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YAZIŞMA ADRESİ | CONTACT ADDRESS

Hitit Üniversitesi Tıp Fakültesi, ÇORUM, TÜRKİYE
Tel: +90 364 222 11 00 Fax: +90 364 222 11 02
hmj@hitit.edu.tr | https://dergipark.org.tr/tr/pub/hititmedj

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Editörden

Değerli Araştırmacılar, Kıymetli Meslektaşlarımız ve Saygıdeğer Okurlarımız,

Bilimsel bilginin hızla değiştiği, teknolojinin sağlık alanındaki uygulamalarını dönüştürdüğü günümüzde, Hitit Tıp Dergisi'nin Ekim 2025 sayısını sizlerle buluşturmanın heyecanını yaşıyoruz. Dergimizin her yeni sayısı, yalnızca güncel bilgilerin paylaşımı değil, aynı zamanda bilimsel düşüncenin evrensel dolaşımına katkı sunma gayretiyle hazırlanmıştır.

Bu sayımızda, farklı uzmanlık alanlarından gelen titiz çalışmalar yer almaktadır: 16 özgün araştırma makalesi, 1 derleme, 5 olgu sunumu ve 1 editöre mektup olmak üzere toplam 23 bilimsel eser, okurlarımızın değerlendirmesine sunulmaktadır.

Yer alan araştırmalar, disiplinler arası iş birliğinin değerli bir ürünü olup hem klinik uygulamalara hem de temel bilimsel yaklaşımlara ışık tutmaktadır. Derleme yazılar güncel literatürün analitik bir bakış açısıyla ele alınmasını sağlarken, olgu sunumları nadir görülen klinik deneyimleri paylaşarak bilimsel pratikte farkındalık yaratmaktadır. Editöre mektuplar ise eleştirel bakış açısını teşvik ederek bilimsel tartışma kültürünün gelişimine katkıda bulunmaktadır.

Hitit Tıp Dergisi olarak, yalnızca bir yayın mecrası değil; aynı zamanda bilimsel dürüstlüğü, eleştirel aklı ve şeffaflığı merkeze alan bir akademik zemin olmayı hedefliyoruz. Bu süreçte araştırmacılarımızın ilgisi, dergimizin daha da güçlenmesi için bizlere ilham vermektedir.

Dergimize değerli katkılarını sunan tüm yazarlarımıza, titiz değerlendirmeleriyle yayın kalitesinin güvencesi olan hakemlerimize ve emeğini esirgemeyen yayın kurulu üyelerimize teşekkür ederiz. Ayrıca bizleri takip eden ve görüşleriyle gelişimimize katkıda bulunan siz değerli okurlarımıza en içten saygılarımızı sunuyoruz.

Bilimsel üretkenliğin ve ortak aklın rehberliğinde, daha nice sayılarda buluşmak dileğiyle...

Hitit Tıp Dergisi Editörlüğü
Ekim 2025

From the Editor

Distinguished Researchers, Esteemed Colleagues, and Respected Readers,

In an era where scientific knowledge evolves rapidly and technological advances continue to transform the field of health sciences, it is our privilege to present to you the October 2025 issue of the Hitit Medical Journal. Each issue of our journal is prepared not only with the aim of sharing up-to-date information, but also with the aspiration of contributing meaningfully to the universal discourse of science.

This issue comprises a diverse collection of scholarly works, reflecting both clinical practice and basic science perspectives. Specifically, it features 16 original research articles, 1 review, 5 case reports, and 1 letters to the editor, for a total of 22 scientific contributions.

The original research articles represent rigorous scientific efforts and embody the principles of methodological soundness and peer-reviewed scrutiny. The review article synthesizes the current body of literature, offering valuable insights into contemporary developments. The case reports present rare clinical encounters that enrich practical knowledge through experiential perspectives, while the letters to the editor encourage scholarly debate and critical reflection.

As Hitit Medical Journal, our mission extends beyond being a publishing platform. We aim to serve as an academic forum that fosters scientific integrity, critical thinking, and transparency, while supporting interdisciplinary dialogue. The growing interest of our contributors and readers is both a source of inspiration and a responsibility that drives us to pursue ever higher standards of quality.

We would like to extend our sincere gratitude to all authors for their invaluable contributions, to our reviewers for their meticulous and dedicated evaluations, and to our editorial board for their commitment to excellence. We also express our appreciation to our readers, whose engagement and constructive feedback continue to shape the progress of our journal.

With the guidance of science, we look forward to meeting you again in forthcoming issues.

Hitit Medical Journal
October 2025

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HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

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Prevalence of Sarcopenia and Its Association with Malnutrition in Hospitalized Elderly Patients

Hastanede Yatan Yaşlı Hastalarda Sarkopeni Prevalansı ve Malnütrisyon ile İlişkisi

Mevlüt Kaçar[1] | Mehmet Uzunlulu[2] | Erhan Eken[2] | Semih Başcı[3]

[1]Celal Bayar University, Faculty of Medicine, Department of Rheumotology, Manisa, Türkiye
[2]İstanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Department of Internal Medicine, İstanbul, Türkiye
[3]Dokuz Eylül University, Faculty of Medicine, Department of Hematology, İzmir, Türkiye

Sorumlu Yazar | Correspondence Author
Erhan Eken
erhan-eken@hotmail.com
Address for Correspondence: İstanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Department of Internal Medicine, İstanbul, Türkiye.

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Prevalence of Sarcopenia and Its Association with Malnutrition in Hospitalized Elderly Patients

ABSTRACT

Objective: To investigate the prevalence of sarcopenia and evaluate the nutritional status in geriatric patients hospitalized at the Internal Medicine Clinic.

Material and Method: A total of 105 patients (54 female and 51 male) aged ≥ 65 years (mean age: 74 ± 6 years) hospitalized between November 2015 and January 2016 were consecutively enrolled in this prospective and observational clinical study. Muscle mass was evaluated by bioelectrical impedance device, muscle function by walking test, and strength by hand grip test. Patients were diagnosed with sarcopenia, pre-sarcopenia, and non-sarcopenic. Mini nutritional assessment (MNA) test was used to define malnutrition.

Results: The number of patients diagnosed with sarcopenia and pre-sarcopenia was 49 (46.7%) and 5 (4.8%), respectively. The prevalence of sarcopenia was higher in female patients than male patients (61.1% vs. 31.4%; *p=0.006*). The prevalence of malnutrition in patients with sarcopenia and without sarcopenia were 51%, 10%, and the rate of patients at risk of malnutrition with sarcopenia and without sarcopenia was 37%, 49%, respectively. The prevalence of malnutrition was significantly higher in patients with sarcopenia (*p<0.001*). 40.8% of sarcopenic patients were overweight or obese. In the logistic regression analysis, female gender (OR=3.3, CI=1.35-8.04) and malnutrition (OR=9.41, CI=3.06-28.95) were significant risk factors for the development of sarcopenia.

Conclusion: Approximately half of the hospitalized geriatric patients were sarcopenic or pre-sarcopenic, and 88% of patients with sarcopenia had malnutrition or at risk of malnutrition. Sarcopenia and malnutrition should be evaluated together in geriatric inpatients and sarcopenic obesity should not be ignored.

Keywords: Bioelectrical Impedance Analysis, Malnutrition, Obesity, Sarcopenia.

ÖZET

Amaç: İç Hastalıkları Kliniğinde yatan geriatrik hastalarda sarkopeni prevalansını araştırmak ve beslenme durumunu değerlendirmek.

Gereç ve Yöntem: Hastanede yatan 65 yaş üstü toplam 105 hasta (54 kadın ve 51 erkek) (ortalama yaş: 74 ± 6 yıl) ardışık olarak çalışmaya dahil edildi. Kas kütlesi biyoelektrik empedans cihazı ile, kas fonksiyonu yürüme testi ile ve kas gücü el kavrama testi ile değerlendirildi. Hastalar sarkopeni, pre-sarkopeni ve sarkopenik olmayan olarak teşhis edildi. Malnütrisyonu tanımlamak için mini nütrisyonel değerlendirme (MNA) testi kullanılmıştır.

Bulgular: Sarkopeni ve pre-sarkopeni tanısı konan hasta sayısı sırasıyla 49 (%46,7) ve 5 (%4,8) idi. Sarkopeni prevalansı kadın hastalarda erkek hastalara göre daha yüksekti (%61,1' e karşı %31,4; *p=0,006*). Sarkopenisi olan hastalarda malnütrisyon prevalansı %51 ve malnütrisyon riski taşıyan hastaların oranı %37; sarkopenisi olmayan hastalarda malnütrisyon prevalansı %10 ve malnütrisyon riski taşıyan hastaların oranı %49 idi. Malnütrisyon prevalansı, sarkopenik olmayan katılımcılara kıyasla sarkopenili hastalarda anlamlı derecede yüksekti (*p<0,001*). Sarkopenik hastaların %40,8' i obez veya kiloluydu. Lojistik regresyon analizinde kadın cinsiyet (OR=3.3, CI=1.35-8.04) ve malnütrisyon (OR=9.41, CI=3.06-28.95) sarkopeni gelişimi için önemli risk faktörleriydi.

Sonuç: Hastanede yatan geriatrik hastaların yaklaşık yarısı sarkopenik veya pre-sarkopenikti ve sarkopenisi olan hastaların %88' inde malnütrisyon vardı veya malnütrisyon riski altındaydı. Yatan geriatrik hastalarda sarkopeni ve malnütrisyon birlikte değerlendirilmeli ve sarkopenik obezite göz ardı edilmemelidir.

Anahtar Sözcükler: Biyoelektrik Empedans Analizi, Malnütrisyon, Obezite, Sarkopeni.

Introduction

Sarcopenia is a syndrome of generalized and progressive loss of muscle mass and strength, resulting in reduced physical performance in geriatric patients (1). The increase in physical disability over time leads to a serious decline in patients' quality of life, poor clinical outcomes and increased mortality. Sarcopenia is associated with aging and can also be caused by immobility, malnutrition, and cachexia (2). It was reported that 1%–29% of individuals aged ≥50 years living in the community, 14%–33% under long-term care, and 10% of inpatients from the same age group were sarcopenic based on the sarcopenia definitions of the European Working Group on Sarcopenia in Older People (EWSGOP) and the International Working Group on Sarcopenia (IWGS) (3). Previous studies reported that sarcopenia had higher prevalence in hospitalized geriatric patients and was associated with physical frailty, functional dependence, decreased quality of life, falls, prolonged hospital stay, increased prevalence of readmission, and increased risk of mortality (4-7). Patients with low muscle mass but normal functioning muscles are defined as "pre-sarcopenia," and patients with low muscle function in terms of physical performance or muscle strength or both are defined as "sarcopenia" pursuant to the diagnostic criteria of EWSGOP (1). Malnutrition is defined as a nutritional condition resulting from a deficiency or excess (or imbalance) of energy, protein, and other nutrients, leading to measurable effects on tissue/body form (body shape, size, and composition), function, and clinical status (8). Malnutrition and sarcopenia are distinct conditions in older adults, sharing common underlying causes such as age-related physiological changes, insufficient protein and energy intake, and inflammation associated with acute or chronic diseases (8,9). Malnutrition is recognized as one of the important key pathophysiological causes of sarcopenia (10,11). The Mini Nutritional Assessment (MNA) has been developed to assess the nutritional status of the geriatric patient population and to provide early intervention for potential malnutrition (12,13).

The aim of this study was to investigate the prevalence of sarcopenia and to evaluate the nutritional status of geriatric patients hospitalized in the Internal Medicine Clinic.

Material and Method

This observational clinical study involved patients aged 65 years and older who were admitted to the Internal Medicine Clinic of Istanbul Medeniyet University Göztepe Training and Research Hospital, from November 2015 to January 2016. Local ethics committee approval was obtained before the commencement of the study, and the principles of the World Medical Association (WMA) Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Participants were complied throughout the study. The study exclusion criteria were as follows: patients with anasarca-type edema, diagnosed malignancy, positive inotrope support, impaired cognitive function, or deformities preventing the participants from performing assessment tests.

Study design: Demographic characteristics and anthropometric measurements, including calf circumference, upper arm circumference, waist circumference, weight, height, and body mass index (BMI), were collected from eligible patients who consented to participate in the study. Additionally, the MNA test was conducted for nutritional evaluation. The prevalence of sarcopenia and pre-sarcopenia was assessed. The study examined the prevalence of malnutrition in patients both with and without sarcopenia.

Sarcopenia classification: The classification of sarcopenia was determined according to the diagnostic criteria suggested by EWGSOP: pre-sarcopenia (low muscle mass), sarcopenia (low muscle mass and either low muscle strength or low physical performance) (1).

Measurements: Muscle mass was evaluated using a bioelectrical impedance device, physical performance with walking test, and muscle strength with hand grip test (1).

Muscle mass measurement: Bioelectrical impedance analysis (BIA) was used to assess the body composition of the patients. The measurements were made by placing two electrodes on the proximal and distal

parts of the right hand and foot in the supine position while the patients were fasting, urine-free, and without any metal (necklace, ring, watch, etc.) attached to their bodies. Muscle mass of the patients was evaluated by measuring fat-free mass index (FFMI) with BIA. In the same population, patients below two standard deviations compared to younger adults aged 18–40 years were included in the group with lower muscle mass.

Muscle strength measurement: Hand grip test was performed using a Jamar Hand Dynamometer. Patients were seated in a chair with their elbows resting on the table and their arms bent at 90 degrees parallel to the floor. Three measurements, with 1 minute rest between repetitions, were then taken in both arms. The largest value was captured from three measurements. Accordingly, readings below 15 kg for men and 10 kg for *women were considered to indicate "low muscle strength."*

Physical performance assessment: Patients underwent the 6-minute walk test to assess their physical performance. During the test, the patients were asked to get out of bed and walk 6 meters. While the patients were walking, walking times were measured using a stopwatch and walking speeds were recorded in meters/second. Those walking less than 0.8m/s were considered to have poor physical performance.

Nutritional assessment: Firstly, the MNA test short form (MNA-SF) was administered to patients as a screening test. The long form of MNA was used in patients who scored ≤11 points on the MNA-SF test. Patients having a total MNA score of less than 17, between 17 and 23.5, and more than 23.5 were classified as malnourished, at risk of malnutrition, and normally nourished, respectively.

Statistical analysis

Analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 27.0 (SPSS Inc, Chicago, IL). Variables were given as mean and standard deviation. The conformity of the variables to normal distribution was examined by Shapiro-Wilk *($p<0.05$)*. Student's t-test was used to compare independent groups for variables conforming to normal distribution. Mann-Whitney U test and Kruskal-Wallis test were preferred for variables that did not fit the normal distribution. Chi-square test or Fisher's exact test was preferred for the comparison of categorical variables. Multivariate analysis of the factors associated with sarcopenia was performed with logistic regression analysis. Continuous variables from independent variables are expressed as mean ± standard deviation. *$p<0.05$* was set as the limit of statistical significance. Analysis was performed with G-power application and 102 patients were considered sufficient for the sample size.

Results

A total of 105 participants, 54 women and 51 men, with a mean age of 74 ± 7 years, were included in the study. Demographic, anthropometric and nutritional data are shown in Table I. Muscle mass (6.6 ± 1.3 kg/m^2 vs. 8 ± 1.3 kg/m^2) and hand grip strength (12.6 ± 6 kg vs. 24.4 ± 10.2 kg) were lower in female participants compared to males (*$p<0.01$* for both). The distribution of sarcopenia, pre-sarcopenia and non-sarcopenia groups according to gender and age is given in Table II. In a total of 105 patients, the number of patients diagnosed with sarcopenia and pre-sarcopenia were 49 (46.7%) and 5 (4.8%), respectively. Of the 49 patients with sarcopenia, 33 (67.3%) were female and 16 (32.7%) were male; of the 5 patients with pre-sarcopenia, 2 (40%) were female and 3 (60%) were male. The prevalence of sarcopenia was significantly higher in female patients than in male patients (61.1% vs. 31.4%, *$p=0.006$*). Of the 56 patients under 75 years, 27 (48.2%) were sarcopenic, whereas 22 (44.9%) of the 49 patients aged 75 years and above were also sarcopenic, with no significant difference seen between the groups (*$p=0.87$*).

Demographic, anthropometric and nutritional status of patients according to sarcopenia groups are shown in Table III. Waist circumference, BMI, calf circumference, arm circumference, muscle mass, hand grip strength, MNA-SF and total MNA scores were significantly decreased in the sarcopenia group compared to the non-sarcopenia group (*$p<0.001$* for all). Looking at the total MNA scores

of sarcopenic patients in our study group, 51% had malnutrition and 37% were at risk of malnutrition. In contrast, 10% of patients without sarcopenia were malnourished and 49% were at risk of malnutrition. The prevalence of malnutrition was significantly increased in patients with sarcopenia compared to non-sarcopenic individuals (*p<0.001*).

Table I. Demographic, Anthropometric, and Nutritional Characteristics of the Patients

	All (n = 105)	Female (n = 54)	Male (n = 51)	*p-value*
Age (years)(mean±SD)	74 ± 7	73 ± 7	74 ± 6	*0.66*
Body mass index (kg/m²)	26.5 ± 6.1	25.6 ± 4.5	25.1 ± 7	*0.40*
Waist circumference (cm)	99.1 ± 17.9	98.8 ± 17.7	98.5 ± 18.6	*0.62*
Arm circumference (cm)	28.2 ± 5.0	27.7 ± 3.8	27.6 ± 5.2	*0.71*
Calf circumference (cm)	33.8 ± 5.2	33.8 ± 6.2	35 ± 6.9	*0.36*
Muscle mass (kg/m²)	7.2 ± 1.1	6.6 ± 1.3	8 ± 1.3	***<0.001***
Hand grip strength (kg)	18.3 ± 10.1	12.6 ± 6.0	24.4 ± 10.2	***<0.001***
Walking speed (s)(n)	0.72 ± 0.15 (16)	0.7 ± 0.15(10)	0.75 ± 0.17(6)	*0.42*
MNA-SF	10.0 ± 2.4	10.0 ± 2.6	10.3 ± 2.7	*0.11*
MNA total	19.0 ± 4.1	18.2 ± 3.7	19.0 ± 4.4	*0.12*

MNA: Mini nutritional assessment, SF: Short form, CI: Confidence İnterval

Logistic regression analysis was performed to evaluate the effect of gender, age and malnutrition independent variables on sarcopenia. Gender (OR=3.3, 95% CI [1.35-8.04], p=0.008) and malnutrition (OR=9.41, 95% CI [3.06-28.95], *p=0.001*) had a significant effect on the occurrence of sarcopenia; the age variable was not significant (OR=0.7, 95% CI [0.291-1.72], *p=0.450*). Female patients were 3.3 times more likely to develop sarcopenia than male patients. Patients with malnutrition were 9.41 times more likely to develop sarcopenia than those without malnutrition.

Table II. Distribution of Sarcopenia, Pre-sarcopenia, and Non-sarcopenic Groups by Sex and Age

	Sarcopenia (n=49)	Pre-sarcopenia (n=5)	Non-sarcopenia (n=51)	*p-value*
Female (n = 54)	33 (61.1)	2 (3.7)	19 (35.2)	***0.006***
Male (n = 51)	16 (31.4)	3 (5.9)	32 (62.7)	
>75 age	27 (48.2)	3 (5.4)	26(46.4)	*0.87*
≤75 age	22 (44.9)	2 (4.1)	25(51)	

When the patients were evaluated according to BMI measurements, 49% of sarcopenic patients had a normal BMI (18-25 kg/m²) compared to 25.5% of patients without sarcopenia, a significant difference (*p<0.001*). In addition, 40.8% of sarcopenic patients were overweight or obese.

