress, nausea, vomiting, diarrhea, and hypotension (1). The annual incidence of severe, life-threatening anaphylaxis with circulatory symptoms is roughly 7.9 to 9.6 cases per 100,000 people (2).

Kounis Syndrome (KS) is an acute coronary syndrome triggered by allergic or anaphylactic reactions. Inflammatory mediators released during mast cell degranulation, along with those derived from the interaction of other immune cells such as T lymphocytes, macrophages, eosinophils, and platelets, play a pivotal role in the pathogenesis of KS. Substances including chymase—which acts as a conversion enzyme—tryptase, histamine, and arachidonic acid derivatives may contribute to acute ischemic events by promoting coronary vasospasm, atheromatous plaque erosion or rupture, and platelet activation. Importantly, KS is not limited to the coronary arteries; it may also involve cerebral, mesenteric, and peripheral vascular beds (3). The incidence in patients undergoing an allergic, hypersensitive, anaphylactic, or anaphylactoid reaction ranges from 1.1% to 3.4% (4). Three types of KS have been described so far:

1. Type I or MINOCA type (myocardial infarction with non-obstructive coronary arteries), which affects 76.6% of patients with normal or nearly normal coronary arteries and is induced by histamine, chymase, or arachidonic acid products (leukotrienes, platelet- activating factor).
2. Type II, which affects 22.3% of patients with quiescent preexisting coronary disease and is induced by the same factors as type I plus platelet activation.
3. Type III is a less common variant, affecting approximately 5.1% of patients, and is characterized by the development of stent thrombosis (subtype IIIa) and/or in-stent restenosis (subtype IIIb). This form is associated with hypersensitivity reactions triggered by various factors, including stent polymers, metallic components of the stent, eluted pharmacologic agents, dual antiplatelet therapies, and environmental exposures (5,6).

The most common heart complaint during application is chest pain (incidence: 86.6%). Diagnosing KS in the emergency department can be challenging due to the variety of clinical symptoms. It should rely on the presence of cardiovascular, allergic, or anaphylactic symptoms and signs, along with supporting evidence from laboratory tests, electrocardiograms, echocardiograms, and angiograms (7). The most common cause of KS is drugs (8) (Table 1). Paclitaxel is a member of the taxane class of chemotherapy medications and is utilized in the treatment of ovarian, breast, advanced non-small cell lung cancer, and Kaposi's Sarcoma associated with AIDS. Although mild allergic reactions such as skin flushing, rash and itching are common, serious allergic reactions such as anaphylaxis, angioedema and heart attacks are uncommon side effects. Hypersensitivity reactions are relatively common and may range from mild clinical manifestations to severe, treatment-resistant, and even fatal outcomes. Approximately 30% of patients receiving taxane-based chemotherapeutic agents experience such reactions. Proposed pathophysiological mechanisms include IgE-mediated anaphylaxis—characterized by elevated serum tryptase levels—direct activation of mast cells and/or basophils, and the involvement of the complement cascade (9). Over 300 cases of KS following exposure to various agents have been reported (2). Although the incidence of KS is quite low, the number of paclitaxel-related KS cases reported in the literature is even lower (10, 11).

In this report, we present a case of anaphylaxis while receiving paclitaxel treatment for lung malignancy in the chemotherapy unit and the diagnosis of Type 2 Kounis Syndrome was established in the emergency department.

CASE

A 62-year-old man with diabetes mellitus, chronic viral hepatitis and non-small cell lung cancer (adenocarcinoma), with no known history of allergies, was diagnosed with lung cancer about 45 days ago. He was admitted to the chemotherapy unit to receive the second dose of carboplatin and paclitaxel one month after his first chemotherapy session. Although he was premedicated with dexamethasone, he developed anaphylaxis during the paclitaxel infusion and was immediately admitted to the emergency department (ED) after receiving adrenaline, pheniramine, dexamethasone, and methylprednisolone in the chemotherapy unit. At the time of admission to the emergency department, the blood pressure was 131/88 mmHg, pulse rate was 88/min, respiratory rate was 16/min, fingertip oxygen saturation was

Table 1: Possible Triggers of Kounis Syndrome

Allergic patients	Drug reactions	Environmental exposure
Angioedema	Antibiotics	Bee stings
Bronchial asthma	Anaesthetics	Anti bites (fire ants)
Urticaria	Radio contrast substances	Latex contact (natural rubber)
Food allergies	Non-steroidal anti-inflammatory drugs	
Serum disease	Corticosteroids	

98%, and temperature was 36.5°C. His general condition was good and Glasgow Coma Scale Score was 15. The patient had mild uvula edema, with no signs of angioedema. Lung sounds were normal and urticarial eruptions were present. The patient described typical chest pain and stated that he had not experienced any chest pain prior to starting chemotherapy. The anamnesis obtained from the patient's relatives also confirmed the patient's statement. An electrocardiogram (ECG) was performed, showing ST segment elevation in the inferior leads and ST segment depression in the reciprocal leads (Figure 1).The patient was immediately consulted with the cardiology department and transferred to the angiography unit for emergency coronary angiography.