Table III. Demographic, Anthropometric, and Nutritional Characteristics of Sarcopenia, Pre-Sarcopenia, and Non-Sarcopenic Groups

	Sarcopenia (n = 49)	Non-sarcopenia (n = 51)	*p-value*
Age (years) (Mean ± SD)	74±7	74±7	*0.93*
Waist circumference (cm)	92.18±16.7	106.8±16.6	***<0.001***
Body mass index (kg/m²)	24.9±6.6	28.5±5.1	***<0.001***
Calf circumference (cm)	32±5.3	35.9±4.6	***<0.001***
Arm circumference (cm)	26,16±5	30,4±4,2	***<0.001***
Muscle mass (kg/m²)	6.4±0.7	8.3±1.1	***<0.001***
Hand grip strength (kg)	11±4.9	24.7±9.28	***<0.001***
Walking speed (s)(n)	0.67±0.14 (11)	0.77±0.18 (3)	***0.456***
MNA-SF	8,14±2,46	10,44±1,94	***<0.001***
MNA total	17,46± 4,4	21,6±3.97	***<0.001***
Prevalence of malnutrition (n, %)	25 (51)	5 (10)	***0.001***
Prevalence of malnutrition risk (n, %)	18 (37)	25 (49)	
Prevalence of normal nutrition (n, %)	6 (12)	21 (41)	
BMI: <18 kg/m² (n,%)	5 (10.2)	-	***<0.001***
18≤ BMI <25 kg/m² (n,%)	24 (49)	13 (25.5)	
25≤ BMI <30 kg/m² (n,%)	10 (20.4)	10 (20.4)	
BMI: ≥30 kg/m² (n,%)	10 (20.4)	20 (39.2)	

MNA: Mini nutritional assessment, SF: Short form, BMI: Body mass index

Discussion

The present study found that almost half of the hospitalized geriatric patients were sarcopenic and 51% of them were malnourished. A total of 88% of patients with sarcopenia or pre-sarcopenia had malnutrition or were at risk of malnutrition. Furthermore, 40.8% of patients with sarcopenia were classified as overweight or obese based on BMI values.

Sarcopenia is a syndrome characterized by generalized and progressive loss of muscle mass, which can lead to adverse health outcomes, including physical disability, poor quality of life, and mortality (1). It has been suggested that the multifactorial causes of sarcopenia may include neurological disorders, hormonal changes, inflammatory pathway activation, activity limitations, chronic diseases, fatty infiltration, and malnutrition (14). Malnutrition,

among the foregoing factors, is considered one of the most important pathophysiologic factors both as a cause of sarcopenia and as a manifestation of comorbid sarcopenia (malnutrition–sarcopenia syndrome), particularly in the geriatric population (15). The results of the present study demonstrated that the rate of patients with sarcopenia constituted approximately half of the geriatric patients included in the study, with half of them having malnutrition, which was consistent with previous reports. On the other hand, the logistic regression analysis revealed that malnutrition increases the risk of developing sarcopenia by 9.4 times. This finding highlights the importance of nutritional assessment in individuals with sarcopenia.

Advanced age is considered an independent risk factor for both sarcopenia and malnutrition. Research investigating the connection between sarcopenia and age revealed that its prevalence in men was 14% for those younger than 70 years, 20% for those aged 70–74, 27% for individuals aged 75–80, and 53% for men older than 80 years. For women in the corresponding age groups, the rates were found to be 23%, 33%, 36%, and 43%, respectively. The findings demonstrated that sarcopenia was more common among women in all age groups except those above 80 years. Additionally, the prevalence of sarcopenia showed an upward trend with increasing age in both men and women (16). A multicenter research examined the risk of sarcopenia and its related variables in inpatients aged ≥65 years, revealing that 48.8% of patients were at risk of sarcopenia, with a greater incidence seen in female participants and older age groups. Furthermore, the duration of hospital stay, prevalence of malnutrition, and incidence of dysphagia were elevated in participants at risk of sarcopenia compared to those without sarcopenia; multivariate analysis indicated that age, female gender, and bedridden condition were independently correlated with the risk of sarcopenia (17). In our study, the logistic regression analysis showed that being female increased the risk of developing sarcopenia by 3.3 times, which appears to be consistent with the literature. The lack of association between the age variable and the risk of sarcopenia may be due to the high average age of the patients and the heterogeneity of the age distribution.

Earlier research has shown varying results concerning the prevalence of sarcopenia, likely due to differences in study methodologies, populations studied, and the diagnostic criteria employed. The imaging methods typically used to measure muscle mass are based on the muscle mass measurements of a younger healthy population. In studies with BIA and bone density scan (DEXA) measurements, participants with -2 standard deviation (SD) muscle mass compared to the younger population were considered sarcopenic. Nevertheless, certain studies classified participants with -1-2 SD muscle mass as sarcopenic. According to the Third National Health and Nutrition Examination Survey (NHANES III) data (1988–1994), in a comprehensive survey in a field on 4504 patients aged >60 years, participants with -1-2 SD were designated as Class 1 sarcopenia and patients with -2 SD as Class 2 sarcopenia upon BIA measurements. Using this classification, the prevalence of Class 1 sarcopenia was observed to be 59% among women and 45% among men. Meanwhile, Class 2 sarcopenia was present in 10% of female participants and 7% of male participants (18). A Japanese study by Tanimoto et al. on 1110 elderly people aged >65 years, who were reached through social assistance centers and local newspaper advertisements, the prevalence of sarcopenia was 14.9% in female and 13.3% in male participants, via BIA measurements (19). Similarly, in this study, it was observed that the prevalence of sarcopenia was high among geriatric patients, also the prevalence of malnutrition was higher in sarcopenic patients and most of these patients were female.

Although sarcopenia occurs in patients with both low and normal BMI, there is increasing evidence that sarcopenia also occurs in overweight and even obese individuals, and this condition has been termed as sarcopenic obesity in the literature. Sarcopenic obesity is a condition marked by the simultaneous presence of diminished skeletal muscle mass and function alongside an increase in body fat (20). With the global aging population and the growing obesity epidemic, the incidence of sarcopenic obesity is rising at a rapid pace. The accompaniment of obesity to the poor clinical outcomes of sarcopenia has led to an increase in various clinical complications such as prolonged hospitalization and increased mortality

in the geriatric population (21). Based on NHANES III survey, the prevalence of sarcopenic obesity in people aged ≥60 years was reported as 18.1% in female and 42.9% in male participants (22). In the present study, 60% sarcopenic participants had low or normal BMI values, and the prevalence of sarcopenia was statistically higher in participants with a BMI between 18 and 25 kg/m^2 compared to non-sarcopenic participants. Nevertheless, the fact that 40.8% of the patients were in the overweight or obesity category based on BMI values is supportive of the fact that sarcopenic obesity should not be ignored in sarcopenic patients.

It has been reported that non-pharmacological treatments, including exercise and nutritional supplements, are safer compared to pharmacological treatments in elderly sarcopenic individuals. Systematic reviews and meta-analyses have shown that both exercises alone and the combination of exercise and nutrition have beneficial effects on muscle strength and physical performance, with resistance exercises in particular improving muscle strength and muscle quality in sarcopenic elderly individuals (23,24).

Limitations of the study

The present study has certain limitations, including the relatively small number of patients and the short follow-up period. The walking test, a sarcopenia screening test based on the EWGSOP diagnostic criteria, could not be performed in many patients in the acute stage of the disease, and only the hand grip test was used to evaluate sarcopenia. And finally, there was no muscle mass cut-off value determined for the Turkish population for the purposes of defining sarcopenia; therefore, the BIA values from foreign studies were used. Since there were no patients with a BMI <18 kg/m^2, logistic regression analysis could not be performed regarding the relationship between BMI and the risk of developing sarcopenia. This can also be considered as a limitation of the study. The study has an observational and cross-sectional design, which limits causality. The lack of analysis of confounding variables such as comorbidities, medications, and inflammation markers also constitutes a limitation in the interpretation of the results. Studies evaluating sociodemographic factors (such as age, marital status, disability for activities of daily living, and underweight), behavioral factors (such as smoking, physical inactivity, malnutrition/malnutrition risk, long and short sleep duration, living alone), and disease-related factors (such as diabetes, cognitive impairment, heart diseases, respiratory diseases, osteopenia/osteoporosis, osteoarthritis, depression, falls, anorexia, and anemia) that may be associated with sarcopenia in the future will shed light on this topic.

Conclusion

In the present study, approximately half of the hospitalized geriatric patients were sarcopenic and approximately half of them were malnourished. These results supported that malnutrition was one of the most important risk factors for sarcopenia and that sarcopenia and malnutrition are two conditions that should be simultaneously evaluated in geriatric patients. The association between sarcopenia and malnutrition, as well as the risk of malnutrition, is substantial, indicating that most hospitalized older adults struggle with both of these debilitating conditions during their hospital stay. This highlights the necessity of including screening tools to assess nutritional status and sarcopenia during comprehensive geriatric assessment before or at the time of hospital admission. All older hospitalized individuals should be followed and treated with an appropriate combination of nutritional support and exercise programs as a priority approach for sarcopenia and malnutrition. Furthermore, 40.8% of patients with sarcopenia were overweight or obese based on BMI values, suggesting that sarcopenic obesity should not be ignored in these patients.

References

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;39:412-423.

2. Meng S, He X, Fu X, et al. The prevalence of sarcopenia and risk factors in the older adult in China: a systematic review and meta-analysis. Front Public Health 2024;12:1415398.

3. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing 2014;43:748-759.

4. Gariballa S, Alessa A. Sarcopenia: prevalence and prognostic significance in hospitalized patients. Clin Nutr 2013;32:772-776.
5. Sousa AS, Guerra RS, Fonseca I, Pichel F, Amaral TF. Sarcopenia among hospitalized patients - A cross-sectional study. Clin Nutr 2015;34:1239-1244.
6. Martone AM, Bianchi L, Abete P, et al. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. J Cachexia Sarcopenia Muscle 2017;8:907-914.
7. Beaudart C, McCloskey E, Bruyère O, et al. Sarcopenia in daily practice: assessment and management. BMC Geriatr. 2016;16:170.
8. Lochs H, Allison SP, Meier R, et al. Introductory to the ESPEN Guidelines on Enteral Nutrition: Terminology, definitions and general topics. Clin Nutr. 2006;25(2):180-186.
9. Ligthart-Melis GC, Luiking YC, Kakourou A, Cederholm T, Maier AB, De van der Schueren MAE. Frailty, Sarcopenia, and Malnutrition Frequently (Co-)occur in Hospitalized Older Adults: A Systematic Review and Meta-analysis. J Am Med Dir Assoc 2020;21:1216-1228.
10. Sieber CC. Malnutrition and sarcopenia. Aging Clin Exp Res 2019;31:793-798.
11. Cruz-Jentoft AJ, Kiesswetter E, Drey M, Sieber CC. Nutrition, frailty, and sarcopenia. Aging Clin Exp Res 2017;29:43-48.
12. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition 1999;15:116-122.
13. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56:366–372.
14. Walston JD. Sarcopenia in older adults. Curr Opin Rheumatol 2012;24:623-627.
15. Hu X, Zhang L, Wang H, Hao Q, Dong B, Yang M. Malnutrition-sarcopenia syndrome predicts mortality in hospitalized older patients. Sci Rep 2017;7:3171.
16. Thomas DR. Sarcopenia. Clin Geriatr Med 2010;26:331-346
17. Ozer FF, Akin S, Tasci İ, et al. Risk of sarcopenia in hospitalized patients and related clinical factors: a multicenter study from Turkey. Eur Geriatr Med 2021;12:863-870.
18. Janssen I, Steven B, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002;50:889-896.
19. Tanimoto Y, Watanabe M, Sun W, et al. Sarcopenia and falls in community-dwelling elderly subjects in Japan: Defining sarcopenia according to criteria of the European Working Group on Sarcopenia in Older People. Arch Gerontol Geriatr 2014;59:295-299.
20. Wei S, Nguyen TT, Zhang Y, Ryu D, Gariani K. Sarcopenic obesity: epidemiology, pathophysiology, cardiovascular disease, mortality, and management. Front Endocrinol (Lausanne) 2023;14:1185221.
21. Prado CM, Batsis JA, Donini LM, Gonzalez MC, Siervo M. Sarcopenic obesity in older adults: a clinical overview. Nat Rev Endocrinol 2024;20:261-277.
22. Batsis JA, Mackenzie TA, Barre LK, Lopez-Jimenez F, Bartels SJ. Sarcopenia, sarcopenic obesity and mortality in older adults: results from the National Health and Nutrition Examination Survey III. Eur J Clin Nutr 2014;68:1001-1007.
23. Wu PY, Huang KS, Chen KM, Chou CP, Tu YK. Exercise, Nutrition, and Combined Exercise and Nutrition in Older Adults with Sarcopenia: A Systematic Review and Network Meta-analysis. Maturitas 2021;145:38-48.
24. Zhao H, Cheng R, Song G, et al. The Effect of Resistance Training on the Rehabilitation of Elderly Patients with Sarcopenia: A Meta-Analysis. Int J Environ Res Public Health 2022;19(23):15491.

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Evaluation of Clinical Findings and NF1 Genetic Variants in Patients Diagnosed with Neurofibromatosis Type 1: a Single-center Experience

Nörofibromatozis Tip 1 Tanılı Hastalarda Klinik Bulgular ve NF1 Genetik Varyantlarının Değerlendirilmesi: Tek Merkez Deneyim

Ünal Akça[1] | Aslıhan Sanrı[2] | Emre Sanrı[3] | Elif Pekmezci Yazgı[4] | Gülfer Akça[3]

[1]Samsun University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Neurology, Samsun, Türkiye
[2]Samsun University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Genetics, Samsun, Türkiye
[3]Samsun University Faculty of Medicine, Department of Pediatrics, Samsun, Türkiye
[4]Samsun University Faculty of Medicine, Department of Child and Adolescent Psychiatry, Samsun, Türkiye

Sorumlu Yazar | Correspondence Author
Ünal Akça
drunalakca@gmail.com
Address for Correspondence: Division of Pediatric Neurology, Department of Pediatrics, Faculty of Medicine, Samsun University, Samsun, Türkiye.

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Evaluation of Clinical Findings and NF1 Genetic Variants in Patients Diagnosed with Neurofibromatosis Type 1: a Single-center Experience

ABSTRACT

Objective: Neurofibromatosis type 1 is a common neurocutaneous syndrome with multisystemic involvement that facilitates tumor formation. The aim of this study was to evaluate the demographic and clinical characteristics as well as genetic results of pediatric patients diagnosed with neurofibromatosis type 1.

Material and Method: This retrospective, cross-sectional descriptive study included 23 patients. Main disease criteria, clinical features, and genetic results obtained using next-generation sequencing and multiple-ligation probe amplification techniques were recorded. Information on zygosity, mutation types, variant positions, American College of Medical Genetics classification, and inheritance models were analyzed.

Results: Café-au-lait spots were present in all patients. Inguinal/axillary freckling was the second most common finding seen in 60.9% of patients. Lisch nodules were observed in patients older than six years, whereas choroidal abnormalities were common in younger patients. Optic glioma was found in 13% of patients and cutaneous neurofibromas in 21.7% of patients, which is lower than that observed in adult patients. Focal signal intensity image was more common in patients with cognitive impairment (Odds Ratio: 4.50, Confidence Interval 95% 0.659-30.715, *p=0.02*). Epilepsy was diagnosed in two patients and treated with a single drug. Macrocephaly (30.4%) was the most common cranial deformity. Missense mutations (43.5%) were the most common, while one frameshift novel mutation (c.6771del. K2257Nfs*8) was identified.

Conclusion: The emergence of new genetic technologies and advances in health care may facilitate earlier diagnosis of neurofibromatosis and the prediction and treatment of complications that may develop.

Keywords: FASI, Neurofibromatosis, Rasopathy, Variant.

ÖZET

Amaç: Nörofibromatozis tip 1, tümör oluşumunu kolaylaştıran multisistemik tutulumu olan yaygın bir nörokutanöz sendromdur. Bu çalışmanın amacı, nörofibromatozis tip 1 tanısı alan çocuk hastaların demografik ve klinik özelliklerinin yanı sıra genetik sonuçlarını da değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif, kesitsel tanımlayıcı çalışmaya 23 hasta dahil edildi. Hastalık ana kriterleri, klinik özellikleri, yeni nesil dizileme ve çoklu ligasyona bağlı prob amplifikasyon teknikleri kullanılarak elde edilen genetik sonuçları kaydedildi. Zigosite, mutasyon tipleri, varyant pozisyonları, Amerikan Tıbbi Genetik Kurulu sınıflandırması ve kalıtım modellerine ilişkin bilgiler analiz edildi.

Bulgular: Café-au-lait lekeleri tüm hastalarda mevcuttu. Kasık/aksiller çillenme, hastaların %60,9'unda görülen ikinci en yaygın bulguydu. Lisch nodülleri altı yaşından büyük hastalarda gözlenirken, koroidal anormallikler daha küçük hastalarda yaygındı. Optik gliom hastaların %13'ünde, kutanöz nörofibromlar ise hastaların %21,7'sinde tespit edilmiş olup bu oran yetişkin hastalarda gözlenenden daha düşüktür. Bilişsel bozukluğu olan hastalarda fokal sinyal yoğunluğu görüntüsü daha yaygındı (Odds Ratio: 4.50, %95 Güven Aralığı 0.659-30.715, *p=0.02*). İki hastada epilepsi tanısı konmuş ve tek bir ilaçla tedavi edilmiştir. Makrosefali (%30,4) en sık görülen kraniyal deformite idi. Missense mutasyonlar (%43,5) en sık görülürken, bir çerçeve kayması yeni mutasyon (c.6771del. K2257Nfs*8) tanımlanmıştır.

Sonuç: Yeni genetik teknolojilerin ortaya çıkması ve sağlık hizmetlerindeki ilerlemeler nörofibromatozisin daha erken tanı almasını ve gelişebilecek komplikasyonların öngörülmesini ve tedavisini kolaylaştırabilir.

Anahtar Sözcükler: FASI, Nörofibromatozis, Rasopati, Varyant.

Introduction

Neurofibromatosis type 1 (NF1) is a common autosomal dominant neurocutaneous disorder with variable expression and complete penetrance. The prevalence is approximately 1 in 3,000 (1). In 95% of cases, at least two of the diagnostic criteria described by the National Institute of Health (NIH) in 1988 must be met (2). The diagnostic criteria include the presence of six or more café-au-lait spots (CALM) larger than 5 mm before puberty and larger than 15 mm after puberty, axillary or inguinal freckling, and the presence of two or more neurofibromas. Additionally, the presence of plexiform neurofibromas, optic gliomas, two or more lisch nodules, and bone findings such as sphenoid dysplasia, thinning of the long bone cortex, and the presence of NF1 in first-degree relatives are indicative of the condition (3). In 2021, Legius et al. revised diagnostic criteria due to its similarity with neurocutaneous disorders such as Legius syndrome, constitutional mismatch repair deficiency (CMMRD) syndrome. They highlighted the importance of clinical and heterozygous pathogenic variants, such as dystrophic scoliosis, choroidal anomalies, and focal signal intensity image (FASI), in the context of these disorders (4).

In some cases, learning disabilities, various skeletal anomalies, attention deficit and hyperactivity disorders, congenital heart diseases, malignant peripheral nerve sheath tumors, and hematologic malignancies have been identified as potential contributing factors (5). By the age of eight years, the major criteria of the disease are clear in patients (6). Although NF1 is a classic monogenic disorder in adulthood, clinical symptoms may vary within families (7,8). The etiology of this phenotypic variability remains poorly understood. Modifier genes, epigenetic variation, and environmental factors are believed to be involved (4,6).

Neurofibromatosis type 1 is the result of a defect in the functioning of the neurofibromin gene, which is located on the long arm of chromosome 17 (17q11.2) (9). The gene in fact functions as a GTPase catalyst and a negative regulator of the RAS/MAPK signaling pathway. A consequence of the loss of function in the neurofibromin gene is the hyperactivation of cell growth, proliferation, and differentiation, which in turn gives rise to the formation of abnormal structures (10). To date, the Human Gene Mismatch Database (HGMD) has cataloged over 3,000 pathogenic variants associated with NF1. Half of the identified genetic variants are familial, while the remaining half are de novo (11,12). Most reported mutations (93%) are small mutations, including missense, nonsense, insertion, deletion, and splicing mutations. The remaining 2% were intragenic, and 5% were large deletions involving NF1 and neighboring genes. These mutations can be identified by multiple ligation-dependent probe amplification (MLPA) (7). Patients with microdeletions are more likely to present with somatic overgrowth, malignant tumors, and dysmorphic features (13). This study aims to describe the clinical symptoms observed in patients with a NF1 genetic diagnosis and to analyze the genetic results.

Material and Method

This study evaluated 23 patients who were admitted to the pediatric neurology outpatient clinic of the Samsun University Pediatrics Department between June 2022 and June 2024 with NF1 clinical findings and whose NF1 gene pathological variants were detected by the pediatric genetic department. Initially, sequence analysis of the NF1 gene was performed for all patients. Genomic DNA was extracted from peripheral blood samples, and all exons of the NF1 gene, including exon-intron boundaries, were analyzed using next-generation sequencing (NGS). The obtained sequences were aligned to the reference genome (GRCh37/hg19), and variants were interpreted in accordance with the American College of Medical Genetics and Genomics (ACMG) guidelines.

For patients in whom no clinically significant variant was identified through sequencing, multiplex ligation-dependent probe amplification (MLPA) was conducted to detect potential deletions or duplications in the NF1 gene. MLPA was performed according to the manufacturer's protocol and results were compared to normal controls for interpretation. The inclusion criteria were as follows: the patients were required to be between the ages of 0 and 18 years and to be a patient whose NF1 diagnosis was confirmed by MLPA and NGS genetic tests. Patients with a clinical diagnosis of NF1 according to NIH (4) diagnostic criteria but without genetic testing were excluded from the study.

Patients were monitored on a regular basis by pediatricians, pediatric neurologists, and child psychiatrists. The patients were examined for any concomitant endocrinological, orthopedic, cardiological, cognitive, and neurological complications. The demographic findings, including age, gender, consanguineous marriage, the presence of NF1 in the family, physical examination findings, abdominal ultrasonography, brain magnetic resonance imaging, echocardiography results, cognitive and psychiatric tests, and treatments received, were analyzed in the patient file records. Genetic results were classified according to zygosity, mutation types, variant positions, ACMG classification, and inheritance types. All data were analyzed retrospectively.

The study was conducted in accordance with the ethical standards of the Samsun University Faculty of Medicine Ethics Committee, which approved the study on 26/06/2024 (decision number 2024/12/6). Prior to participation, informed consent was obtained from the legal guardians of all patients.

Statistical Analysis

The analyses were conducted using IBM SPSS Statistics 25.0. Numerical variables were expressed as mean ± standard deviation, while categorical variables were expressed as number and percentage. Tests were used to ascertain whether a relationship existed between the categorical variables and whether there were any significant differences between the demographic and clinical findings of the patients. The significance level was set at $p<0.05$.

Results

Demographic Characteristics

A total of 23 patients participated in the study, with 13 males (56.5%) and 10 females (43.5%). The mean age of the patients at the time of enrollment was 6.4 years (ranging from 1 to 14 years). 47.8% of the patients were less than six years old. 10 patients (43.5%) had no first-degree relatives with neurofibromatosis type 1.

Clinical Findings

All patients exhibited a minimum of six CALMs spots. Axillary or inguinal freckling was identified in 60.9% of patients. Upon examination of ocular involvement, 30.4% of patients exhibited Lisch nodules, while 13% demonstrated choroidal abnormalities. The mean age of patients with Lisch nodules was 11.5 years (range: 10-14 years), and the mean age of patients with choroidal abnormalities on optical coherence tomography was 3.6 years (range: 3-5 years). None of the patients exhibited severe visual loss or blindness. The frequency of NF1 findings is presented in Table I.

Table I. Neurofibromatosis type 1 Clinical Characteristics of Participants and Mean Age at Diagnosis.

	n	%	Mean age (years)
Female/Male	10/13		
6 CALMs	23/23	100	6.4
Freckling	14/23	60.9	7.9
Lisch nodule	7/23	30.4	11.6
Choroidal abnormalities	4/23	17.4	3.7
Cutaneous neurofibromas	5/23	21.7	8.8
Optic glioma	3/23	13.0	9.7
Sphenoid wing dysplasia	3/23	13.0	5.7
Long bone dysplasia	1/23	4.3	14.0
Epilepsy	2/23	8.7	8.6
Short stature	11/23	47.8	7.5
Macrocephaly	7/23	30.4	5.3
Scoliosis	6/23	26.0	8.2
Focal areas of high signal intensity	8/23	34.8	7.9
Attention deficit hyperactivity disorder	6/23	26.1	7.2
Pulmonary artery stenosis	2/23	8.7	12.5

Three patients presented with optic gliomas. All had pre-chiasmatic localization and did not receive chemotherapy due to the absence of visual acuity impairment. None exhibited proptosis, pupillary dysfunction, or optic atrophy. Two patients with optic gliomas had precocious puberty. The prevalence of cutaneous neurofibroma was 21.7%. The majority were located on the back and trunk. None had peripheral nerve sheath tumors, glomus tumors, or stromal tumors.

Scoliosis was observed in 26.1% of cases. Sphenoid wing dysplasia was observed in 13% of cases, with two patients exhibiting grade 1 and one patient exhibiting grade 2 dysplasia. Additionally, anterolateral curvature of the tibia was identified in a 14-year-old male patient.

The analysis of neurological anomalies revealed that learning retardation was present in 60.9% of

Table II. Comprehensive Clinical Characteristics of Patients

Patient	CALMs	Freckling	Ocular features	Tumors	Bone abnormalities	Short stature	Neurological abnormalities	Family history of NF1	FASI	Other lesions
1	+					+		+		Growth retardation
2	+	+	LN	CN	S		LD	+	+	ADHD
3	+		CA					+		Frontal bossing, hemangioma
4	+		CA		SWD			+		Dysmorphic face
5	+	+	LN	OG	SWD		LD	+	+	Dysmorphic face, premature puberty
6	+	+	LN			+	LD			
7	+	+	LN			+		+		Growth retardation
8	+			OG	S	+	LD		+	Macrocephaly, downward and slanting eyes, ADHD
9	+							+		
10	+	+		CN			LD			Macrocephaly
11	+	+					LD	+		Macrocephaly
12	+					+	LD		+	Macrocephaly, ADHD
13	+	+				+	LD, E		+	Brachycephaly, epilepsy, downward and slanting eyes, ADHD
14	+	+	CA							
15	+			CN			LD	+		Speech delay, ADHD
16	+	+				+	LD			Short stature, pectus excavatum, speech impairment, delayed walking.
17	+	+	LN	OG	S	+	LD		+	Pectus excavatum, scoliosis, hypertelorism, strabismus, premature puberty
18	+	+	CA		S	+	LD			Speech retardation, scoliosis, pectus excavatum, pes planus, ADHD
19	+	+			S, SWD	+		+	+	Polydactyly, dysmorphic face, epicanthus, tele canthus, depressed nasal root
20	+	+	LN				LD	+		Depressed nasal root, pulmonary artery stenosis, hypertelorism
21	+									Macrocephaly,
22	+			CN				+		Macrocephaly, speech retardation,
23	+	+	LN	CN	LBD, S	+	LD, E	+	+	Macrocephaly, pulmonary artery stenosis

LN: lisch Nodule, CA: Choroidal abnormalities, CN: Cutaneous neurofibromas, OG: Optic glioma, LBD: Long bone dysplasia's: sphenoid wing dysplasia, S: scoliosis, LD: learning disabilities, E: epilepsy, ADHD: Attention deficit hyperactivity disorder, FASI: Focal areas of high signal intensity

the participants, while no patient exhibited severe intellectual disability. Four patients were undergoing language therapy for speech retardation. Epilepsy was diagnosed in two patients. Both patients were monitored for seizures and remained seizure-free following single valproate treatment. FASI imaging was identified in 34.8% of patients undergoing neuroimaging. Six patients were followed up in the pediatric psychiatry clinic with a diagnosis of ADHD. Two patients were receiving risperidone, and two patients were receiving stimulant support.

The frequency of learning disabilities was found to be statistically significantly higher in patients with FASI images (odds ratio: 4.50, CI 95 %0.659-30.715, *p=0.02*). Macrocephaly was observed in 30.4% of the patients. One patient exhibited brachycephaly,

Table III. Evaluation of the Neurofibromatosis Type 1 Variant Mutations of the Participants

Patient	Age	Gender	Zygosity	Mutation	Protein	Mutation Type	Variant Position	ACMG Classification	References	Inheritance
1*	8	M	Heterozygous	c.7415del	p. P2472Lfs*17	Frameshift	Exon 50	Pathogenic	Reported	Paternal
2*	12	M	Heterozygous	c.2530C>T	p. L844F	Missense	Exon 21	Pathogenic	Reported	Maternal
3*	3	M	Heterozygous	c.4247C>T	p. P1416L	Missense	Exon 32	Likely Pathogenic	Reported	Maternal
4*	3	F	Heterozygous	c.1A>G	p. M1V	Missense	Exon 1	Pathogenic	Reported	Paternal
5**	12	M	Heterozygous			Deletion	Exon 24	Pathogenic	Reported	Maternal
6*	10	M	Heterozygous	c.1466A>G	p. Y489C	Missense	Exon 13	Pathogenic	Reported	De novo
7*	12	F	Heterozygous	c.2T>G	p.M1R	Missense	Exon 1	Pathogenic	Reported	Maternal
8*	7	F	Heterozygous	c.6771delA	p. K2257Nfs*8	Frameshift	Exon 45	Likely Pathogenic	Novel	De novo
9*	1	M	Heterozygous	c.2511G>A	p.W837*	Nonsense	Exon 21	Pathogenic	Reported	Maternal
10*	7	M	Heterozygous	c.5305C>T	p.R1769*	Nonsense	Exon 38	Pathogenic	Reported	De novo
11*	1	M	Heterozygous	c.62T>C	p. L21P	Missense	Exon2	VUS	Reported	Maternal
12*	4	F	Heterozygous	c.1466A>G	p. Y489C	Missense	Exon 13	Pathogenic	Reported	De novo
13**	3	M	Heterozygous	c.3709-2A>G		Splice Acceptor		Pathogenic	Reported	De novo
14**	5	M	Heterozygous	c.7458-1G>C		Splice Acceptor		Pathogenic	Reported	De novo
15*	8	M	Heterozygous	c.1882dup	p. Y628Lfs*6	Frameshift	Exon 17	Pathogenic	Reported	Maternal
16*	8	F	Heterozygous	c.3461A>T	p. N1154I	Missense	Exon 26	Likely Pathogenic	Reported	De novo
17*	10	F	Heterozygous	c.3834C>G	p. N1278K	Missense	Exon 28	Pathogenic	Reported	De novo
18**	4	M	Heterozygous			Deletion	Whole gene	Pathogenic	Reported	De novo
19**	2	M	Heterozygous			Deletion	Whole gene	Pathogenic	Reported	Maternal
20*	11	F	Heterozygous	c.7415del	p. P2472Lfs*17	Frameshift	Exon 50	Pathogenic	Reported	Paternal
21*	1	F	Heterozygous	c.4243A>T	p. N1415Y	Missense	Exon 32	Pathogenic	Reported	De novo
22*	3	F	Heterozygous	c.186del	p.L62*6	Frameshift	Exon 29	Pathogenic	Reported	Maternal
23*	14	M	Heterozygous	c.501del	p.C167Qfs*10	Frameshift	Exon 31	Pathogenic	Reported	Maternal

*Next-generation sequencing (NGS), ** Multiple ligation dependent probe amplification (MLPA)
ACMG: The American College of Medical Genetics and Genomics, F: female, M: male; VUS: Variant of Uncertain Significance

and one patient demonstrated frontal bossing. Pulmonary artery stenosis was identified in two patients. The comprehensive clinical findings of the patients are presented in Table II.

Genetic testing revealed that all patients exhibited heterozygous inheritance. A novel frameshift mutation was identified in one patient, who was subsequently classified as likely pathogenic according to ACMG. The remaining mutations were distributed as follows: 43.5% were missense, 26.1% were frameshift, 13% were deletions, 8.7% were nonsense, and 8.7% were splice acceptors. The mutations identified in this study are presented in Table III.

Discussion

Neurofibromatosis type 1 (NF1) is a multisystemic neurocutaneous disorder characterized by pigmentary changes, benign peripheral nervous system gliomas (also known as neurofibromas) and an increased risk of malignant tumors, as well as learning difficulties. The most prominent features are multiple café-au-lait spots and associated cutaneous neurofibromas. Neurofibromatosis type 1 is an autosomal dominant disease caused by pathogenic variants in the NF1 gene. The diagnostic criteria are met in the first year of life, with almost all patients fulfilling the criteria by the age of eight years (1,2).

CALMs are uniform hyperpigmented macules that typically manifest in the first year after birth and increase in size and number during early childhood. It has been reported that the probability of a CALM not reaching six in the first five years is low in individuals who are subsequently diagnosed with NF (14). In the present case series, more than six café-au-lait macules were observed in all patients, including those aged one year.

Inguinal and axillary freckles are defined as hyperpigmented macules in the form of clusters, which are typically smaller in size compared to CALMs, particularly in the fold areas. They are less

frequently observed in individuals younger than three years of age (15). In our study, the presence of freckles was observed in 60% of patients, with a mean age of 7.9 years. The mean age of patients without freckles was 3.7 years, which is consistent with the findings in the literature.

Ocular involvement represents the most significant finding associated with NF1, following the identification of cutaneous manifestations. Lisch nodules and choroidal anomalies, discernible through optical coherence tomography (OCT), are incorporated into the diagnostic criteria for NF1. The incidence of these anomalies is less than 10% in children under the age of six and 90% in adults (16). In our study, the incidence was 34.8%, with the youngest age of detection being eight years.

Choroidal anomalies are defined as clusters of melanocytes, which can be identified using OCT. In comparison to Lisch nodules, these anomalies are more prevalent in younger age groups and in pediatric cases (17). The mean age of the patients included in our study was 3.6 years, and it is postulated that this conclusion was reached due to the inability to perform the examination in younger patients. It is hypothesized that this will prove to be a more sensitive indicator of NF1 in younger patients with CALMs.

Individuals with NF1 are at an increased risk of developing both benign and malignant tumors over the course of their lifetime. The incidence of cancer is higher in those with NF1 than in the general population (18). Cutaneous neurofibromas are the most common intradermal benign tumors. They tend to occur just before puberty (19). They were observed in 21.7% of our patients, with a mean age at presentation of 9 years. Malignant transformation is not expected. Optic gliomas are low-grade pilocytic astrocytoma and occur in all visual pathways. In a study comprising 562 NF1 patients, the overall prevalence was determined to be 9.3%. Most localizations were prechiasmatic, with optic tract involvement representing the most common visual impairment (20). In our study, the prevalence of optic glioma was found to be 13%, with all cases exhibiting prechiasmatic involvement.

MPNSTs are characterized by severe pain, progressive hardening and rapid growth, arising from pre-existing plexiform or atypical neurofibromas. Differential diagnosis from benign cutaneous neurofibromas can be made by positron emission tomography. It typically develops in young adults (21). Our cohort did not include any individuals with MPNSTs, as the oldest participant was only 14 years old.

Bone abnormalities and short stature are also common findings associated with NF1. There is a high degree of clinical overlap between NF1 and other conditions, such as Legius syndrome, McCune Albright syndrome, Noonan syndrome, and CMMRD, which are associated with CALMs (22). Genetic investigations are becoming increasingly important in this context. The prevalence of scoliosis in individuals with NF1 has been reported to range from 10 to 25% (23). A reduction in birth weight and an increase in head circumference have been observed in infants born to mothers with NF1 (24). In our study, the prevalence of macrocephaly was found to be 30.1%, which is considerably higher than that observed in the general population.

Long bone dysplasia encompasses a range of conditions, including antero-tibial curvature, which may progress to medullary canal narrowing, cortical thickening and fractures (25). One of our patients exhibited this finding. Sphenoid wing dysplasia, which can lead to facial asymmetry, is another significant condition (26). It was identified in 13% of our patients. Short stature is a characteristic observed in patients with NF1. The underlying cause of this phenomenon is believed to be a significant reduction in the growth rate during puberty, particularly in males. It has been demonstrated that the impact of short stature is more pronounced, particularly in males with pronounced macrocephaly (27). In our patient cohort, no gender-based differences in short stature were identified.

Neurological abnormalities may manifest as cognitive impairments, learning difficulties and seizures. Although the risk of intellectual disability is slightly higher than the population average, a lower IQ level is a more realistic observation. Learning difficulties, attention deficits, speech disorders and impaired social skills are more prevalent (28). The series revealed a prevalence of learning disabilities in 65% of cases, with ADHD occurring in 30-40% of instances (29). The prevalence of these conditions

was found to be almost identical in our patient cohort. The incidence of seizures is twofold that observed in the general population. The number of cases exhibiting treatment resistance is low, and new-onset seizures may necessitate neuroimaging (30).

Pulmonary stenosis has the highest association with NF1 when congenital heart diseases are analyzed. A study of 493 patients revealed that 21 (4.2%) of them had both congenital heart disease and pulmonary stenosis (31). In the present study, pulmonary stenosis was identified in two patients. The patients in question were demonstrated to be more prone to exhibiting phenotypic characteristics associated with Noonan syndrome.

Neuroimaging features are summarized as increased brain volume and the presence of bright spots, which are associated with NF1. FASI is most frequently observed in the basal ganglia, cerebellum, and subcortical white matter in 40–95% of patients (32). It is hypothesized that this is associated with dysplastic glial proliferation and fluid increase, which are linked to vacuolar myelopathy. One of the most significant findings of our investigation is that learning disabilities and neurological complications are more prevalent in individuals with FASI. Similarly, two studies have demonstrated that patients with FASI exhibit lower IQ values and a higher prevalence of mental retardation (33,34).

In cases where a diagnosis is suspected, it has been deemed appropriate to either confirm the diagnosis or to perform targeted testing on the proband, rather than undertaking a comprehensive mutation range of the entire gene. It should be noted that a positive NF1 mutation test does not necessarily indicate the severity of the disorder or the potential for complications, with a few exceptions (12). Nevertheless, recent years have seen a proliferation of studies mapping nonsense mutations at specific codons in terms of their specificity in causing heart diseases, susceptibility to the Noonan phenotype, dysmorphic facial features or mental retardation (35-37). As genetic investigations become more prevalent, there is a corresponding increase in genotype-to-phenotype correlation studies.

Conclusion

Neurofibromatosis type 1 is a genetic disease with multisystemic involvement and an increased risk of malignancy. The necessity for genetic examinations in patients with CALM who do not meet the criteria for age-related NF1 is becoming increasingly apparent. The clinical, diagnostic, and predictive advances in healthcare facilitate the early recognition of disease complications and the planning of appropriate treatments. It is anticipated that the advent of new pharmaceuticals and a multidisciplinary approach to treatment will result in a significant reduction in the feared aspects of the disease, following the complete elucidation of the pathogenesis.