Coronary angiography revealed a 100% occlusion of the obtuse marginal artery (OMA) branch of the circumflex artery (Figure 2, 3), and the angiography report indicated that this occlusion was successfully opened. During the follow-up, it was noted that oncologic treatment was planned with the discontinuation of paclitaxel. According to the hospital data system, carboplatin and pemetrexed were administered in combination with dexamethasone and premedication during the next chemotherapy. The treatment continued with gemcitabine approximately 9 months later. It was determined that brain metastases had developed, and the patient also received radiotherapy. The patient was followed up infrequently in the cardiology outpatient clinic for

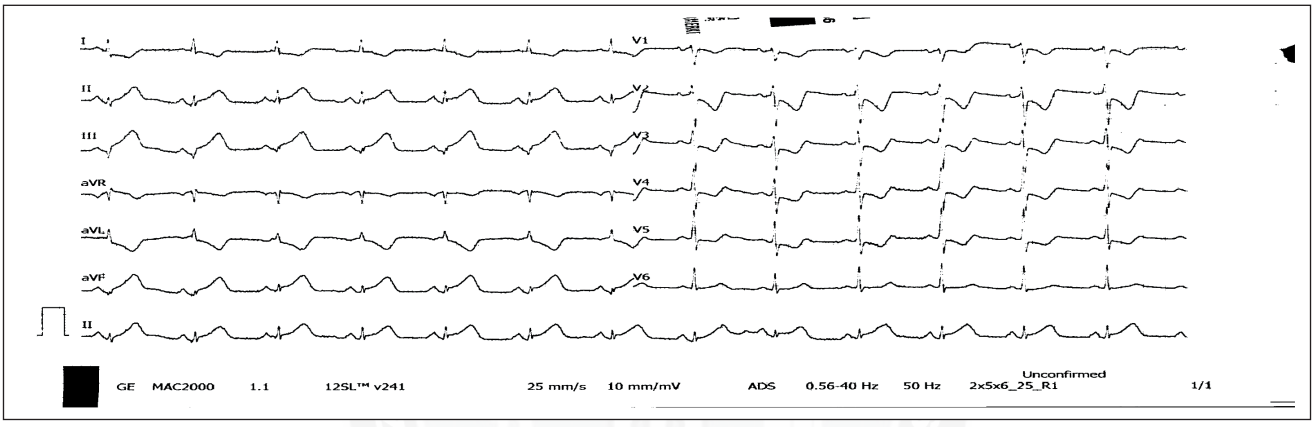


Figure 1: The ECG image of the patient showed ST elevation in the inferior leads and ST depression in the reciprocal leads, indicating acute inferior myocardial ischemia.

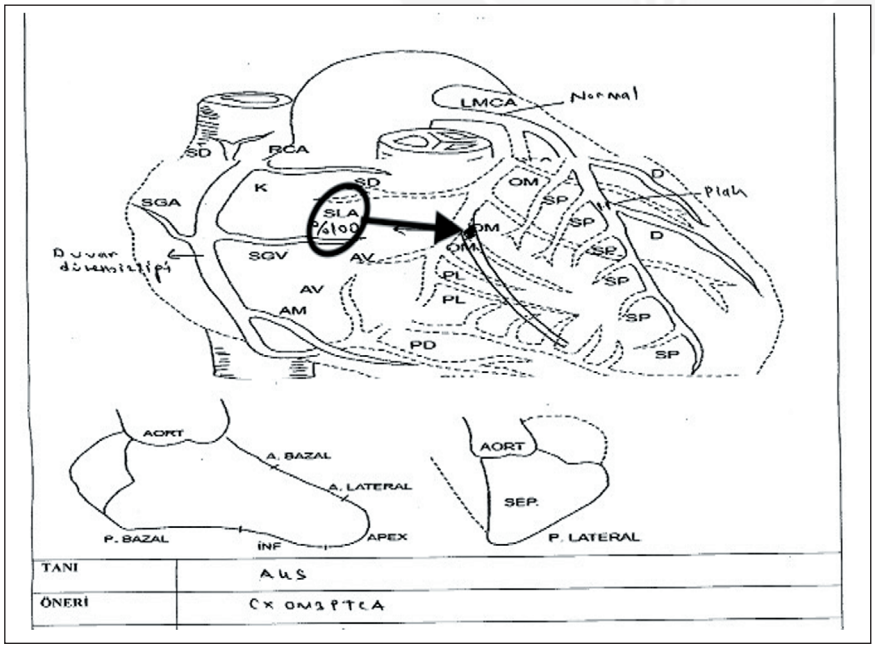


Figure 2: The coronary angiography report of the patient revealed a 100% occlusion of the obtuse marginal artery 3 (OMA3) branch of the circumflex artery.