References

1. Ly KI, Blakeley JO. The Diagnosis and Management of Neurofibromatosis Type 1. Med Clin North Am 2019;103(6):1035-1054.

2. Kehrer-Sawatzki H, Cooper DN. Challenges in the diagnosis of neurofibromatosis type 1 (NF1) in young children facilitated by means of revised diagnostic criteria including genetic testing for pathogenic NF1 gene variants. Hum Genet 2022;141(2):177-191.

3. Cimino PJ, Gutmann DH. Neurofibromatosis type 1. Handb Clin Neurol 2018; 148:799-811.

4. Legius E, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. Genet Med 2021;23(8):1506-1513.

5. Jett K, Friedman JM. Clinical and genetic aspects of neurofibromatosis 1. Genet Med 2010;12(1):1-11.

6. Sabatini C, Milani D, Menni F, Tadini G, Esposito S. Treatment of neurofibromatosis type 1. Curr Treat Options Neurol 2015;17(6):355.

7. Abdel-Aziz N, Y El-Kamah G, A Khairat R, et al. Mutational spectrum of NF1 gene in 24 unrelated Egyptian families with neurofibromatosis type 1. Mol Genet Genomic Med 2021;9(12):e1631.

8. Mao B, Chen S, Chen X, et al. Clinical characteristics and spectrum of NF1 mutations in 12 unrelated Chinese families with neurofibromatosis type 1. BMC Med Genet 2018;19(1):101.

9. Viskochil D, Buchberg AM, Xu G, et al. Deletions and a translocation interrupt a cloned gene at the neurofibromatosis type 1 locus. Cell 1990;62(1):187-192.

10. Jafry M, Sidbury R. RASopathies. Clin Dermatol 2020;38(4):455-461.

11. Anderson JL, Gutmann DH. Neurofibromatosis type 1. Handb

Clin Neurol 2015; 132:75-86.
12. Mudau MM, Dillon B, Smal C, et al. Mutation analysis and clinical profile of South African patients with Neurofibromatosis type 1 (NF1) phenotype. Front Genet 2024; 15:1331278.
13. Mautner VF, Kluwe L, Friedrich RE, et al. Clinical characterization of 29 neurofibromatosis type-1 patients with molecularly ascertained 1.4 Mb type-1 NF1 deletions. J Med Genet 2010;47(9):623-630.
14. Jha SK, Mendez MD. Cafe Au Lait Macules. In: StatPearls. Treasure Island (FL): StatPearls Publishing; July 31, 2023.
15. Lalvani S, Brown RM. Neurofibromatosis Type 1: Optimizing Management with a Multidisciplinary Approach. J Multidiscip Healthc 2024; 17:1803-1817.
16. Pinti E, Nemeth K, Staub K, Lengyel A, Fekete G, Haltrich I. Diagnostic difficulties and possibilities of NF1-like syndromes in childhood. BMC Pediatr 2021;21(1):331.
17. Târtea AE, Mocanu CL, Ștefănescu Dima AȘ, et al. Neurofibromatosis Type 1-Retinal Alterations Detectable with Optical Coherence Tomography Angiography. Diagnostics (Basel) 2024;14(13):1447.
18. Landry JP, Schertz KL, Chiang YJ, et al. Comparison of Cancer Prevalence in Patients with Neurofibromatosis Type 1 at an Academic Cancer Center vs in the General Population From 1985 to 2020. JAMA Netw Open 2021;4(3):e210945.
19. Sur ML, Armat I, Sur G, et al. Neurofibromatosis in Children: Actually, and Perspectives. Children (Basel. 2022;9(1):40.
20. Sellmer L, Farschtschi S, Marangoni M, et al. Serial MRIs provide novel insight into natural history of optic pathway gliomas in patients with neurofibromatosis 1. Orphanet J Rare Dis 2018;13(1):62.
21. Pannu AK, Sharma N. Neurofibromatosis type 1 and disseminated malignant peripheral nerve sheath tumor. QJM 2017;110(9):583-584.
22. Peduto C, Zanobio M, Nigro V, Perrotta S, Piluso G, Santoro C. Neurofibromatosis Type 1: Pediatric Aspects and Review of Genotype-Phenotype Correlations. Cancers (Basel) 2023;15(4):1217.
23. Elefteriou F, Kolanczyk M, Schindeler A, et al. Skeletal abnormalities in neurofibromatosis type 1: approaches to therapeutic options. Am J Med Genet A 2009;149A(10):2327-2338.
24. Leppävirta J, Kallionpää RA, Uusitalo E, et al. Neurofibromatosis type 1 of the child increases birth weight. Am J Med Genet A 2019;179(7):1173-1183.
25. Chauvel-Picard J, Lion-Francois L, Beuriat PA, et al. Craniofacial bone alterations in patients with neurofibromatosis type 1. Childs Nerv Syst 2020;36(10):2391-2399.
26. Naran S, Swanson JW, Ligh CA, Shubinets V, Taylor JA, Bartlett SP. Sphenoid Dysplasia in Neurofibromatosis: Patterns of Presentation and Outcomes of Treatment. Plast Reconstr Surg 2018;142(4):518e-526e.
27. Clementi M, Milani S, Mammi I, Boni S, Monciotti C, Tenconi R. Neurofibromatosis type 1 growth charts. Am J Med Genet 1999;87(4):317-323.
28. North KN, Riccardi V, Samango-Sprouse C, et al. Cognitive function and academic performance in neurofibromatosis. 1: consensus statement from the NF1 Cognitive Disorders Task Force. Neurology 1997;48(4):1121-1127.
29. Eijk S, Mous SE, Dieleman GC, et al. autism spectrum disorder in an Unselected Cohort of Children with Neurofibromatosis Type 1 (NF1). J Autism Dev Disord 2018;48(7):2278-2285.
30. Khair AM, Falchek S, Nikam R, Kaur G. Epilepsy and Electroencephalogram Characteristics in Children with Neurofibromatosis Type 1, What We Have Learned from a Tertiary Center Five Years' Experience. Child Neurol Open 2022; 9:2329048 X221131445.
31. Pinna V, Daniele P, Calcagni G, et al. Prevalence, Type, and Molecular Spectrum of NF1 Mutations in Patients with Neurofibromatosis Type 1 and congenital heart disease. Genes (Basel) 2019;10(9):675.
32. Mentzel HJ, Seidel J, Fitzek C, et al. Pediatric brain MRI in neurofibromatosis type I. Eur Radiol 2005;15(4):814-822.
33. Denckla MB, Hofman K, Mazzocco MM, et al. Relationship between T2-weighted hyperintensities (unidentified bright objects) and lower IQs in children with neurofibromatosis-1. Am J Med Genet 1996;67(1):98-102.
34. North K, Joy P, Yuille D, et al. Specific learning disability in children with neurofibromatosis type 1: significance of MRI abnormalities. Neurology 1994;44(5):878-883.
35. Koczkowska M, Chen Y, Callens T, et al. Genotype-Phenotype Correlation in NF1: Evidence for a More Severe Phenotype Associated with Missense Mutations Affecting NF1 Codons 844-848. Am J Hum Genet 2018;102(1):69-87.
36. Koczkowska M, Callens T, Chen Y, et al. Clinical spectrum of individuals with pathogenic NF1 missense variants affecting p.Met1149, p.Arg1276, and p.Lys1423: genotype-phenotype study in neurofibromatosis type 1. Hum Mutat 2020;41(1):299-315.
37. Napolitano F, Dell'Aquila M, Terracciano C, et al. Genotype-Phenotype Correlations in Neurofibromatosis Type 1: Identification of Novel and Recurrent NF1 Gene Variants and Correlations with Neurocognitive Phenotype. Genes (Basel) 2022;13(7):1130.

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A Comparison of Laparotomy and Laparoscopic Surgery in the Treatment of Adnexal Torsion in the Reproductive Age Group at a Tertiary Care Hospital in Türkiye

Türkiye'de Tersiyer Bir Hastanede Üreme Çağı Grubunda Adneksiyal Torsiyon Tedavisinde Laparotomi ve Laparoskopik Cerrahinin Karşılaştırılması

Bekir Sıtkı İsenlik[1] | Ödül Özkan Kalfagil[1] | Sinem Tuzcuoğlu[2] | Orkun Han[1] Zeynep Öztürk İnal[3] | Hasan Ali İnal[1]

[1]Antalya Training and Research Hospital, Department of Obstetrics and Gynecology, Antalya, Türkiye
[2]Kepez State Hospital, Department of Obstetrics and Gynecology, Antalya, Türkiye
[3]Konya City Hospital, Department of Obstetrics and Gynecology, Konya, Türkiye

Sorumlu Yazar | Correspondence Author
Zeynep Öztürk İnal
zeynephafiza@gmail.com
Address for Correspondence: Konya City Hospital, Department of Obstetrics and Gynecology, 04200, Konya, Türkiye.

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A Comparison of Laparotomy and Laparoscopic Surgery in the Treatment of Adnexal Torsion in the Reproductive Age Group at a Tertiary Care Hospital in Türkiye

ABSTRACT

Objective: To retrospectively evaluate the sociodemographic and clinical characteristics, and laboratory and pathology results of patients who underwent surgical intervention due to adnexal torsion in our clinic over the previous 10 years.

Material and Method: One hundred and seventy-six patients who underwent surgical procedures due to adnexal torsion, 146 of whom were treated with laparoscopy (L/S) (Group 1) and 30 with laparotomy (Group 2), between January 2014 and December 2023, were retrospectively and consecutively included in the study. The participants' sociodemographic and clinical characteristics, and laboratory and histopathology results were retrospectively recorded and compared.

Results: While no difference was observed between the groups in terms of age, body mass index, smoking status, alcohol use, gravidity, mass size, symptoms on admission, torsion turn number, the torsioned site, presence of necrosis, pre- and postoperative hemoglobin levels, white blood cell count, neutrophil, lymphocyte, monocyte, and platelet counts, red cell distribution width, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, C-reactive protein, or erythrocyte sedimentation rate values, significant differences were determined in operative times (40.81 ± 18.09 in Group 1 vs 82.33 ± 18.03 in Group 2, *p<0.001*) and hospitalization days (3.12 ± 1.15 in Group 1 vs 4.33 ± 1.54 in Group 2, *p=0.002*). Detorsion + cystectomy was the most commonly performed surgical procedure, while mature cystic teratoma was the most frequently observed histopathological finding.

Conclusion: This study showed that L/S has a shorter operation time and hospital stay in surgical treatment of adnexal torsion in reproductive-age women. The results of this study should now be confirmed by research involving larger numbers of participants.

Keywords: Adnexial torsion, Clinical feature, Laparoscopy, Laparotomy.

ÖZET

Amaç: Kliniğimizde son 10 yıl içinde adneksiyal torsiyon nedeniyle cerrahi müdahale geçiren hastaların sosyodemografik ve klinik özelliklerini, laboratuvar ve patoloji sonuçlarını geriye dönük olarak değerlendirmek.

Gereç ve Yöntem: Ocak 2014 ile Aralık 2023 arasında adneksiyal torsiyon nedeniyle cerrahi işlemler geçiren 176 hasta çalışmaya geriye dönük ve ardışık olarak dahil edilmiştir; bunlardan 146'sı laparoskopi (L/S) ile (Grup 1) ve 30'u laparotomi ile (Grup 2) tedavi edilmiştir. Katılımcıların sosyodemografik ve klinik özellikleri ile laboratuvar ve histopatoloji sonuçları geriye dönük olarak kaydedilmiş ve karşılaştırılmıştır.

Bulgular: Gruplar arasında yaş, vücut kitle indeksi, sigara durumu, alkol kullanımı, gravidisite, kitle boyutu, başvuru sırasında semptomlar, torsiyone tur sayısı, torsiyone taraf, nekroz varlığı, preoperatif ve postoperatif hemoglobin seviyeleri, lökosit, nötrofil, lenfosit, monosit ve trombosit sayıları, kırmızı hücre dağılım genişliği, nötrofil-lenfosit oranı, trombosit-lenfosit oranı, C-reaktif protein veya eritrosit sedimentasyon hızı değerleri açısından herhangi bir fark gözlemlenmemiştir; ancak operasyon süresinde (Grup 1'de 40.81 ± 18.09 vs Grup 2'de 82.33 ± 18.03, *p<0.001*) ve hastanede yatış gününde (Grup 1'de 3.12 ± 1.15 vs. Grup 2'de 4.33 ± 1.54, *p=0.002*) anlamlı farklılıklar belirlenmiştir. Detorsiyon + kistektomi en sık gerçekleştirilen cerrahi prosedür olurken, olgun kistik teratom en sık gözlemlenen histopatolojik bulgudur.

Sonuç: Bu çalışma, L/S'nin üreme çağındaki adneksiyal torsiyon cerrahisinde daha kısa operasyon ve hastanede yatış süresine sahip olduğunu göstermiştir. Bu çalışmanın sonuçları, daha fazla katılımcı içeren araştırmalarla doğrulanmalıdır.

Anahtar Sözcükler: Adneksiyal torsiyon, Klinik özellik, Laparoskopi, Laparotomi

Introduction

Adnexal torsion, which occurs due to the rotation of the ovary and/or fallopian tube around their vascular and ligamentous structures, accounts for approximately 3% of gynecological emergencies, and is the fifth most common of these. Although it can be seen in all age groups, it is most common during the reproductive years. If not diagnosed and treated in time, it can lead to adnexal loss and even death (1). Known risk factors include controlled ovarian stimulation, a history of adnexal torsion, polycystic ovary syndrome, tubal ligation, and pregnancy (2). Adnexal torsion is more commonly caused by follicular cysts, corpus luteum cysts, benign cystic teratomas, and cystadenomas. Endometriomas and malignant masses are less likely to cause torsion due to adhesions (3). Adnexal torsion is more commonly observed on the right side due to the lower mobility of the sigmoid colon, the greater mobility of the ileum and cecum, and the greater length of the right ligamentum ovarii proprium (4).

The most common symptom is acute onset of continuous or intermittent abdominal pain, while nausea-vomiting and fever may also be observed. In the event of adnexal torsion, venous blood flow is initially interrupted, leading to edema due to ongoing arterial flow, and eventually to complete cessation of arterial flow. If the necessary intervention is not performed, symptoms of peritonitis may also develop due to necrosis and inflammation (2). Acute appendicitis, pyelonephritis, ectopic pregnancy, pelvic inflammatory disease, cyst rupture, nephrolithiasis, and colitis should also be clinically differentiated in the diagnosis (3). A palpable pelvic mass in the lower genital region, rebound tenderness, and defense due to peritoneal irritation may be observed at physical examination (2).

Transvaginal ultrasonography (TVUSG) should represent the first-choice imaging option in the diagnosis of adnexal torsion. Important TVUSG findings include the presence of a mass, peripheral small follicles located centrally in the edema (a string of pearls), free fluid in the Douglas pouch, and the appearance of the follicular ring sign (whirlpool) (5). Blood flow may be observed in the early stages of Doppler ultrasound, while flow loss is seen in the later stages. Other diagnostic options include computed tomography (CT) and magnetic resonance imaging (MRI) (6).

Laparoscopy is the preferred surgical procedure in the treatment of adnexal torsion due to such advantages as less postoperative pain, less blood loss, a rapid healing time, quicker return to daily activities, a shorter hospital stays, the avoidance of a large abdominal surgical incision, and reduced socioeconomic losses (3).

The type of surgical intervention should be personalized, taking into account the patient's age and fertility desires, and the appearance of the adnexal mass. Detorsion and aspiration of the cyst content or cystectomy represent conservative approaches, while oophorectomy or salpingo-oophorectomy are more invasive surgical options (2,3). The prevention of adnexal torsion by means of oophoropexy and shortening of the ligamentum ovarii proprium is controversial (3,5). This study retrospectively evaluated the sociodemographic and clinical characteristics, as well as the laboratory and pathology results, of patients who underwent surgical interventions for adnexal torsion in our clinic over the previous 10 years.

Material and Method

This retrospective cohort study was conducted at the Antalya Training and Research Hospital Gynecology Unit, Türkiye, between January 2014 and December 2023. Ethics committee approval was obtained on 23.05.2024 under decision number 2024/145. The study was carried out in accordance with the principles of the Declaration of Helsinki, and no conflict of interest was declared by the authors. Written informed consent to the use of their data was obtained from the participants prior to hospitalization. Premenstrual and postmenopausal patients were excluded from the study, since premenstrual torsion cases in our hospital are evaluated by the pediatric surgery department and postmenopausal cases by the gynecological oncology department. A hundred and seventy-six patients underwent surgical procedures due to adnexal torsion during the study period, 146 of whom were treated with laparoscopy (Group 1), while 30 underwent laparotomy (Group 2).

Data were collected for age, body mass index (BMI) (kg/m^2), smoking status, alcohol use, gravidity,

parity, mass size, symptoms on admission, torsion turn number, torsioned site, presence of necrosis, operative time, length of hospitalization, pre- and postoperative hemoglobin (Hb), white blood cell (WBC), neutrophil, lymphocyte, monocyte, and platelet counts, red cell distribution width (RDW), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) values on admission, surgical interventions applied, and pathological findings from hospital automation system and patient file archive. Ovarian stromal edema with or without peripherally displaced antral follicles, the follicular ring sign, the whirlpool sign, and absence of vascularization in the twisted organ are considered abnormal findings in adnexal torsion in USG and Doppler USG (5).

Sociodemographic and clinical characteristics, laboratory results, and surgical and pathological findings, were compared between the groups.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0 for Windows software (SPSS, Chicago, IL, USA). The Shapiro-Wilk test was used to examine continuous variables with normal and non-normal distributions, while Student's t-test was used to examine the normally distributed continuous variables. The Mann-Whitney U test was used for non-normally distributed continuous variables. Categorical data were analyzed using Pearson's chi-square test, while Fisher's exact test was applied if the expected frequency was less than five in >20% of all cells. Continuous variables were presented as mean ± standard deviation (SD) or median (25th and 75th percentiles) and categorical variables as the number of cases and percentages. A *p<0.05* value was regarded as statistically significant. In the post-hoc power analysis, the power of the study was found to be 92% with an effect size of 0.69 for operation time.

Results

A comparison of the groups' sociodemographic and clinical characteristics is shown in Table I. No differences were observed between the groups in terms of age (24.74+7.53 in Group 1 vs 23.73+7.70 in Group 2, *p=0.692*), BMI (27.81+4.20 vs 26.20+2.66, *p=0.159*), smoking status (44 [30.1%] vs 12 [40.0%], *p=0.455*), alcohol use (28 [19.2%] vs 6 [20.0%], p=0.941), gravidity (1.0 [0-1.0] vs 0 [0-0], *p=0.099*), parity (0 [0-0] vs 0 [0-0], *p=0.426*), mass size (8.64+2.66 vs 8.07+2.51, *p=0.651*), symptoms on admission (pelvic pain 142 [97.3%] vs 28 [93.3%], *p=0.433*; pelvic mass 138 [94.5%] vs 26 [86.7%], *p=0.270*; peritoneal signs 122 [83.6%] vs 20 [66.7%], *p=0.156*; nausea/vomiting 100 [68.5%] vs 14 [46.7%], *p=0.107*; fever 16 [11.0%] vs 4 [13.3%], *p=0.677*; abnormal Doppler ultrasound findings 106 [72.6%] vs 18 [60.0%], *p=0.330*), torsion turn number (2.27+1.20 vs 2.47+1.59, *p=0.596*), the torsioned site (left 68 [46.6%] vs 14 [46.7%], right 78 [53.4%] vs 14 [46.7%], bilateral 0 [0%] vs 2 [6.7%], *p=0.161*), or presence of necrosis (52 [35.6%] vs 12 [40.0%], *p=0.748*). However, operative time (40.81+18.09 minutes in Group 1 vs 82.33 =+18.03 minutes in Group 2, *p<0.001*) and days of hospitalization (3.12+1.15 days vs 4.33+1.54 days, *p=0.002*) differed significantly.

Table I. The Participants' Sociodemographic and Clinical Characteristics

		Laparoscopy (n=146)	Laparotomy (n=30)	p
Age (years)		24.74±7.53	23.73±7.70	*0.692*
BMI (kg/m²)		27.81±4.20	26.20±4.66	*0.159*
Tobacco use (n, %)		22 (30.11%)	6 (40.0%)	*0.455*
Alcohol use (n, %)		14 (19.2%)	3 (20.0%)	*0.941*
Gravidity		1 (0-1.0)	0 (0-0)	*0.099*
Mass size (cm)		8.64±2.66	8.07±2.51	*0.651*
Symptoms (n, %)	**Pelvic pain**	138 (94.5%)	26 (86.7%)	*0.270*
	Pelvic mass	142 (97.3%)	28 (93.31%)	*0.433*
	Peritoneal signs (Rebound/ Defense)	132 (86.6%)	20 (66.7%)	*0.156*
	Nausea/Vomiting	100 (68.6%)	14 (46.7%)	*0.107*
	Fever	16 (11.0%)	4 (13.3%)	*0.677*
	Abnormal Doppler ultrasound findings	106 (72.6%)	18(60.0%)	*0.330*
Torsion turn number		2.27±1.20	2.47±1.59	*0.596*
The torsioned side (n, %)	**Left**	**68 (46.6%)**	14 (46.7%)	*0.161*
	Right	**78 (53.4%)**	14 (46.7%)	
	Bilateral	0	2 (6.4%)	
Presence of necrosis (n, %)		26 (35.6%)	6 (40%)	*0.748*
Operative time (min)		40.81±18.09	82.33±18.03	***<0.001****
Length of hospitalization (days)		3.12±1.15	4.33±1.54	***0.002****

BMI: body mass index, *Statistically significant

The groups' laboratory outcomes are given in Table II. Preoperative (12.23+2.66 in Group 1 vs 11.61+2.39 in Group 2, *p=0.177*) and postoperative Hb (10.73+2.38 vs 10.28+2.49, *p=0.258*) levels, WBC (12.69+3.26 vs 12.14+3.37, *p=0.631*), neutrophil (11.80+2.22 vs 12.28+2.44, *p=0.452*), lymphocyte (1.51+0.33 vs 1.67+0.45, *p=0.117*), monocyte (0.41+0.09 vs 0.45+0.12, *p=0.213*), and platelet counts (222.42+59.65 vs 231.665516, *p=0.177*), and RDW (15.62+4.65 vs 14.78+2.04, *p=0.273*), NLR (7.84+0.48 vs 7.49+0.82, *p=0.131*), PLR (15.14+4.98 vs 19.20+5.65, *p=0.101*), CRP (19.58+6.35 vs 19.06+6.21, *p=0.868*), and ESR (42.57+12.86 vs 43.33+13.73, *p=0.596*) values were comparable between the groups.

Table II. The Patients' Laboratory Outcomes

	Laparoscopy (n=146)	Laparotomy (n=30)	*p*
Preoperative Hb (g/dl)	12.23±2.66	11.61±2.39	*0.177*
Postoperative Hb (g/dl)	10.73±2.38	10.29±2.49	*0.258*
Leukocyte count (10^3) (mcl)	12.69±3.26	12.14±3.37	*0.631*
Neutrophil count (10^3) (mcl)	11.80±2.22	12.28±2.44	*0.452*
Lymphocyte count (10^3) (mcl)	1.51±0.33	1.67±0.45	*0.117*
Monocyte count (10^3) (mcl)	0.41±0.09	0.45±0.12	*0.213*
RDW	15.62±4.65	14.78±2.04	*0.273*
Platelet count (10^3) (mcl)	222.42±59.65	231.66±55.16	*0.177*
NLR (%)	7.84±0.48	7.49±0.82	*0.131*
PLR (%)	15.14±4.98	19.20±5.65	*0.101*
CRP (mg/dL)	19.58±6.35	19.06±6.21	*0.868*
ESR (mm/h)	42.571±2.86	43.33±13.73	*0.882*

Hb: hemoglobin, Htc: hemotocrit, RDW: red cell distribution width, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate

Table III summarizes the patients' surgical intervention and pathological findings. No difference was determined between the groups in terms of surgical interventions performed (detorsion 46 [31.51%] vs 14 [46.7%], detorsion + cystectomy 82 [56.2%] vs 16 [53.3%], salpingo-ooferectomy 8 [5.5%] vs 0 [0%], hysterectomy + salpingo-ooferectomy 10 [6.8%] vs 0 [0%], *p=0.114*) and pathological findings (serous cystadenoma 32 [21.9%] vs 8 [26.7%], musinous cystadenoma 10 [6.8%] vs 2 [6.7%], hemorrhagic cyst 14 [9.6%] vs 2 [6.7%], mature cystic teratoma 44 [30.1%] vs 8 [26.7%], endometrioma 14 [9.6%] vs 4 [13.3%], corpus luteum cyst 8 [5.5%] vs 2 [6.7%], borderline tumor 10 [6.8%] vs 2 [6.7%], unclassified 14 [9.6%] vs 2 [6.7%]) *p=0.757*).

Table III. A Comparison of the Patients' Surgical Intervention and Pathological Findings

		Laparoscopy (n=146)	Laparotomy (n=30)	*p*
Surgical intervention (n, %)	**Detorsion**	46 (31.5%)	14 (46.7%)	*0.114*
	Detorsion + Cystectomy	82 (56.2%)	16 (53.3%)	
	Salpingo-oopherectomy	8 (5.5%)	-	
	Hysterectomy + Salpingo-oopherectomy	10 (6.8%)	-	
Pathological findings (n, %)	**Serous cystadenoma**	32 (21.9%)	4 (26.7%)	*0.757*
	Mucinous cystadenoma	10 (6.8%)	1 (6.7%)	
	Hemorrhagic cyst	14 (9.6%)	1 (6.7%)	
	Mature cystic teratomas	44 (30.1%)	4 (26.7%)	
	Endometrioma	14 (9.6%)	1 (6.7%)	
	Borderline tumor	10 (6.8%)	1 (6.7%)	
	Corpus luteum cyst	8 (5.5%)	1 (6.7%)	

Discussion

This retrospective study examined the sociodemographic and clinical characteristics and laboratory and pathology results of patients who underwent surgical interventions for adnexal torsion in our clinic over the previous 10 years. Analysis showed that patients undergoing laparoscopic surgery (L/S) had shorter operative times and lengths of hospitalization.

Adnexal torsion accounts for approximately 3% of gynecological surgical emergencies, and 70% of cases are seen in women of reproductive age. The condition is defined as a partial or complete rotation of the adnexal vascular pedicle and may involve the ovary, fallopian tube, or both. It is the fifth most common gynecological condition following ectopic pregnancy, corpus luteum rupture and bleeding, pelvic inflammatory disease, and acute appendicitis. In case of torsion, venous blood flow is initially disrupted, followed by impairment of arterial flow. Congestion, adnexal edema, ischemia, and ultimately necrosis develops as a result (2,3,7).

Elongation of the ligaments supporting the adnexa and the presence of a corpus luteum cyst increases the risk of adnexal torsion during pregnancy. Fifty-

five percent of cases of adnexal torsion during pregnancy occur in the first trimester, 34% in the second trimester, and 11% in the third (8). In the present study, five patients with adnexal torsion were in the first trimester, with four undergoing laparoscopic surgery (L/S) and one undergoing a laparotomic surgical procedure.

Although it can occur on both sides, adnexal torsion is typically observed more frequently on the right due to the longer right utero-ovarian ligament or the proximity of the left ovary to the sigmoid colon (9). In the present study, adnexal torsion was more frequently present on the right side, although this was not statistically significant. Adnexal torsion typically presents with acute, unilateral sharp pain (70%) or stabbing pain (60%) in the lower abdomen. Nausea and vomiting are observed in 60% to 70% of cases. Fever is usually seen in approximately 10% of cases, particularly in cases of necrosis. A palpable mass is found in approximately 60-90% of adults at physical examination, while in children the figure is 20-35%. Peritoneal irritation symptoms are observed in approximately 30% of cases (10). The most common symptoms in the current study were pelvic pain, pelvic mass, peritoneal signs, nausea/vomiting, and fever, with no statistically significant difference being observed between the L/S and laparotomy cases.

Ultrasound, with color Doppler if possible, should represent the preferred imaging modality for suspected adnexal torsion. The most commonly observed findings at ultrasound examination include an increased ovarian size and volume, and the absence of blood flow on Doppler ultrasound. The appearance of peripheral follicles ranging from 8 to 12 mm (whirlpool sign) in size due to ovarian congestion is moderately sensitive and highly specific for the diagnosis of adnexal torsion. Intraperitoneal fluid accumulation may be observed due to fluid leakage into the interstitial space (11). CT (with findings such as thickening of the uterine tube (74%), eccentric or concentric wall thickening (54%), and eccentric septal thickening (50%)) and MRI (with abnormal T1 and T2 images in the presence of hemorrhagic infarction) can also be used to detect adnexal torsion (12). In the present study, abnormal Doppler ultrasound findings were observed in 72.6% of the L/S group and 60.0% of the laparotomy group, with a total incidence of 70.5% across the entire case group.

While specific histological findings such as ischemia, necrosis, and infarction are observed in 80% of torsioned adnexa, these findings may not be present in 20% (13). There is no specific laboratory test for the diagnosis of adnexal torsion. Serum WBC (>12×10^9) may be elevated in 56% of cases, and serum CRP levels rise in the presence of necrosis (13,14). Elevated WBC and CRP levels were observed in the present study.

The management of adnexal torsion has changed significantly over the past decade, with detorsion via laparoscopic surgical procedures, with or without cystectomy, despite the necrotic appearance of the ovary, being recommended (15). A previous study reported a shorter operative time, lower postoperative fever rates, and shorter hospital stays in a group of 179 patients with adnexal torsion treated with laparoscopic surgery (16). However, gynecologists with limited experience in laparoscopic surgery tend to prefer laparotomy. Oelsner et al. (17) observed fewer postoperative complications, and shorter hospital stays in cases of adnexal torsion treated with L/S. Cohen et al. retrospectively compared 102 cases of adnexal torsion treated with L/S and laparotomy. Those authors also concluded that L/S should constitute the primary approach for the definitive diagnosis and treatment of adnexal torsion, particularly in premenopausal patients (18). In the current study, the L/S group had shorter operative times (40.81 ± 18.09 min vs 82.33 ± 18.03 min) and shorter lengths of hospitalization (3.12 ± 1.15 days vs 4.33 ± 1.54 days). These findings were consistent with the literature.

The time elapsing from the onset of adnexal torsion to the surgical procedure has been shown to affect the management of the condition, longer delays being associated with a lower rate of adnexal salvage (19). In our clinic, patients hospitalized with suspected adnexal torsion undergo surgical interventions as soon as possible, within 24 hours of symptom onset.

Laparoscopic detorsion with or without cystectomy should represent the primary treatment method for both adults and children, in preference to salpingo-oophorectomy. This is because ovarian function has

been shown both histologically and biochemically to be preserved postoperatively (17,20). If the torsioned adnexa is excessively edematous, cystectomy may be delayed for 6-8 weeks, since it is highly sensitive to rupture (19).

In a previous study of 981 patients with adnexal torsion, 672 underwent detorsion and/or cystectomy, while 309 were managed conservatively. Pulmonary embolism was observed in only two of the entire patient group (21). No cases of thromboembolic events were observed in two large retrospective studies in which only detorsion was performed. This finding supports the conservative approach to managing adnexal torsion (17,18). In the present study, and consistent with the literature, no thromboembolic events were observed in any cases.

Malignancy has been detected in 3% of adult adnexal torsion cases. In postmenopausal patients, however, this can rise to 22%. Salpingo-oophorectomy is recommended in ovarian torsion occurring post-menopause (22). No malignancy was determined in any of the cases included in the present study, which were all in the premenopausal period. All our patients who underwent hysterectomy were in the perimenopausal period, and this surgical procedure was performed due to their own wishes and consent, with no evidence of malignancy found in any of them. However, it should be kept in mind that borderline tumors may be present in these patients.

Although adnexal torsion can occur without ovarian pathology, it is most commonly associated with benign ovarian cysts. The most frequently observed associated condition is mature cystic teratoma (2,3). The most commonly detected histopathological diagnosis (mature cystic teratoma) in the present study was consistent with the previous literature.
The potential limitations of this study include its retrospective design and its being conducted at a tertiary center. However, one particular strength is that the surgical procedures were performed by two senior surgeons (BSI and HAI).

Adnexal torsion should be considered in cases presenting with acute abdominal pain and findings at Doppler ultrasound such as reduced or absent blood flow, along with increased adnexal size and volume. However, the decision to perform surgical intervention should not be based solely on ultrasound findings. Rapid diagnosis and prompt surgical intervention can reduce the risk of trauma and ischemia to the ovary. Even in an adnexal structure that has acquired a blue-black color, detorsion should be performed first, and cystectomy only if necessary. Salpingo-oophorectomy should only be considered in postmenopausal women or in cases with an increased risk of malignancy. Oophoropexy can be considered in cases in which the adnexal ligament is congenitally long, in patients with recurrent torsion, or when no clear cause of torsion can be identified. In conclusion, laparoscopic surgical procedures should be preferred in adnexal torsion, especially for young reproductive-age patients who wish to preserve their fertility. The results of this study should now be confirmed by further research involving larger numbers of participants.

References

1. Melcer Y, Maymon R, Pekar-Zlotin M, Vaknin Z, Pansky M, Smorgick N. Does she have adnexal torsion? Prediction of adnexal torsion in reproductive age women. Arch Gynecol Obstet 2018;297:685-690.
2. Sasaki KJ, Miller CE. Adnexal torsion: review of the literature. J Minim Invasive Gynecol 2014;21:196-202.
3. Chang-Patel EJ, Palacios-Helgeson LK, Gould CH. Adnexal torsion: a review of diagnosis and management strategies. Curr Opin Obstet Gynecol 2022;34:196-203.
4. Ling-Shan C, Jing L, Zheng-Qiu Z, et al. Computed Tomography Features of Adnexal Torsion: A Meta-Analysis. Acad Radiol 2022;29:317-325.
5. Moro F, Bolomini G, Sibal M, et al. Imaging in gynecological disease (20): clinical and ultrasound characteristics of adnexal torsion. Ultrasound Obstet Gynecol 2020;56:934-943.
6. Sugi MD, Patel AG, Yi J, Patel MD. The Flipped Ovary Sign in Ovarian Torsion. J Ultrasound Med 2021;40:839-843.
7. Birsen MB, Erturk D, Onder D, et al. Practicability of Serum Kallistatin Levels as a Biomarker in the Diagnosis of Tubo-Ovarian Abscess. Surg Infect (Larchmt) 2024;25:668-673.
8. Inal ZO, Inal HA. Bilateral Dermoid Cysts of the Ovaries in a Term Pregnant Woman: A Case Report. Anatol JFM 2018;2:67-69.
9. Smorgick N, Maymon R, Mendelovic S, Herman A, Pansky M. Torsion of normal adnexa in postmenarcheal women: can ultrasound indicate an ischemic process? Ultrasound Obstet Gynecol 2008;31(3):338-341.
10. Tsafrir Z, Azem F, Hasson J, et al. Risk factors, symptoms, and treatment of ovarian torsion in children: the twelve-year

experience of one center. J Minim Invasive Gynecol 2012;19:29-33.
11. Shadinger LL, Andreotti RF, Kurian RL. Preoperative sonographic and clinical characteristics as predictors of ovarian torsion. J Ultrasound Med 2008;27:7-13.
12. Lee JH, Park SB, Shin SH, et al. Value of intra-adnexal and extra-adnexal computed tomographic imaging features diagnosing torsion of adnexal tumor. J Comput Assist Tomogr 2009;33:872-876.
13. Tobiume T, Shiota M, Umemoto M, Kotani Y, Hoshiai H. Predictive factors for ovarian necrosis in torsion of ovarian tumor. Tohoku J Exp Med 2011;225:211-214.
14. McCloskey K, Grover S, Vuillermin P, Babl FE. Ovarian torsion among girls presenting with abdominal pain: a retrospective cohort study. Emerg Med J 2013;30:e11.
15. Galinier P, Carfagna L, Delsol M, et al. Ovarian torsion. Management and ovarian prognosis: a report of 45 cases. J Pediatr Surg 2009;44:1759-1765.
16. Lo LM, Chang SD, Horng SG, Yang TY, Lee CL, Liang CC. Laparoscopy versus laparotomy for surgical intervention of ovarian torsion. J Obstet Gynaecol Res 2008;34:1020-1025.
17. Oelsner G, Cohen SB, Soriano D, Admon D, Mashiach S, Carp H. Minimal surgery for the twisted ischaemic adnexa can preserve ovarian function. Hum Reprod 2003;18:2599-2602.
18. Cohen SB, Wattiez A, Seidman DS, et al. Laparoscopy versus laparotomy for detorsion and sparing of twisted ischemic adnexa. JSLS 2003;7:295-299.
19. Ghandehari H, Kahn D, Glanc P. Ovarian Torsion: Time Limiting Factors for Ovarian Salvage. Emerg Med (Los Angel) 2015;5:273.
20. Celik A, Ergün O, Aldemir H, et al. Long-term results of conservative management of adnexal torsion in children. J Pediatr Surg 2005;40:704-708.
21. Weitzman VN, DiLuigi AJ, Maier DB, Nulsen JC. Prevention of recurrent adnexal torsion. Fertil Steril 2008;90:2018.e1-3.
22. Eitan R, Galoyan N, Zuckerman B, Shaya M, Shen O, Beller U. The risk of malignancy in post-menopausal women presenting with adnexal torsion. Gynecol Oncol 2007;106:211-214.

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The Relationship Between Pain, Depression, and Job Satisfaction in Employees with Chronic Neck Pain

Kronik Boyun Ağrısı Olan Çalışanlarda Ağrı, Depresyon ve İş Tatmini İlişkisi

Öznur Kutluk[1] | Tuğba Yalçın[2]

[1]Antalya Training and Research Hospital, Department of Rheumatology, Antalya, Türkiye
[2]Medical Park Hospital, Department of Physical Medicine and Rehabilitation, Adana, Türkiye

Sorumlu Yazar | Correspondence Author
Öznur Kutluk
oznurkutluk@gmail.com
Address for Correspondence: Antalya Training and Research Hospital, Department of Rheumatology, Varlık, Kazım Karabekir Cd., 07100 Muratpaşa/Antalya, Türkiye.

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The Relationship Between Pain, Depression, and Job Satisfaction in Employees with Chronic Neck Pain

ABSTRACT

Objective: The aim of this study is to investigate the relationships between factors such as occupation, pain, depression, and kinesiophobia with job satisfaction in employees with chronic neck pain.

Material and Method: This study was designed as a cross-sectional observational study. Individuals aged between 18 and 50 years, working in non-physically demanding occupations (such as nurses and secretaries), without neurological deficits and suffering from chronic neck pain lasting more than 3 months, were included in the study. The severity of neck pain was determined using the Visual Analog Scale (VAS). Disability was assessed using the Neck Disability Index (NDI). Depression symptoms were evaluated with the Beck Depression Inventory, and kinesiophobia was assessed using the Tampa Scale for Kinesiophobia (TSK). Job satisfaction was measured using the Minnesota Satisfaction Questionnaire. The data were analyzed using SAS 9.4 software.