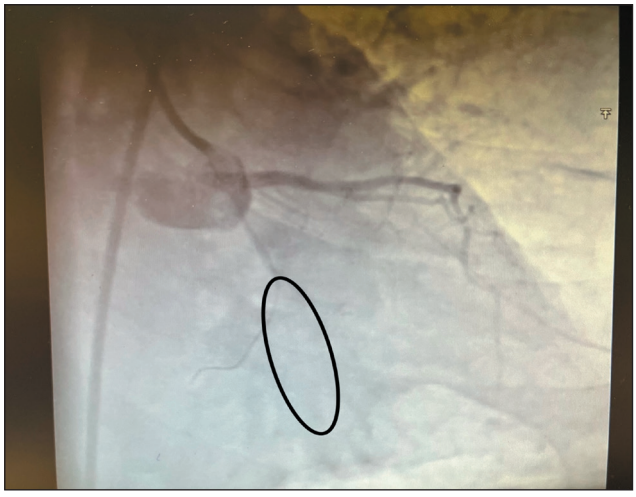


Figure 3: The fluoroscopic image of the patient's coronary angiography shows the area of occlusion, with the circled region indicating a 100% occlusion of the OMA3 (obtuse marginal artery 3) branch.

11 months after the development of KS, but did not require another coronary angiography. Approximately 11 months later, two days after receiving chemotherapy, the patient developed a cerebral hemorrhage due to a fall and passed away after being followed up in the intensive care unit for a period of time.

DISCUSSION

Drug antigens are linked to the formation of specific IgE after repeated exposure in patients, leading to sensitization (12). Through the cross-linking of drug antigens to specific IgE via high-affinity IgE receptors on mast cells and/or basophils, inflammatory mediators are released from these cells. These mediators include vasoactive amines (histamine), proteolytic enzymes (tryptase), arachidonic acid metabolites (prostaglandins and leukotrienes), proteoglycans (heparin) and some symptoms are caused by their release. Organ systems such as cutaneous, respiratory, cardiovascular and gastrointestinal systems may be affected and deaths due to anaphylaxis may occur (13,14).

Early hypersensitivity reactions due to non-immunologic mechanisms are reactions that may occur at the first encounter with the drug antigen without prior sensitization. Mediator release from mast cells and/or basophils occurs without a known IgE mechanism. The responsible mechanism is usually complement activation and/or direct mediator release. Clinical symptoms and signs are similar to IgE-mediated reactions (15).

In the pathogenesis of KS, a variety of inflammatory mediators are thought to be involved, including proteases, tryptase, arachidonic acid metabolites, platelet-activating factor, as well as various cytokines and chemokines released during mast cell activation (5). Recent studies suggest an increased risk of allergic reactions in patients with similar pathogenesis, such as cancer, diabetes, viral hepatitis, and low immune sensitivity, as seen in our case. A recently published study identified 31 immunophenotypes associated with urticaria, with 4 showing a strong causal relationship with the condition. Specifically, the presence of HLA DR^+ $CD4^+$ activated T cells, expression of CD45 in CD8 br, and increased HLA DR expression in plasmacytoid dendritic cells have been associated with a heightened risk. In contrast, CD8dim natural killer T (NKT) lymphocytes appear to exert a protective effect (16).

KS has been categorized into three distinct subtypes in the literature (5, 6). Type I is characterized by coronary vasospasm occurring in individuals with no underlying coronary artery disease or identifiable cardiovascular risk factors, and with angiographically normal coronary arteries. Type II refers to patients with pre-existing coronary atherosclerosis, in whom an acute allergic reaction can trigger plaque erosion or rupture, subsequently leading to acute myocardial infarction. Type III is associated with stent thrombosis occurring after an allergic event in individuals who have previously received a drug-eluting stent (17). Our case represents Type 2 KS because of ST segment elevation in inferior leads and occlusion in coronary angiography. Previously reported cases in the literature were Type 1 KS and our case is Type 2 KS. Therefore, this case report is a rare case report (10,11).

Patients with KS typically present to the emergency department with cardiac symptoms associated with either acute or chronic allergic reactions. The clinical picture may include ischemic chest pain, dyspnea, coronary vasospasm, angina pectoris, myocardial infarction, and syncope secondary to heart failure. Common clinical signs of KS also comprise cold extremities, pallor, palpitations, hypotension, tachycardia, or bradycardia. If left untreated, KS can result in cardiorespiratory arrest or sudden death. In a study conducted in the USA, it was reported that the prevalence of KS was 1.1% and it was responsible for 7% of hospital deaths (18). Our case also had a fatal condition such as ST segment elevation, but the patient survived because of early recognition and rapid intervention. In patients exhibiting systemic allergic reactions, KS should be carefully considered in the differential diagnosis, particularly when clinical, electrocardiographic, echocardiographic, angiographic, or laboratory findings suggest acute myocardial ischemia. A prior history of atopic conditions or allergic episodes should be regarded as a significant diagnostic indicator in such cases. Paclitaxel, docetaxel and other taxanes are commonly used agents in cancer treatment, and hypersensitivity reactions to taxanes are common. In early studies with paclitaxel and docetaxel, reactions of up to 30% were reported in patients. Antihistamine (H1 and H2 histamine receptor antagonists)

and corticosteroid premedication and slow infusion rates reduced the rate of severe reactions to less than 10% (19). However, it should be noted that severe hypersensitivity reactions may occur with both paclitaxel and docetaxel despite premedication. Symptoms typically begin within the first few minutes of infusion and usually occur on the first or second administration of the drug. Symptoms may include dyspnea, urticaria, flushing, severe pain in the back or chest, gastrointestinal symptoms, hypo- or hypertension, musculoskeletal pain, paresthesia and loss of consciousness. There are also cases that report death (15,19).

Although cases of ischemic events or myocardial infarction associated with paclitaxel use have been reported in the literature, the majority of these patients had established cardiovascular risk factors such as hypertension, a history of smoking, or pre-existing coronary artery disease. These confounding variables make it difficult to attribute the observed cardiac effects solely to paclitaxel administration (20). Conversely, reports involving patients who experienced ischemic events in the absence of known coronary artery disease or significant cardiovascular risk factors remain scarce (1). In our case, there was no history of coronary artery disease and no previous symptoms suggestive of acute coronary syndrome.

Hypersensitivity reactions to anticancer chemotherapy can lead to discontinuation of first-line treatment options. Identification of these reactions can lead to rapid drug desensitization and specific diagnosis and treatment. One study investigated the symptoms seen in the presence of immediate hypersensitivity reactions (IHSR) in patients receiving anticancer chemotherapy and found that urticaria was more common with carboplatin, back pain with paclitaxel, dyspnea with oxaliplatin and docetaxel, and cardiovascular symptoms with monoclonal antibodies (22). The debate on the management of IHSR to paclitaxel continues and various management approaches including desensitization have been proposed. In a study of 425 patients, 29.2% of patients experienced IHSR and 11.8% of them met the criteria for anaphylaxis according to the Brighton scale. Of the patients who experienced IHSR, 83.8% completed their treatment by adding antihistamines, leukotriene blockers and corticosteroids and also by slowing the infusion rate (23). In our case, anaphylaxis developed despite desensitization treatment and chest pain was observed in the foreground. The medical oncology unit was informed about the patient, our patient could not continue paclitaxel treatment and the chemotherapeutic drug had to be changed.

It is known that ST segment elevations in the inferior leads usually originate from the right coronary artery (RCA). Although the ECG findings and coronary angiography findings of our case seem to be contradictory, it has been reported in the literature that the circumflex artery (CX) may be the cause of inferior wall STEMI along with the RCA (24,25). Our case is also rare that will contribute to the literature in this respect.

There have been some reports of acute coronary syndromes developing during paclitaxel use. However, many patients also have other important risk factors for cardiovascular diseases. Direct cardiotoxic damage was not reported in these studies (26,27). Gemici et al. suggested that paclitaxel has an allergic effect on the myocardium and causes acute coronary syndrome (20). However, paclitaxel-related Type 2 KS has been reported rarely in the literature. Therefore, we think that our case will contribute to the literature. We recommend that chest pain should be questioned when allergy, anaphylaxis and angioedema develop in patients receiving chemotherapeutic drugs and that they should be alert for KS.

The 2022 European Society of Cardiology (ESC) guidelines on cardio-oncology, developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO), and the International Cardio-Oncology Society (IC-OS), do not address hypersensitivity reactions or the coronary form of KS associated with hypersensitivity. This omission is noteworthy, given the frequent reports in the literature of hypersensitivity reactions and KS as significant cardiovascular side effects of cancer therapies (28).

From the perspective of public health and patient benefit, cardiac toxicity, cardiovascular hypersensitivity, and Kounis Syndrome are three critical conditions in cardio-oncology that every general practitioner and specialist should be aware of.

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None.

Author Contributions

Author contributions are equal.

Conflicts of Interest

Authors declare no conflict of interest.

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None.

Ethical Approval

This study is not an experimental and clinical research. Because of it was a case report, the ethical approve was not needed. Written informed consent was obtained from the patient for the publication of the case report.

Review Process

Externally and extremely peer-reviewed.