Results: A total of 64 healthcare workers with chronic neck pain were included in the study. Among the participants, 33% were found to have low job satisfaction. In the group with low job satisfaction, pain severity (VAS: 7.6 vs. 6.5; *p=0.011*), disability level (NDI: 24.5 vs. 17.4; *p=0.013*), and depression level (BDI: 22.5 vs. 12.6; *p<0.001*) were significantly higher. Furthermore, among healthcare workers with chronic neck pain, higher levels of depression were associated with increased pain (VAS: *p=0.024*), disability (NDI: *p=0.007*), and kinesiophobia (TSK: *p=0.011*), as well as decreased job satisfaction (MSQ-Total: *p=0.004*, MSQ-Intrinsic: *p=0.003*, MSQ-Extrinsic: *p<0.001*).

Conclusion: In this study, a significant association was found between low job satisfaction and higher levels of pain, disability, and depression. Additionally, an increase in depression levels was observed to be associated with decreased job satisfaction and increased pain severity. These findings suggest that physical and psychological factors may be related to job satisfaction in healthcare workers with chronic neck pain.

Keywords: Healthcare workers, Job satisfaction, Neck pain.

ÖZET

Amaç: Bu çalışmanın amacı, kronik boyun ağrısı olan çalışanlarda ağrı, depresyon ve kinezyofobi gibi faktörlerin iş tatmini ile olan ilişkilerini incelemektir.

Gereç ve Yöntem: Bu çalışma, kesitsel gözlemsel bir çalışma olarak tasarlanmıştır. Çalışmaya, 18-50 yaş aralığında, fiziksel efor gerektirmeyen işlerde (örneğin hemşire, sekreter) çalışan, nörolojik defisiti bulunmayan ve 3 aydan uzun süredir devam eden kronik boyun ağrısı şikayeti olan hastalar dahil edilmiştir. Boyun ağrısının şiddeti Görsel Analog Skala (GAS) kullanılarak belirlenmiştir. Engellilik durumu Boyun Engellilik İndeksi (BEI) ile değerlendirilmiştir. Depresyon semptomları Beck Depresyon Envanteri ile değerlendirilmiş ve kinezyofobi, Tampa Kinezyofobi Ölçeği (TSÖ) ile ölçülmüştür. İş tatmini Minnesota İş Tatmini Anketi ile değerlendirilmiştir. Veriler SAS 9.4 yazılımı kullanılarak analiz edilmiştir.

Bulgular: Çalışmaya kronik boyun ağrısı olan 64 sağlık çalışanı dahil edilmiştir. Katılımcıların %33'ünde düşük iş tatmini saptanmıştır. Düşük iş tatminine sahip grupta ağrı düzeyi (VAS: 7.6 vs. 6.5; *p=0.011*), engellilik düzeyi (NDI: 24.5 vs. 17.4; *p=0.013*) ve depresyon düzeyi (BDI: 22.5 vs. 12.6; *p<0.001*) istatistiksel olarak anlamlı şekilde daha yüksek bulunmuştur. Ayrıca, kronik boyun ağrısı olan sağlık çalışanlarında depresyon düzeyi arttıkça ağrı (VAS: *p=0.024*), engellilik (NDI: *p=0.007*) ve kinezyofobi (TSK: *p=0.011*) düzeylerinde artış; iş tatmini düzeyinde ise azalma (MSQ-Total: *p=0.004*, MSQ-Intrinsic: *p=0.003*, MSQ-Extrinsic: *p<0.001*) gözlemlenmiştir.

Sonuç: Bu çalışmada, düşük iş tatmini ile daha yüksek düzeyde ağrı, engellilik ve depresyon arasında anlamlı bir ilişki saptanmıştır. Ayrıca, depresyon düzeyindeki artışın, iş tatmininde azalma ve ağrı düzeyinde artış ile ilişkili olduğu gözlemlenmiştir. Elde edilen bulgular, kronik boyun ağrısı olan sağlık çalışanlarında fiziksel ve psikolojik değişkenlerin iş tatmini ile ilişkili olabileceğini göstermektedir.

Anahtar Sözcükler: Boyun ağrısı, İş tatmini, Sağlık çalışanları.

Introduction

Pain is one of the most common reasons for seeking medical attention and is known to have physical, emotional, and cognitive dimensions, making it a complex biopsychosocial experience (1). Chronic pain can coexist with depression and secondarily lead to reduced activity, social, and economic problems for the individual (2). It is reported that the prevalence of depression in individuals with chronic pain is generally over 50% (3,4).

Non-specific neck-arm pain is defined as pain or discomfort originating from muscles, connective tissue, bursa, tendons, or joint capsules, and is used to describe symptoms in the upper quadrant associated with increased nerve mechanosensitive without accompanying neurological deficits. Occupational groups such as office workers, teachers, and healthcare workers are at risk for such pain. In one study, it was found that low back pain (71.6%) was the most common pain among healthcare workers, followed by shoulder pain (46.8%) and neck pain (42.2%) (5). Physical, psychological, and sociocultural factors related to the profession, as well as negative aspects of job satisfaction, can lead to a decrease in productivity and efficiency. Observational studies indicate that psychological risk factors such as depressive mood, a tendency towards somatization (generally the tendency to worry about common somatic symptoms), job dissatisfaction, and work stress are closely associated with musculoskeletal pain (6,7).

The relationship between pain and occupational stress may arise from stress increasing the sensitivity to and expression of pain. However, it should also be noted that pain may make individuals more prone to perceiving and expressing occupational stress. One study demonstrated that perceived stress has a small but significant effect on the development of musculoskeletal symptoms (8).

Previous studies have been conducted on job satisfaction in occupational groups that do not involve physical labor (such as teachers, nurses, and doctors). However, our study aims to investigate the relationship between factors such as chronic pain and depression and job satisfaction among employees with chronic neck pain.

Material and Method

Selection and Description of Participants: This study was designed as a cross-sectional observational study. The participants were selected from patients aged 18–50 years who presented to the Rheumatology (Physical Medicine and Rehabilitation) outpatient clinic of Antalya Training and Research Hospital in Antalya, Türkiye, between January 2023 and January 2024. Employees with chronic neck pain lasting more than 3 months were included in the study. In accordance with the literature, participants were selected to represent non-specific neck pain, characterized by the absence of identifiable structural, surgical, or neurological causes. Participants were from non-physical labor occupations (secretaries, nurses). The participants' prior medical histories and imaging reports were reviewed using the national electronic health record system (e-Nabız) and hospital databases. Individuals with a history of surgery on the head/neck region, cervical disc disease, or cervical disc pathology identified on MRI were excluded. Additionally, those diagnosed with myelopathy, fractures, infections, dystonia, tumors, inflammatory diseases, fibromyalgia, or osteoporosis were not included in the study. Patients with neurological deficits or clinical signs of radiculopathy were also excluded.

Data sources/measurement: After collecting demographic information such as age, gender, and occupation, the severity of neck pain was assessed using the Visual Analog Scale (VAS). Disability was evaluated using the Neck Disability Index (NDI). Symptoms of depression were assessed using the Beck Depression Inventory (BDI), and kinesiophobia was evaluated using the Tampa Scale of Kinesiophobia (TSK). Job satisfaction was measured using the Minnesota Satisfaction Questionnaire (MSQ)

Visual Analog Scale (VAS): The meaning of the numbers placed from zero to ten on a 10 cm line. Zero indicates no pain, ten indicates unbearable pain, and five indicates moderate pain. Following this explanation, patients were asked to indicate their chronic neck pain on a 10 cm line (9,10).

Neck Disability Index (NDI): Various scales have been developed for the evaluation of self-rated disability in neck pain patients. The Neck Disability Index (NDI) (11) is the first such scale published. It

was modified from the Oswestry Low Back Pain Disability Questionnaire (12) by Vernon and Mior (11). The NDI is the most widely used scale for evaluating neck pain related disability throughout the World (13). The Turkish validity and reliability of NDI have been confirmed by Kesiktaş et al. (14). The total score ranges from 0 to 50, with higher scores indicating higher disability.

Beck Depression Inventory (BDI): The scale is a psychological assessment questionnaire consisting of a total of 21 questions, evaluated by summing the scores between 0 and 3 obtained from each answer. In accordance with the corresponding score ranges, the scale is evaluated as follows: minimal depression between 1-9, mild depression between 10-16, moderate depression between 17-29, and severe depression between 30-63. The Turkish validity and reliability study of the scale were conducted by Hisli (15).

Tampa Scale of Kinesiophobia (TSK): Assessment of Kinesiophobia was conducted using the Tampa Scale for Kinesiophobia (TSK) in patients. The original version of the Tampa Scale for Kinesiophobia (TSK) was developed by Miller, Kopri, and Todd in 1991 but was not published. Vlaeyen and colleagues republished the original scale consisting of 17 questions with permission from the developers in 1995. TSK is a 17-item scale developed to measure fear of movement/reinjury. The scale includes parameters related to work-related activities, injury/reinjury, and fear-avoidance (16,17). With Turkish validity and reliability established, individuals receive a total score ranging from 17 to 68 on this scale (18). The higher the score obtained on the scale, the higher the degree of kinesiophobia experienced by the individual.

The Minnesota Satisfaction Questionnaire-short form (MSQ-short form): The MSQ-short form is a 20-item questionnaire consisting of two dimensions: intrinsic job satisfaction and extrinsic job satisfaction. Each item is rated on a 5-point Likert scale, ranging from 1 (very dissatisfied) to 5 (very satisfied). Intrinsic job satisfaction comprises 12 items, while extrinsic job satisfaction comprises eight items. The neutral satisfaction score is 3, based on the sum of the score (19). A final score higher than 3 indicates high job satisfaction, while a score smaller than 3 indicates low job satisfaction. The Turkish version of MSQ-short form has been validated and shown to be reliable (20).

The evaluation of job satisfaction includes total job satisfaction, intrinsic job satisfaction, and extrinsic job satisfaction. Intrinsic job satisfaction focuses on factors related to the nature of the job itself, such as the job content, responsibility, and opportunities for advancement and promotion. Extrinsic job satisfaction, on the other hand, primarily involves factors external to the job, such as company policies and management, relationships with coworkers and supervisors, working conditions, and salary.

This project received approval from the Ethics Committee of Antalya Training and Research Hospital on January 26, 2023 (protocol number 2/10). Informed consent was obtained from all individual participants included in the study. In accordance with the principles of the Helsinki Declaration, this research was conducted with full adherence to ethical standards and the protection of human rights. All aspects of the study involving human participants were carried out in strict compliance with the Helsinki Declaration's guidelines and regulations.

Statistical Analysis

The normality of the data was assessed using visual methods (histograms and Q–Q plots) as well as the Kolmogorov–Smirnov test. Although certain variables showed minor deviations from normal distribution, descriptive statistics were presented as mean ± standard deviation throughout the manuscript to ensure consistency and to facilitate clinical interpretation. Accordingly, parametric summaries were preferred. For group comparisons, non-parametric tests (Kruskal–Wallis) were used in cases where assumptions of normality were not sufficiently met. Categorical variables were compared using the Chi-square test. A p-value of less than 0.05 *($p<0.05$)* was considered statistically significant.

Results

Patients General Characteristics

A total of 64 patients were included in the study, consisting of 47 (73.4%) females and 17 (26.6%) males, with a mean age of 34.6 years. The occupational distribution of the patients in the study was 31 nurses and 33 medical secretaries. Among the 64 patients,

the mean pain (VAS) score was 6.9 (range = 4–10). Patients average scores for total job satisfaction and intrinsic job satisfaction exceeded 3, whereas the average score for extrinsic job satisfaction was below 3. Among the patients, 34% exhibited a severe Neck Disability Index (NDI) score, while 27% showed mild disability. Additionally, 36% of the patients had a mild Beck Depression Inventory (BDI) score, and 11% exhibited severe depression. The average score for the Tampa Scale of Kinesiophobia (TSK) was 42. The demographic characteristics of the study population and the evaluation results are summarized in Table I.

Table I. General characteristics of the study population

	Total (N=64)
Gender, n (%)	
Female	47 (73.4%)
Male	17 (26.6%)
Profession, n (%)	
Nurse	31 (48.4%)
Medical secretary	33 (51.6%)
NDI, n (%)	
Mild	17 (26.6%)
Moderate	21 (32.8%)
Severe	22 (34.4%)
BDI, n (%)	
Minimal	17 (26.6%)
Mild	23 (35.9%)
Moderate	17 (26.6%)
Severe	7 (10.9%)
Age (year)	
Mean (SD)	34.6 (9.25)
VAS	
Mean (SD)	6.9 (1.45)
TSK	
Mean (SD)	42.3 (9.21)
MSQ-Total	
Mean (SD)	3.2 (0.87)
MSQ-Intrinsic	
Mean (SD)	3.4 (0.88)
MSQ-Extrinsic	
Mean (SD)	2.9 (1.03)

NDI: Neck Disability Index, BDI: Beck Depression Inventory, VAS: Visual Analog Scale,TSK: Tampa Scale for Kinesiophobia, MSQ: Minnesota Satisfaction Questionnaire

Gender-specific Patient Characteristics

Among female patients, there were 26 nurses and 21 medical secretaries, while among male patients, there were 5 nurses and 12 medical secretaries. The average pain (VAS) score was higher in female patients (7.3) compared to males (5.8), and this difference was statistically significant (*p=0.0009*). Scores for depression status, disability, and kinesiophobia (BDI, NDI, TSK) were higher in females compared to males, and these differences were statistically significant (*p=0.0147, p=0.0016, p=0.0158*) In the evaluation of the Minnesota Job Satisfaction Scale, total, extrinsic, and intrinsic job satisfaction scores were lower in females compared to males, but only intrinsic job satisfaction showed a statistically significant difference *(p=0.0306*), with females reporting significantly lower intrinsic satisfaction than males. The assessment results of patients according to gender are shown in Table II.

Table II. Gender-specific Patient Characteristics:

	Gender		
	Female (N=47)	**Male (N=17)**	***p*-value**
Profession, n (%)			0.067[1]
Nurse	26 (55.3%)	5 (29.4%)	
Medical secretary	21 (44.7%)	12 (70.6%)	
NDI, n (%)			0.001[1]
Mild	7 (14.9%)	10 (58.8%)	
Moderate	18 (38.3%)	3 (17.6%)	
Severe	20 (42.6%)	2 (11.8%)	
BDI, n (%)			0.014[1]
Minimal	8 (17.0%)	9 (52.9%)	
Mild	17 (36.2%)	6 (35.3%)	
Moderate	15 (31.9%)	2 (11.8%)	
Severe	7 (14.9%)	0 (0.0%)	
Age (year)			0.493[2]
Mean (SD)	35.1 (9.60)	33.1 (8.30)	
VAS			0.000[2]
Mean (SD)	7.3 (1.29)	5.8 (1.38)	
TSK			0.015[2]
Mean (SD)	44.0 (8.35)	37.5 (10.06)	
MSQ-Total			0.097[2]
Mean (SD)	3.1 (0.90)	3.6 (0.65)	
MSQ-Intrinsic			0.030[2]
Mean (SD)	3.2 (0.92)	3.8 (0.57)	
MSQ-Extrinsic			0.241[2]
Mean (SD)	2.8 (1.04)	3.2 (0.97)	

[1]Chi-Square p-value; [2]Kruskal-Wallis p-value NDI: Neck Disability Index BDI: Beck Depression Inventory VAS: Visual Analog Scale TSK: Tampa Scale for Kinesiophobia MSQ: Minnesota Satisfaction Questionnaire

Occupational Group Characteristics of Patients

By occupation group, patient characteristics were assessed, revealing that the secretary group was younger in age (32) compared to the nurse group (37). In the nurse patient group, female gender was dominant (n:26), while in the secretary patient group, male gender was dominant (n:21). No significant differences were found between the two professions in terms of disability, pain scores, kinesiophobia, and job satisfaction (NDI, VAS, TSK, MSQ). However, in the nurse group, BDI depression scores were significantly higher compared to the secretary group (*p=0.0481*). Occupational Group Characteristics of Patients are Presented in Table III.

Table III. Occupational Group Characteristics of Patients

	Nurse (N=31)	Medical secretary (N=33)	*p*-value
Gender, n (%)			0.067[1]
Female	26 (83.9%)	21 (63.6%)	
Male	5 (16.1%)	12 (36.4%)	
BDI			0.0482
Mean (SD)	18.5 (10.71)	13.4 (8.94)	
Age (year)			0.015[2]
Mean (SD)	37.4 (9.57)	32.0 (8.24)	
VAS			0.592[2]
Mean (SD)	6.8 (1.25)	6.9 (1.64)	
MSQ-Total			0.332[2]
Mean (SD)	3.1 (0.84)	3.3 (0.90)	

[1]Chi-Square p-value; [2]Kruskal-Wallis p-value NDI: Neck Disability Index BDI: Beck Depression Inventory VAS: Visual Analog Scale TSK: Tampa Scale for Kinesiophobia MSQ: Minnesota Satisfaction Questionnaire

The Relationship Between the Minnesota Satisfaction Questionnaire and Other Parameters

Minnesota total job satisfaction was high (3 and above) in 43 people, while it was low in 21 people. The pain, disability, and depression scale scores (VAS, NDI, and BDI) of those with low total job satisfaction were statistically significantly higher than those with high total job satisfaction (*p=0.0112, p=0.0130, p=0.0004*). However, no significant relationship was found between total job satisfaction and kinesiophobia (TAMPA) scores.

In individuals with low Minnesota intrinsic job satisfaction (n:14), the BDI was significantly higher(*p<0.001*). No significant relationship was found between disability, pain, and kinesiophobia (NDI, VAS, TAMPA) scores and intrinsic job satisfaction. In individuals with low Minnesota extrinsic job satisfaction (n:28), the scores for pain, depressive state, and kinesiophobia (VAS, BDI, TAMPA) were significantly higher compared to those with high job satisfaction (*p=0.0627, p=0.0001, p=0.0426*) However, no significant relationship was found between disability (NDI) scores and extrinsic job satisfaction. (Table IV)

Table IV. The Relationship Between the Minnesota Satisfaction Questionnaire and Other Parameters

	MSQ-Total		
	≥3 (N=43)	<3 (N=21)	*p*-value
VAS			0.011[2]
Mean (SD)	6.5 (1.47)	7.6 (1.16)	
NDI			0.013[2]
Mean (SD)	17.4 (10.37)	24.5 (8.28)	
BDI			0.000[2]
Mean (SD)	12.6 (7.71)	22.5 (11.22)	
TSK			0.061[2]
Mean (SD)	41.0 (9.15)	44.8 (9.01)	
	MSQ-Intrinsic ≥ 3 **(N=50)**	< 3 **(N=14)**	
VAS			0.124[2]
Mean (SD)	6.7 (1.47)	7.5 (1.22)	
NDI			0.341[2]
Mean (SD)	19.0 (10.48)	22.4 (9.14)	
BDI			<.000[2]
Mean (SD)	12.8 (8.17)	26.6 (8.98)	
TSK			0.092[2]
Mean (SD)	41.2 (9.78)	45.9 (5.64)	
	MSQ-Extrinsic ≥3 **(N=36)**	<3 **(N=28)**	
VAS			0.062[2]
Mean (SD)	6.6 (1.42)	7.3 (1.43)	
NDI			0.070[2]
Mean (SD)	17.6 (10.96)	22.5 (8.65)	
BDI			0.000[2]
Mean (SD)	11.6 (7.78)	21.3 (10.22)	
TSK			0.042[2]
Mean (SD)	40.0 (10.40)	45.1 (6.50)	

[1]Chi-Square p-value; [2]Kruskal-Wallis p-value, NDI: Neck Disability Index BDI: Beck Depression Inventory VAS: Visual Analog Scale TSK: Tampa Scale for Kinesiophobia MSQ: Minnesota Satisfaction Questionnaire

The Relationship Between the Beck Depression Inventory and Other Parameters

The Beck Depression Inventory was divided into four categories: minimal, mild, moderate, and severe. As the severity of BDI increased, statistically significant increases were observed in patients' pain, disability, and kinesiophobia scores (VAS, NDI, TSK), particularly between the severe and minimal groups. Conversely, job satisfaction scores (MSQ-total, intrinsic, and extrinsic) significantly decreased, with the lowest scores seen in the severe group. Specifically, pain intensity scores (VAS) significantly increased across BDI categories, with the highest scores observed in patients with severe depression (*p=0.024*) (Table V)

Table V. The Relationship Between the Beck Depression Inventory and Other Parameters

	BDI				
	Minimal (N=17)	Mild (N=23)	Moderate (N=17)	Severe (N=7)	*p*-value
Gender, n (%)					0.014[1]
Female	8 (47.1%)	17 (73.9%)	15 (88.2%)	7 (100.0%)	
Male	9 (52.9%)	6 (26.1%)	2 (11.8%)	0 (0.0%)	
Profession, n (%)					0.305[1]
Nurse	6 (35.3%)	10 (43.5%)	10 (58.8%)	5 (71.4%)	
Medical secretary	11 (64.7%)	13 (56.5%)	7 (41.2%)	2 (28.6%)	
VAS					0.024[2]
Mean (SD)	5.9 (1.60)	7.0 (1.40)	7.4 (1.12)	7.6 (0.98)	
NDI					0.007[2]
Mean (SD)	13.8 (10.68)	19.2 (9.49)	22.5 (8.84)	29.1 (5.55)	
TSK					0.011[2]
Mean (SD)	36.2 (12.91)	43.3 (6.66)	43.6 (4.33)	50.3 (6.60)	
MSQ-Total					0.004[2]
Mean (SD)	3.7 (0.66)	3.4 (0.73)	2.9 (0.77)	2.2 (1.04)	
MSQ-Intrinsic					0.003[2]
Mean (SD)	3.9 (0.57)	3.5 (0.77)	3.1 (0.83)	2.5 (1.07)	
MSQ-Extrinsic					0.000[2]
Mean (SD)	3.5 (0.74)	3.1 (0.92)	2.5 (0.97)	1.8 (0.87)	

[1]Chi-Square p-value; [2]Kruskal-Wallis p-value; NDI: Neck Disability Index BDI: Beck Depression Inventory VAS: Visual Analog Scale TSK: Tampa Scale for Kinesiophobia MSQ: Minnesota Satisfaction Questionnaire

Discussion

In this study, we found that lower job satisfaction among healthcare workers with chronic neck pain was significantly associated with higher levels of pain, disability, depression, and kinesiophobia. Notably, pain severity was not only higher in those with lower job satisfaction but also increased in parallel with depression severity. These findings highlight the bidirectional impact of pain on both psychological well-being and occupational satisfaction. The results underscore the complex interplay between physical symptoms and psychosocial factors in employees with chronic neck pain.

Pain is an unpleasant sensation that negatively affects individuals' daily functioning and quality of life, with responses varying between individuals depending on pain tolerance and acceptance (21). In a study involving individuals with back and neck pain, it was found that their physical functioning was more impaired than that of healthy controls, and they experienced greater limitations in work and daily activities (22). Similarly, in a study on job satisfaction among healthcare workers, the rate of dissatisfaction was reported as 35%, close to the 33% rate found in our study (23). In our study, workers with lower job satisfaction had significantly higher levels of pain, disability, and depression, indicating a multifaceted interaction between physical and psychological well-being in the workplace.

In our study, the professional groups consisted of nurses and medical secretaries, whereas the referenced study involved research assistant physicians working at a university hospital (23). The mean age of the participants in our study was 35, slightly higher than the 30 years reported in the physician group. Previous research has suggested that younger age and shorter professional experience may be associated with lower job satisfaction (24). While we did not collect data on years of employment, it is noteworthy that medical secretaries and nurses typically enter the workforce at an earlier age compared to physicians, due to shorter educational training. This difference in career trajectories may partly account for variation in job satisfaction across occupational groups.

In another study conducted with nurses and physicians, the average job satisfaction score of physicians was significantly higher compared to nurses (25). In the same study, significant differences were found between male and female employees in terms of total job satisfaction as well as intrinsic and extrinsic job satisfaction, with female employees

having lower job satisfaction (25). In our study, 73.4% of the participants were female, and there was no difference in the average age between genders. While no differences were found between men and women in terms of total job satisfaction and extrinsic satisfaction, intrinsic satisfaction was significantly lower in women. Additionally, pain intensity, disability, kinesiophobia, and depression were found to be significantly higher in women compared to men. A recent systematic review and meta-analysis involving over 347,000 individuals with chronic pain reported that approximately 40% experienced clinically significant symptoms of depression and anxiety, with notably higher prevalence among women and younger individuals. Similarly, in our study, depressive symptoms were significantly more common in female participants, who also reported higher levels of pain intensity compared to males. These findings support the growing evidence of a gender-related vulnerability to psychological distress in individuals with chronic pain (26).

In patients with chronic pain, there is often a reluctance to exercise and kinesiophobia due to the fear of exacerbating the pain (27). In a study conducted with men and women suffering from chronic low back pain, similar to our study, disability and kinesiophobia were found to be higher in women compared to men. Additionally, the same study found that pain intensity was also higher in women (28). Although our study did not statistically evaluate the relationship between pain intensity and kinesiophobia, previous studies have reported a positive association between these two variables. For instance, in a study conducted on sedentary individuals with and without chronic pain, kinesiophobia was found to be more common in those with chronic pain (28).

Previous studies have shown that chronic low back and neck pain are closely associated with depression, with depression being more common in patients with chronic pain compared to the normal population (29). While the prevalence of depression in the general population is 5-8%, this rate is between 30-54% in patients with chronic pain (30). In our study, consistent with the literature, a positive relationship was found between pain intensity and depression. It was also found that as the severity of depression increased in patients, both disability and job dissatisfaction increased. In our study, it was determined that the increase in the severity of depression not only reduced total job satisfaction but also negatively affected the subgroups of job satisfaction, such as intrinsic and extrinsic job satisfaction. There are also studies reporting a positive correlation between the severity of depression and the duration of pain (31). In our study, patients with a pain duration of 3 months or more were included, but the exact duration was not specified; therefore, the relationship between depression and pain duration could not be evaluated.

In a study conducted between medical secretaries and administrative staff working in hospitals, it was found that the BDI scores were low in medical secretaries, similar to those of administrative staff who do not have direct contact with patients (32). In our study, total BDI scores in the patient group were significantly lower in medical secretaries compared to the nurse patient group. Additionally, while the number of nurses was higher in the female patient group (55.3%), the number of medical secretaries was higher in the male patient group (70.6%). Therefore, it is considered that the difference in the severity of depression between female and male healthcare workers in our study may be related not only to gender but also to the profession. It is thought that besides encountering patients, the communication of medical secretaries with patients on matters other than diagnosis/treatment and clinical follow-up, as required by their job description, may be a factor contributing to this difference.

A study conducted in Nigeria among 355 academic staff examined the relationship between job satisfaction and musculoskeletal problems. The findings revealed that as the severity and frequency of musculoskeletal symptoms—such as back pain, neck pain, and upper limb discomfort—increased, overall job satisfaction decreased. The study emphasizes the negative impact of musculoskeletal complaints on employees' perceived satisfaction with their work and highlights the importance of addressing physical health in occupational well-being strategies. Similarly, in our study, we found that increased neck pain severity was associated with reduced job satisfaction (33).

The main limitations of this study include the absence of data on factors such as work duration, educational background, marital status, number of children, and shift duration, which are commonly considered in job satisfaction research. The study focused on healthcare workers with chronic neck pain, specifically secretaries and nurses in Antalya, Turkey, limiting the generalizability of findings to other regions or healthcare worker populations. Moreover, although both groups were selected from non-physical labor occupations, the job demands, responsibilities, and work-related stress levels of secretaries and nurses may differ considerably, which may have influenced the study variables and further limited generalizability.

Additionally, the lack of a control group of healthcare workers without chronic pain restricts the ability to establish causal relationships between pain, depression, and job satisfaction. Future research with more diverse samples and control groups is recommended to enhance the generalizability and provide clearer insights into these dynamics.

Conclusion

This study highlights the associations between depression, pain, and disability and their potential influence on job satisfaction among healthcare workers with chronic neck pain. The findings suggest that lower job satisfaction is related to higher levels of pain, disability, and depression. Furthermore, greater severity of depression appears to be associated with reduced job satisfaction and increased pain intensity. These observations underline the importance of addressing pain and depressive symptoms in this population, which may contribute to improving job satisfaction. Further research, particularly involving control groups, is recommended to better understand the interplay between chronic pain, job satisfaction, and depression. Such studies could help clarify causal relationships and support the development of strategies aimed at improving the overall well-being of healthcare workers.

References

1. Treede RD, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the ICD-11. Pain 2019;160(1):19–27.
2. Peters L, Simon EP, Folen RA, Umphress V. The COPE program: treatment efficacy and medical utilization outcome of a chronic pain management program at a major military hospital. Mil Med 2000;165(12):954-960.
3. Krishnan KRR, France RD, Davidson J. Depression as a psychopathological disorder in chronic pain. Chronic Pain 1988:195-218.
4. Rudy TE, Kerns RD, Turk DC. Chronic pain and depression: toward a cognitive-behavioral mediation model. Pain 1988;35:129-140.
5. Ganuyi SO, Olabode JA, Stanley MM, Muhammed I. Patterns of occurrence of work-related musculoskeletal disorders and its correlation with ergonomic hazards among health care professionals. Nig J Exp Clin Bio 2015;3(1):18-23.
6. Linton SJ. A review of psychological risk factors in back and neck pain. Spine 2000;25(9):1148-1156.
7. Macfarlane GJ, Hunt MI, Silman AJ. Role of mechanical and psychosocial factors in the onset of forearm pain: prospective population based study. BMJ 2000;321(7262):676.
8. Lang J, Ochsmann E, Kraus T, Lang JW. Psychosocial work stressors as antecedents of musculoskeletal problems: a systematic review and meta-analysis of stability-adjusted longitudinal studies. Soc Sci Med 2012;75(7):1163-1174.
9. Boonstra AM, Preuper HRS, Balk GA, Stewart RE. Cut-off points for mild, moderate, and severe pain on the visual analogue scale for pain in patients with chronic musculoskeletal pain. Pain 2014;155(12):2545-2550.
10. Dixon JS, Bird HA. Reproducibility along a 10 cm vertical visual analogue scale. Ann Rheum Dis 1981;40(1):87-89.
11. Vernon H, Mior S. The neck disability index: a study of reliability and validity. J Manipulative Physiol Ther 1991;14(7):409-415.
12. Fairbank JCT, Cooper J, Davies JB, O'Brien JP. The Oswestry low back pain disability index. Physiotherapy 1980;66:271-273.
13. Vernon H. The neck disability index: state of the art 1991-2008. J Manipulative Physiol Ther 2008;31(7):491-502.
14. Kesiktas N, Ozcan E, Vernon H. Clinimetric properties of the Turkish translation of a modified neck disability index. BMC Musculoskelet Disord 2012;13:1-6.
15. Hisli N. Beck Depresyon Envanterinin Üniversite Öğrencileri İçin Geçerliği, Güvenirliği. Psikoloji Dergisi 1989;7:3-13.
16. Vlaeyen JW, Kole-Snijders AM, Boeren RG, Van Eek H. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. Pain 1995;62(3):363-372.
17. Kori SH, Miller RP, Todd D. Kinesophobia: a new view of chronic pain behaviour. Pain Management 1990;3:35-43.
18. Yılmaz ÖT, Yakut Y, Uygur F, Uluğ N. Tampa Kinezyofobi

Ölçeği'nin Türkçe versiyonu ve test-tekrar test güvenirliği. Fizyoter Rehabil 2011;22(1):44-49.
19. Hirschfeld RR. Does revising the intrinsic and extrinsic subscales of the Minnesota Satisfaction Questionnaire short form make a difference? Educ Psychol Meas 2000;60(2):255-270.
20. Baycan AF. Analysis of Several Effects of Job Satisfaction between Different Occupational Groups. [Master's thesis]. İstanbul: Boğaziçi University Institute of Social Science; 1995.
21. Fidaner H, Elbi H, Fidaner C, Eser SY, Eser E, Göker E. Yaşam kalitesinin ölçülmesi. WHOQOL-100 ve WHOQOL-BREF. 3P Dergisi 1999;7:5-13.
22. Yazıcı K, Tot Ş, Biçer A, Yazıcı A, Buturak V. Bel ve boyun ağrısı hastalarında anksiyete, depresyon ve yaşam kalitesi. Klinik Psikiyatri Dergisi 2003;6(2):95-101.
23. Yaşan A, Eşsizoğlu A, Yalçın M, Özkan M. Bir üniversite hastanesinde çalışan araştırma görevlilerinde iş memnuniyeti, anksiyete düzeyi ve ilişkili etmenler. Dicle Tıp Dergisi 2008;35(4):228-233.
24. Öztürk Z, Çelik G, Örs E. Sağlık çalışanlarında tükenmişlik ve iş doyumu ilişkisi: bir kamu hastanesi örneği. Ulus Sağlık Yön Strateji Arş Derg 2020;6(2):328-349.
25. Erşan EE, Yıldırım G, Doğan O, Doğan S. Sağlık çalışanlarının iş doyumu ve algılanan iş stresi ile aralarındaki ilişkinin incelenmesi. Anadolu Psikiyatri Dergisi 2013;14(2):115-121.
26. Aaron RV, Ravyts SG, Carnahan ND, et al. Prevalence of depression and anxiety among adults with chronic pain: A systematic review and meta-analysis. JAMA Network Open 2025;8(3):e250268
27. Usta N. Kronik bel ağrılı hastalarda farklı cinsiyetlerde ağrı yönetiminin kinezyofobi, fiziksel aktivite ve özürlülük düzeyi ile ilişkisi. [Yüksek Lisans Tezi]. Denizli: Pamukkale Üniversitesi Sağlık Bilimleri Enstitüsü; 2021.
28. Altuğ F, Ünal A, Kılavuz G, Kavlak E, Çitişli V, Cavlak U. Investigation of the relationship between kinesiophobia, physical activity level and quality of life in patients with chronic low back pain. J Back Musculoskelet Rehabil 2016;29(3):527-531.
29. Dworkin RH, Gitlin MJ. Clinical aspects of depression in chronic pain patients. Clin J Pain 1991;7:79-94.
30. Haythornthwaite JA, Sieber WJ, Kerns RD. Depression and the chronic pain experience. Pain 1991;46:177-184.
31. Altındağ Ö, Altındağ A, Soran N. Kronik ağrılı hastalarda depresyon düzeyinin ağrı şiddeti ve süresi ile ilişkisinin araştırılması. Symposium Journal 2006;44(4):178-181.
32. Çetin E, Özdengül F, Yargıç MP, Aydın L. Tıp fakültesinde çalışan tıbbi sekreterlerin ve idari personelin mesleki doyumları, tükenmişlikleri, depresyon düzeyleri ve fiziksel aktivite düzeyleri. Sağlık Bilimleri Dergisi 2021;30(1):37-42.
33. Yongu WT, Iorvaa T, Burbwa SN, Zwawua O, Efu ME. Correlation between job satisfaction and musculoskeletal disorders among academic staff of universities in Benue State: A theoretical narrative. Educational Research and Reviews 2024;19(10):135–142.

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Analysis of Predictors of Progression-free Survival and Early Response in Young Adult Classical Hodgkin Lymphoma

Genç Erişkin Klasik Hodgkin Lenfomada Progresyonsuz Sağkalım ve Erken Yanıt Öngörücülerinin Analizi

Tuğcan Alp Kırkızlar[1] | Erge Karadağ[2] | Ahmet Yiğitbaşı[1] | Onur Kırkızlar[1] Elif Gülsüm Ümit[1] | Ahmet Muzaffer Demir[1]

[1]Trakya University Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Edirne, Türkiye
[2]Trakya University Faculty of Medicine, Department of Internal Medicine, Edirne, Türkiye

Sorumlu Yazar | Correspondence Author
Tuğcan Alp Kırkızlar
tugcanalp82@hotmail.com
Address for Correspondence: Trakya University Faculty of Medicine, Department of Internal Medicine, Division of Hematology, 22030, Edirne, Türkiye.

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Analysis of Predictors of Progression-free Survival and Early Response in Young Adult Classical Hodgkin Lymphoma

ABSTRACT

Objective: Classical Hodgkin lymphoma (HL) is a common malignancy among adolescents and young adults (AYA). As this age group has biological, clinical, and psychosocial differences compared to other age groups, it is referred to as the AYA group. The present study aimed to evaluate young adult patients diagnosed with classical HL at our center and identify predictors of complete response (CR) at interim evaluation and progression-free survival (PFS).

Material and Method: Patients aged 18-39 years diagnosed with classical HL who were treated and followed up at our center between 2015 and 2023 were retrospectively analyzed.

Results: The median age of 54 patients was 30 years, and 53.7% were female. Nodular sclerosis was the most common subtype, observed in 61.1% of cases. At diagnosis, 48.1% of patients were in the early stage, while 51.9% were in the advanced stage. Among early-stage patients, 53.8% were categorized as unfavorable risk, whereas 46.4% and 7.1% of advanced-stage patients were classified as intermediate and high risk, respectively. In the first-line treatment, 92.6% of patients were treated with the ABVD protocol. At the interim evaluation, the CR rate was 66.1%, while the CR rate at the end of treatment was 88%. The mortality rate was 3,7% during a median follow-up of 47.5 months. The mean overall survival was 107.4 months. The mean PFS was 83.5 months, with no statistically significant difference between the early CR and non-CR groups (*p=0.197*). When the predictors of PFS and CR at interim assessment were analyzed in multivariate analyses, no significant variables were found.

Conclusion: In our study, our results are similar to the literature, and the survival and response rates in the patient population, almost all of whom were on the ABVD protocol, are also encouraging. Despite analyzing potential predictors of PFS and early CR for guiding treatment and follow-up, no significant factors were identified. Furthermore, achieving early CR did not significantly impact PFS.

Keywords: Hodgkin disease, Progression-free survival, Young adults.

ÖZET

Amaç: Klasik Hodgkin lenfoma (HL) ergen-genç erişkin yaş grubunda (AYA) sık görülen bir malignitedir. Bu yaş grubu diğer yaş gruplarına göre biyolojik, klinik ve psikososyal farklılıklara sahip olduğundan AYA grubu olarak ifade edilmektedir. Biz de bu çalışmayla merkezimizdeki genç erişkin grupta Klasik HL tanılı olgularımızı değerlendirmeyi, ara değerlendirmede tam yanıtın (CR-erken yanıt) ve progresyonsuz sağkalım (PFS) öngörücülerini belirlemeyi amaçladık.

Gereç ve Yöntem: 2015-2023 tarihleri arasında merkezimizde klasik HL tanısı alarak tedavi ve izlemi yapılan 18-39 yaş grubundaki hastalar retrospektif olarak incelendi.