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CASE REPORT

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Batı Karadeniz Tıp Dergisi

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Type II Mirizzi Syndrome: A Case Report

Tip II Mirizzi Sendromu: Olgu Sunumu

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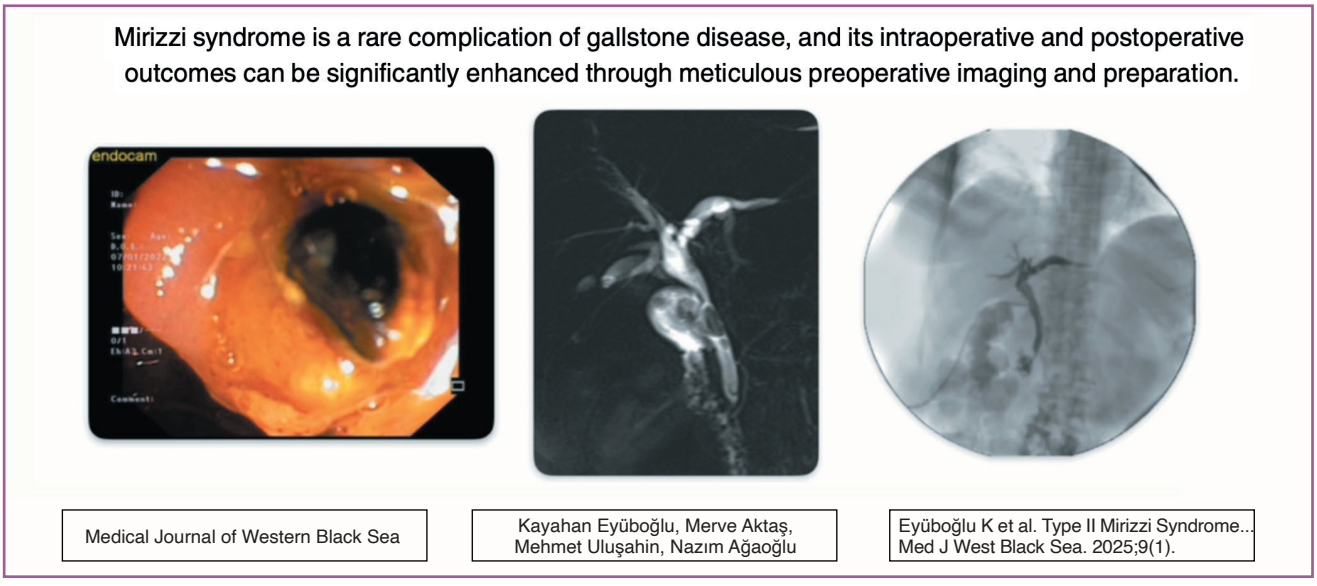
GRAPHICAL ABSTRACT



ABSTRACT

Mirizzi syndrome (MS) is characterized by the blockage of the bile duct due to external compression caused by a large stone located in the Hartmann pouch or cystic duct of the gallbladder. These patients present with obstructive jaundice accompanied by fever and right upper quadrant pain. If it cannot be detected in the preoperative or intraoperative period, it may cause biliary tract injuries during surgery. In this case, a 60-year-old female patient complains of abdominal pain, jaundice, nausea, and vomiting. This case report emphasizes the diagnostic and surgical approach in type II Mirizzi Syndrome and highlights the importance of preoperative imaging, contributing to the literature. ng and was diagnosed with cholelithiasis and choledocholithiasis is presented. The diagnosis of Mirizzi syndrome was clarified with MR cholangiopancreatography (MRCP) after the procedure of endoscopic retrograde cholangiopancreatography (ERCP) for choledochal stone was unsuccessful. Cholecystectomy, common bile duct (CBD) exploration, and T-tube drainage were performed on the patient for whom surgical intervention was decided. The postoperative period ended uneventfully.

Keywords: Mirizzi syndrome, cholelithiasis, choledochal exploration

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GRAFİKSEL ÖZET

Mirizzi sendromu, safra taşı hastalığının nadir görülen bir komplikasyonudur ve dikkatli preoperatif görüntüleme ve hazırlık ile intraoperatif ve postoperatif sonuçlar önemli ölçüde iyileştirilebilir.

Batı Karadeniz Tıp Dergisi

Kayahan Eyüboğlu, Merve Aktaş, Mehmet Uluşahin, Nazım Ağaoğlu

Eyüboğlu K ve ark. Type II Mirizzi... Med J West Black Sea. 2025;9(1).

ÖZ

Mirizzi sendromu (MS), safra kesesinin Hartmann poşu veya sistik kanalında yer alan büyük bir taşın dıştan basısının neden olduğu safra kanalının tıkanıklığıyla karakterizedir. Bu hastalarda, obstruktif sarılığa eşlik eden ateş ve sağ üst kadranda ağrı görülür. Eğer preoperatif veya intraoperatif dönemde tespit edilemezse, ameliyat sırasında safra yolları yaralanmalarına sebebiyet verebilir. Bu makalede, karın ağrısı, sarılık, bulantı ve kusma şikâyetleri olan ve kolesistit ve koledokolitiazis teşhisi konulan 60 yaşında bir kadın hasta sunulmuştur. Mirizzi sendromu teşhisi, koledok taşı nedeniyle yapılan endoskopik retrograd kolanjiyopankreatografi (ERCP) işleminin başarısız olması sonrasında MR Kolanjiyopankreatografi (MRCP) ile netleştirilmiştir. Cerrahi müdahaleye karar verilen hastaya kolesistektomi, ortak safra kanalı (CBD) eksplorasyonu ve T-tüp drenajı uygulanmıştır. Hastanın postoperatif dönemi komplikasyonsuz geçmiştir. Bu olgu sunumu, Tip II Mirizzi Sendromu'nun tanı ve cerrahi tedavisindeki yaklaşımı ile preoperatif görüntülemenin önemini vurgulayarak literatüre katkı sağlamaktadır.

Anahtar Sözcükler: Mirizzi sendromu, kolelitiazis, koledok eksplorasyonu

INTRODUCTION

Gallstones (cholelithiasis) are a prevalent gastrointestinal condition and are usually asymptomatic. Their incidence increases significantly in certain populations, such as fertile women aged forty to fifty and those with certain risk factors, including obesity, rapid weight loss, or a family history of gallstone disease. In most cases, gallstones remain clinically silent; however, complications can arise when stones migrate or obstruct biliary structures. Mirizzi Syndrome (MS) is a rare, although potentially serious, consequence of cholelithiasis. MS results from the common bile duct (CBD) mechanical obstruction caused by a large gallstone located in the infundibulum (Hartmann's pouch) or cystic duct, leading to extrinsic compression and biliary obstruction.

Mirizzi Syndrome was first described by Pablo Luis Mirizzi in 1948, who identified the syndrome as a significant cause of obstructive jaundice due to external compression of the bile duct. Since then, the syndrome has been further studied and categorized. In 1982, McSherry et al. introduced two categories of MS; subsequently, Csendes et al. broadened this categorization in 1989 to include four subtypes. These classifications aid in differentiating the extent of bile duct involvement, encompassing the existence of cholecystobiliary fistulas and the severity of biliary wall degradation (1).

The ethology of MS encompasses persistent inflammation, fibrosis, and ultimately adhesion between the gallbladder and biliary tree components, and it is considered an important risk factor for bile duct injuries (2). Untreated cholelithiasis may eventually result in problems including cholecystitis, choledocholithiasis, and Mirizzi Syndrome. The symptoms generally include obstructive jaundice, right upper quadrant pain, and fever. In some cases, the disease progresses insidiously, making early diagnosis difficult. Especially dangerous anatomic alterations make the surgical intervention more complex and riskier. It is important to the importance of preoperative determination of surgical strategies and optimal surgical intervention when diagnosis is done at

the time of operation, particularly for those whose classification was high grade (3). Advanced imaging techniques, including Magnetic Resonance Cholangiopancreatography (MRCP) and Endoscopic Retrograde Cholangiopancreatography (ERCP), are essential for identifying and validating MS when traditional diagnostic methods are inadequate.

This case report highlights the diagnostic and therapeutic challenges related to type II Mirizzi Syndrome, focusing on a 60-year-old female patient who presented with symptoms of abdominal pain, jaundice, nausea, and vomiting. Imaging modalities such as MRCP and ERCP were critical in diagnosing the condition after initial interventions failed. The surgical approach included cholecystectomy, common bile duct exploration, and T-tube drainage, which resulted in a successful recovery. This article highlights the importance of preoperative imaging and a multidisciplinary surgical strategy to prevent problems like biliary damage and postoperative morbidity. The objective is to enhance the knowledge regarding the care of this rare event to improve patient outcomes and address analogous circumstances in clinical practice.

CASE REPORT

A 60-year-old female patient has come to the emergency department complaining of upper abdominal pain and nausea. The patient's history revealed ongoing pain and loss of appetite for several weeks.

Laboratory findings showed cholestasis: ALT 121 U/L, AST 62 U/L, GGT 328 U/L, ALP 246 U/L, direct/total bilirubin 3.92/7.08 mg/dL. White blood cell count was 6.220 μl, and CRP was 87.9. Initial abdominal ultrasonography showed diffuse thickening of the gallbladder wall (5.5 mm), multiple millimetric stones, and slight prominence in the intrahepatic bile ducts. To clarify the preliminary diagnosis of obstructive icterus, endoscopic retrograde cholangiopancreatography (ERCP) was performed and revealed a stone approximately 2 cm in size at the junction of the common bile duct and cystic duct, which could not be removed. Instead, a 7 cm 10 Fr plastic stent was placed in the common bile duct. Magnetic Resonance Cholangiopancreatography (MRCP) imaging was performed in the preoperative preparation phase after the failed ERCP procedure. In MRCP several stones were observed within 15mm diameter located at cystic duct - choledochal junction common bile duct & neck region exerting pressure on main bile causing dilatation on proximal main hepatic & intrahepatic tract respectively (Figure 1 and 2).

Based on clinical, laboratory, and imaging findings, the patient was diagnosed with type II Mirizzi Syndrome. Subsequently, open cholecystectomy was planned. Through a right subcostal incision, the gallbladder was removed, and adhesions between the cystic duct and common bile duct were released. The gallbladder neck was opened, and multiple stones were removed by irrigation, followed by the removal of the stent. A T-tube was inserted into the common bile duct, and the defect on the duct's wall was repaired using a flap from Hartmann's pouch. Intraoperative cholangiography confirmed clear bile ducts, and the surgery was completed with the placement of a suction drain in the subhepatic area.

Postoperatively, the patient's liver function tests improved, and bilirubin levels decreased (Table 1).

Oral intake began on the second postoperative day. The drain was removed on the fourth day, and T-tube cholangiography on the tenth day showed no complications. The T-tube was removed two days later, and the patient was discharged fully recovered. (Figure 3).

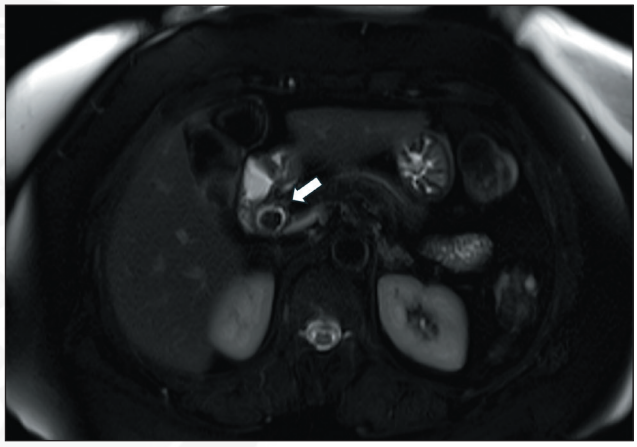

Figure 1: MRCP shows that the gallbladder appears contracted. At the junction of the cystic duct and choledochal duct, several stones, the largest of which is 15 mm in diameter, are observed in the choledochal and gallbladder neck. The stone in the neck of the gallbladder compresses the common bile duct and there is dilatation of the proximal common hepatic bile duct and intrahepatic bile ducts (Mirizzi syndrome).

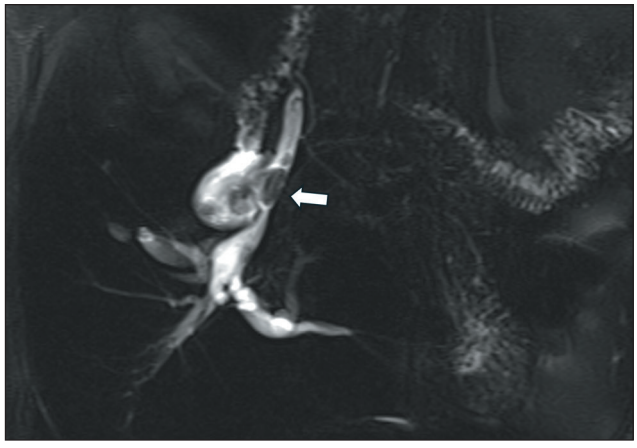

Figure 2: A view of the biliary tree

Table 1. Patient's laboratory results.

Blood Tests	Normal Range	Emergency Department	After ERCP	Post-op 1st day	Post-op 2nd day	Post-op 3rd day	Discharge Day 12th
ALT	0-45 U/L	121	69	56	35	23	25
AST	0-35 U/L	62	69	43	29	18	20
GGT	0-55 U/L	328	25	30	25	29	44
ALP	30-120 U/L	246	72	62	61	64	77
T.Bil.	0.3-1.2 mg/dL	3.92	0.33	0.43	0.52	0.29	0.1
D.Bil.	0-0.2 mg/dL	7.08	1.99	2.47	2.82	1.8	0.48
WBC	3710-10190 μL	6220	16860	16350	11310	8670	6750
CRP	<5 mg/L	87.9	4.5	74.5	217	182.5	4.9

ALT: Alanine Aminotransferase, **AST:** Aspartate Aminotransferase, **GGT:** Gamma-Glutamyl Transferase, **ALP:** Alkaline Phosphatase, **T.Bil.:** Total Bilirubin, **D.Bil.:** Direct Bilirubin, **WBC:** White Blood Cell, **CRP:** C-Reactive Protein, **ERCP:** Endoscopic Retrograde Cholangiopancreatography.

Figure 3: Evaluation of the biliary tract by postoperative t-tube cholangiography.

DISCUSSION

Partial biliary duct obstruction due to gallstones was first reported by Hans Kehr in 1905. In 1948, Pablo Luis Mirizzi drew attention to this situation with his article titled "Sindrome del conducto hepatico" and MS was first described.

MS was divided into four types with the Csendes classification in 1989, and in 2007, having a colo-enteric fistula with one of these types was defined as type 5 (4,5):

There are five different varieties of Mirizzi syndrome, and each one is characterized by a unique set of symptoms. The external compression of the common bile duct that is induced by a gallstone is what distinguishes Mirizzi type I from other types. On the other hand, the occurrence of a cholecystobiliary fistula that affects about one-third of the bile duct's circumference is what distinguishes Mirizzi type II from type I. The cholecystobiliary fistula can involve up to two-thirds of the bile duct's circumference if it is a Mirizzi type III, which is the most severe form of the condition. The most severe form, known as type IV Mirizzi, happens when the cholecystobiliary fistula not only grows to an extensive size but also causes the destruction of the wall of the bile duct, which encompasses the entirety of the duct's perimeter. Any variant of the Mirizzi syndrome that is linked with a bilioenteric fistula is considered to be Mirizzi type V, regardless of whether or not gallstone ileus is present in the patient (6). The purpose of all definitions is to ease the decompression of the biliary tree, prevent a recurrence, and decrease biliary tract injuries and morbidity during the operation.

Diagnosing MS can be challenging due to the lack of distinct signs and symptoms that are unique to the condition. The most observed symptom is abdominal pain, which is often followed by jaundice and cholangitis. Nausea, vomiting, and itching are less frequently encountered (7). ERCP and MRCP are valuable imaging methods in preoperative diagnosis. Especially in ERCP, obstruction in the common bile duct, presence of impacted stone in the gallbladder neck or cystic duct, size of the stone, presence of biliobiliary fistula, duodenal, pancreatic and ampullary pathologies and possible findings of malignancy can be detected. It allows biliary decompression by placing a stent in the same session (8). However, in cases where ERCP cannot be technically performed due to external compression, MRCP is a guiding method with high sensitivity and specificity (9).

The significance of MR Cholangiopancreatography (MRCP) in accurately diagnosing Mirizzi syndrome, particularly when conventional methods like endoscopic retrograde cholangiopancreatography (ERCP) prove inadequate, is

underscored in this case study. Furthermore, surgical interventions, encompassing cholecystectomy and exploration of the common bile duct, have proven to be highly effective in managing this condition and facilitating a successful patient recovery, as exemplified by the presented case.

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None.

Author Contributions

Concept: **Nazım Agaoglu, Mehmet Ulusahin, Kayahan Eyüboğlu,** Design: **Mehmet Ulusahin, Kayahan Eyüboğlu, Merve Aktas,** Data collection or processing: **Mehmet Ulusahin, Kayahan Eyüboğlu, Merve Aktas,** Analysis or Interpretation: **Nazım Agaoglu, Mehmet Ulusahin, Merve Aktas,** Literature search: **Mehmet Ulusahin, Kayahan Eyüboğlu, Merve Aktas,** Writing: **Mehmet Ulusahin, Kayahan Eyüboğlu, Merve Aktas,** Approval: **Nazım Agaoglu, Mehmet Ulusahin.**

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Ethical Approval

Written informed consent was obtained from the patient for the publication of the case report.

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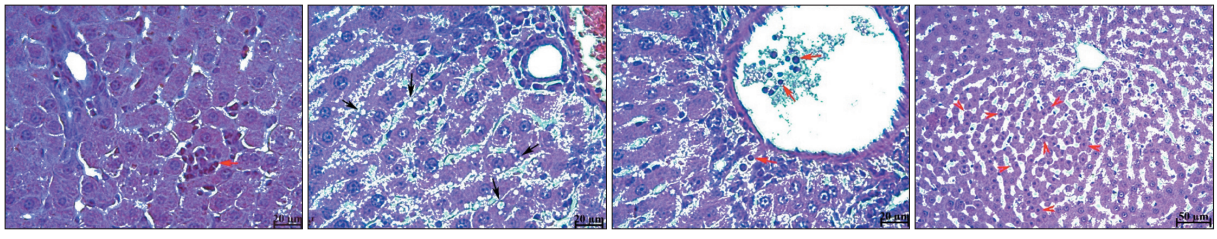

GLP-1 Receptor Agonist Liraglutide Modulates the Oxidative Stress and SIRT1/PGC1 Alpha Levels on Liver Tissue in Ovariectomized Rats

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TURKJOD

(Zonguldak Bülent Ecevit Üniversitesi ile Türkiye Obezite Araştırma Derneği arasında işbirliği protokolü çerçevesinde ortak yayın platformudur)