Bulgular: Elli-dört hastanın ortanca yaşı 30 yıl ve %53,7'i kadındı. En sık alt tip nodüler sklerozan olup olguların %61,1'inde görüldü. Tanı anında, hastaların %48,1'i erken evredeyken %51,9'u ileri evreydi. Erken evre hastaların %53,8'i olumsuz risk grubundayken ileri evre hastaların %46,4've %7,1'i orta ve yüksek riske sahipti. İlk sıra tedavide hastaların %92,6'sına ABVD protokolü uygulanmıştı. Ara değerlendirmede CR oranı %66,1 iken tedavi sonunda CR oranı %88 idi. Ortanca 47,5 aylık izlem sürecinde mortalite oranı %3,7 idi. Ortalama toplam sağkalım süresi 107.4 aydı. Ortalama PFS süresi 83,5 ay olup, erken yanıt sağlanan ve sağlanamayan gruplar arasında istatiksel fark bulunmadı (*p=0.197*). PFS ve ara değerlendirmede CR öngörücüleri multivariate analizlerde incelendiğinde anlamlı değişken saptanmadı.

Sonuç: Çalışmamızda sonuçlarımız literatürle benzerlik göstermekte olup, tamamına yakınına ABVD protokolü uygulanan hasta grubumuzda sağkalım ve tedavi yanıt oranları da yüz güldürücüdür. Hastaların tedavi yaklaşımı ve izleminde katkı sağlayabilecek PFS ve erken CR öngörücüleri incelenmiş ancak anlamlı değişkenler saptanamamıştır. Bunun yanında erken CR sağlanmasının PFS farkı anlamlı bulunmamıştır.

Anahtar Sözcükler: Genç erişkin, Hodgkin hastalığı, Progresyonsuz sağkalım.

Introduction

Hodgkin lymphoma (HL) is a lymphoid malignancy classified into two main groups based on morphology and immunophenotype: classical and nodular lymphocyte predominant. Classical Hodgkin lymphoma accounts for approximately 90% of all HL cases. It includes four subtypes: 'nodular sclerosis,' 'lymphocyte-rich,' 'lymphocyte-depleted,' and 'mixed cellularity.' While different types and subtypes of HL have a bimodal age distribution or peak in different age groups, overall HL peaks in the 15-35 and over 55 age groups (1-3).

The National Cancer Institute (NCI) defines the 15–39 age group as adolescents and young adults (AYA), considering their distinct pathogenesis, treatment, and psychosocial characteristics. This concept, widely accepted, is also applied to solid tumors and some hematological malignancies, particularly acute lymphoblastic leukemia. The highest incidence of HL occurs in the AYA group. Although there is extensive literature on the management and treatment of older HL patients, research specific to the AYA group remains limited (4-6).

From a treatment point of view, pediatric or adult protocols can be used for this age group, but the results of the studies are controversial. In our country, adult-based protocols are generally preferred for young adults. According to guidelines, initial treatment with the ABVD chemotherapy protocol (adriamycin, vinblastine, dacarbazine, bleomycin) is recommended, except in selected cases of advanced-stage disease. Depending on interim assessment responses, options include dose-reduced or bleomycin-excluded protocols (AVD: adriamycin, vinblastine, dacarbazine), combination with radiotherapy, or intensified treatments (BEACOPP: bleomycin, etoposide, doxorubicin, cyclophosphamide, vinblastine, procarbazine, prednisone), or second-line therapies (7).

In our study, we aimed to evaluate epidemiological, clinical, and treatment outcomes of AYA patients diagnosed with classical HL at our center and to identify predictors of early complete response (CR) and progression-free survival (PFS).

Material and Method

This retrospective study was conducted on patients aged 18–39 years newly diagnosed with classical Hodgkin lymphoma (HL) at the Trakya University Faculty of Medicine, Department of Hematology, between January 2015 and December 2023. The study was performed in compliance with the principles of the Declaration of Helsinki and approved by the Trakya University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (TÜTF-GOBAEK 2024/417). All of the patients' data were obtained from both electronic and hand-written medical records. Fifty-four patients aged 18–39 years who had been diagnosed with classical HL and whose treatments and evaluations were conducted at our center were included in the study. Patients with classical HL subtypes—'nodular sclerosis,' 'lymphocyte-rich,' 'lymphocyte-depleted,' and 'mixed cellularity'—based on morphological and immunophenotypical evaluations were included. However, nodular lymphocyte predominant HL was considered a separate entity and excluded (3). Data on patients' age, sex, date of diagnosis, B symptoms, morphological and immunohistochemical findings, disease subtypes, presence of extranodal disease, bulky disease, bone marrow involvement, laboratory parameters (hemoglobin, leukocyte, lymphocyte, lactate dehydrogenase (LDH), albumin, and erythrocyte sedimentation rate (ESR) levels, imaging studies (ultrasound (US), computed tomography (CT), positron emission tomography/CT (PET/CT), magnetic resonance imaging (MRI)), lymph node/tissue/bone marrow biopsy evaluations, treatments received, and treatment responses were collected. Staging was performed using the Lugano classification, derived from the Ann Arbor staging system, based on PET/CT imaging findings (8,9). The presence of B symptoms was defined as fever >38°C within the past month, recurrent night sweats, or unintended weight loss exceeding 10% of body weight in the previous six months. Extranodal involvement was classified as limited to nodal-adjacent or closely proximal extranodal sites or as widespread extranodal involvement. Bulky disease was defined as abdominal lymph nodes or masses ≥10 cm in greatest dimension, or mediastinal masses ≥10 cm or exceeding one-third of the thoracic transverse diameter as determined by CT, MRI or US (8,9). Bone marrow involvement was assessed

through morphological and immunohistochemical analyses of unilateral bone marrow aspiration and biopsy samples. Prognosis was assessed using the European Organisation for Research and Treatment of Cancer (EORTC) unfavorable factors for stage I-II patients and the International Prognostic Score-7 (IPS-7) for stage III-IV patients (10,11).

During first-line treatment, clinical, laboratory and PET/CT imaging evaluations were conducted for interim assessment after 2–4 cycles and for end-of-treatment assessment upon planned treatment completion. Response status was classified according to the Lugano response criteria, based on metabolic response assessed using the Deauville score (a 5-point scale) from PET/CT reports. Complete response (CR) was defined as a Deauville score of 1–3 in nodal or extranodal sites, with or without a residual mass. Partial response (PR) was defined as a score of 4 or 5 with reduced uptake compared to baseline and residual mass(es) of any size. Stable disease (SD) was defined as a score of 4 or 5 with no significant change in uptake from baseline. Progressive disease (PD) was defined as a score of 4 or 5 with increased uptake from baseline and/or the presence of new FDG-avid foci consistent with disease. Relapsed disease was defined as the recurrence of the disease in existing or new foci confirmed through morphological and immunohistochemical analysis after achieving CR, while primary refractory disease was defined as a lack of CR or PR to initial therapy. For first-line treatment, patients received the ABVD protocol (doxorubicin, vinblastine, dacarbazine, bleomycin) or the A-AVD protocol (brentuximab vedotin, doxorubicin, vinblastine, dacarbazine) in cases of advanced-stage disease, known pulmonary pathology, or pulmonary involvement with impaired pulmonary function tests. Autologous hematopoietic stem cell transplantation (AHSCT) was performed in cases of relapse or primary refractory disease where chemosensitivity was demonstrated following salvage therapy.

Patients were followed until their last outpatient visit or death. Progression-free survival (PFS) was defined as the time from treatment initiation to disease progression. Overall survival (OS) was calculated from the date of diagnosis to the last follow-up or death.

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 26, 2019). Continuous variables were expressed as mean and median values, while categorical variables were expressed as percentages. Overall survival (OS) and progression-free survival (PFS) analyses, as well as group comparisons, were conducted using Kaplan-Meier and log-rank survival analyses. A *p-value of <0.05* was considered statistically significant. Logistic regression analysis was used to evaluate predictors of complete response (CR) at interim evaluation, while Cox regression analysis assessed predictors of progression-free survival (PFS). Variables with p-values of 0.20 or less in univariate analyses were included in multivariate analyses. Variables with *p-values of <0.05* in multivariate analyses were considered statistically significant. A comprehensive set of clinical and laboratory variables—including age, sex, disease subtype, stage at diagnosis, presence of B symptoms, extranodal involvement, bulky disease, splenomegaly, bone marrow involvement, hemoglobin level, leukocyte and lymphocyte counts, serum albumin, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), and first-line treatment regimen—was included in the analysis to evaluate their potential as predictors of complete response and progression-free survival (PFS). For PFS, interim and end-of-treatment response assessments were also incorporated into the analysis.

Results

Among the 54 patients aged 18–39, 53.7% were female, and the median age was 30 years. The distribution of classical Hodgkin lymphoma subtypes was as follows: nodular sclerosis (61.1%), mixed cellularity (25.9%), lymphocyte-rich (11.1%), and lymphocyte-depleted (1.9%). At diagnosis, 18.6% of the patients were stage IV according to the Lugano classification, and 29.6% presented with B symptoms. Splenomegaly was present in 27.8%, bulky disease in 5.6%, extranodal involvement in 16.7%, and bone marrow involvement in 5.5% of patients. For patients in stages I and II (26 patients, 48.1%), EORTC risk assessment categorized 46.2% as favorable risk and 53.8% as unfavorable risk. In advanced-stage patients (stages III and IV) categorized by IPS-7, 46.5% were low risk, 46.4% medium risk and 7.1% high risk. At

diagnosis, the median erythrocyte sedimentation rate was 35.5 mm/hour, LDH level was 243.5 U/L, albumin level was 4.15 g/dL, leukocyte count was 9.750/mm^3, lymphocyte count was 1.540/mm^3 and hemoglobin level was 11.9 g/dL (Table I).

Table I. Distribution Characteristics of 54 Newly Diagnosed Patients with Classical Hodgkin Lymphoma Aged 18-39 Years

Variable	
Age (median) (n:54)	30 years (min-max:18-39 years)
Sex (n:54) (%)	Female: 53,7 Male: 46,3
Subtype of classical Hodgkin Lymphoma (n:54) (%)	Nodular sclerosis: 61,1 Lymphocyte-rich: 11,1 Lymphocyte-depleted: 1,9 Mixed cellularity: 25,9
Stage of disease based on the Lugano classification (n:54) (%)	I: 7,4 II: 40,7 III: 33,3 IV: 18,6
B symptoms (n:54) (%)	29,6
Extranodal involvement (n:54) (%)	16,7
Bulky disease (n:54) (%)	5,6
Splenomegaly (n:54) (%)	27,8
Bone marrow involvement (n:54) (%)	5,5
Median hemoglobin level (n:54)	11,95 g/dL (7,4-17,4)
Median leukocyte level (n:54)	9.750/mm3 (1.010-26.920)
Median lymphocyte level (n:54)	1.540/mm3 (190-3.400)
Median albumin level (n:54)	4,15 g/dL (2,6-5)
Median lactate dehydrogenase level (n:54)	243,5 U/L (122-763)
Median erythrocyte sedimentation rate level (n:54)	35,5 mm/hour (2-109)
Risk assessment based on EORTC (n: 26) (%)	Favourable: 46,2 Unfavourable: 53,8
Risk assessment based on IPS-7 (n: 28) (%)	0: 3,6 1: 14,3 2: 28,6 3: 32,1 4: 14,3 5: 7,1
First-line treatment (n:54) (%)	ABVD: 92,6 A-AVD: 7,4
Complete response with first-line treatment (n:54) (%)	88,9
Median follow-up time (n:54) (month)	47,5 (7-112)
Mean PFS time (n:54) (month)	83,5 (±5,15) (%95CI)
Mortality rate (n:54) (%)	3,7

EORTC: European Organisation for Research and Treatment of Cancer; IPS-7: International Prognostic Score-7; ABVD: Adriamycin, Bleomycin, Vinblastine, Dacarbazine; A-AVD: Brentuximab vedotin, Adriamycin, Vinblastine, Dacarbazine; PFS: Progression-free survival.

Initial treatment involved the ABVD protocol (adriamycin, vinblastine, dacarbazine, bleomycin) in 92.6% of patients, while the remaining patients received the A-AVD protocol (brentuximab vedotin, adriamycin, vinblastine, dacarbazine) per the specified indications. Interim evaluations after 2–4 courses of first-line treatment revealed complete response (CR) in 61.1%, partial response (PR) in 35.2%, and stable disease (SD) in 3.7% of patients. End-of-first-line treatment assessments showed CR in 88.9% of patients, while 11.1% had SD or progressive disease (PD). Two patients received radiotherapy. Six patients were considered to have primary refractory disease and four patients experienced relapse.

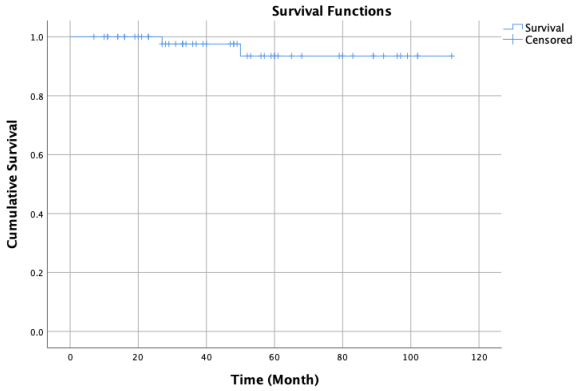

Figure I. Kaplan-Meier Survival Plot for the Entire Patient Group

Second-line treatments included brentuximab-ICE (ifosfamide, carboplatin, etoposide) in five patients, ICE in four patients, and brentuximab-bendamustine combination in one patient. These therapies achieved CR in eight patients, PR in one patient, SD in one patient and PD in one patient. Of the patients who achieved CR after second-line treatment, seven underwent autologous hematopoietic stem cell transplantation (AHSCT) and one declined. Three remaining patients received single-agent brentuximab, nivolumab, or nivolumab-brentuximab. Three patients required ≥4 lines of treatment.

During follow-up, of the eight patients who underwent AHSCT, one was evaluated as having PD at the 3-month follow-up, and another relapsed at the 9-month follow-up. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) was performed in one patient. Over a median follow-up of 47.5 months, two patients died: one due to complications following allo-HSCT and the other, a primary refractory disease

patient, from COVID-19 Pneumonia.

Kaplan-Meier survival analysis revealed a mean overall survival (OS) of 107.4 (±3.16) months (95% CI), with the median OS not reached (Figure I). The mean progression-free survival (PFS) was 83.5 (±5.15) months. When comparing groups with and without CR at interim evaluation using Kaplan-Meier log-rank analysis, the mean PFS was 88.10 (±5.63) months in the CR group and 64.40 (±7.23) months in the non-CR group, although this difference was not statistically significant (*p=0.197*, Figure II).

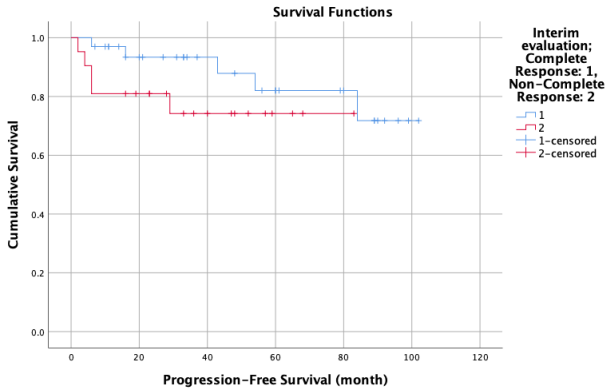

Figure II. Progression-free Survival Kaplan-Meier (log-rank) Analysis Plot of Patients with and without Complete Response at Interim Assessment

Logistic regression analysis assessed variables predictive of achieving CR at interim evaluation. In univariate analysis, male gender, higher hemoglobin levels, and receiving ABVD therapy were associated with increased CR rates (*p=0.041, p= 0.073, p=0.160,* respectively). However, these factors lost significance in multivariate analysis (*p=0.116, p=0.556, p=0.179,* respectively).

Factors predictive of PFS were evaluated using Cox regression analysis. In univariate analysis, lymphocyte-depleted subtype and A-AVD therapy were associated with shorter PFS (*p=0.030, p=0.042,* respectively). These factors lost significance in multivariate analysis (*p=0.329 and p=0.328,* respectively).

Discussion

Hodgkin lymphoma (HL) accounts for 10% of all lymphomas in developed countries. According to data from the United States, the median age at diagnosis is 39 years, with the highest incidence observed in the 20–34 age group (12). For the adolescent and young adult (AYA) group, representing the most frequently affected age range, differences in epidemiological, clinical, and treatment approaches have been proposed to result in distinct disease courses. Compared to studies on older age groups in HL, the literature focusing on the AYA group remains limited.

In a single-center study by Zawati et al. comparing AYA (15–39 years) and adult (≥40 years) classical HL patients in terms of epidemiological, clinical, and treatment outcomes, a total of 112 HL patients were included, of whom 66 represented the AYA group and 46 the adult group. The AYA group had a median age of 27.5 years, and 61% were male. Among these patients, 58% had the nodular sclerosing subtype, and 33% had the mixed cellularity subtype. Furthermore, 72% of the patients were stage II (46%) and III (26%), with B symptoms present in 54% of cases at diagnosis (13). The Pediatric Health Information System database was used to analyse age-related differences in HL in another study by Kendel et al. 3.034 patients aged 0-39 years were included, with 58% in the 15-39 age group. The median age in this age group was 17.2 years. Gender distribution analysis showed that males predominated in younger age groups, while females became more prevalent as age increased. For the 15-39 age range, 52% of the patients were female. Regarding subtype distribution, 66% of patients had the nodular sclerosis subtype, while 5% had the mixed cellularity subtype (14).

A 2021 study using Surveillance, Epidemiology, and End Results (SEER) data analyzed 15.889 patients aged 15-39 years who had survived at least five years post-diagnosis between 1980 and 2009. This study evaluated age, ethnicity, and socioeconomic status. Among these patients, 50% were male, and the median age at diagnosis was 27 years. Approximately half of the patients were stage II at diagnosis, while 12.8% were stage IV (15). The results from our clinic, which included patients aged 18 years and older, revealed a median age of 30 years—slightly higher than that reported in the literature for populations aged 15 years and above. Furthermore, the female predominance of 53.7% observed in our study aligns with similar findings reported by Kendel et al. In terms of subtype distribution, the nodular sclerosis subtype accounted for 61.1% of cases, and 40.7%

of patients were stage II at diagnosis, aligning with trends reported in previous studies.

In the adolescent and young adult (AYA) age group, there are differences in treatment protocols, with pediatric- or adult-based approaches showing varying outcomes and long-term effects. These differences continue to be debated. Supporting the efficacy of adult protocols, the 2006 study by Foltz et al evaluated HL patients between 1981 and 2004. The study compared treatment outcomes of the ABVD protocol, an adult regimen, in 16-21 and 22-45 age groups, concluding similar efficacy. 10-year progression-free survival (PFS) rates were 77% and 80%, respectively, and overall survival (OS) rates for limited disease were 96% in both groups, while in advanced disease they were 88% and 86%, respectively (16). Similarly, the German Hodgkin Study Group's 2009 comparison of 15-20 and 21-45 age groups reported similar survival outcomes (17). However, both studies lacked comparisons with pediatric regimens and assessments of long-term complications. Conversely, studies advocating pediatric-based treatments suggest superior outcomes. Although differences in case distribution between groups, staging, and response assessment criteria are noted, a 2017 study contrasting pediatric and adult protocols did not align with prior findings. In the 17-21 age group, five-year survival to treatment failure was 85% with pediatric protocols but only 68% with adult protocols. Comparing the 17-21 and 22-45 age groups treated with adult regimens, survival to treatment failure was lower in the younger group, at 68% versus 76%, demonstrating a disadvantage for younger patients treated with adult protocols (5). In the study by Marr et al. comparing 55 pediatric patients <18 years and 154 young adults aged 18-25 years, all treated with ABVD, no significant differences in sex, subtype, tumour burden or risk assessment distributions were found between the groups. They concluded that ABVD is an effective treatment (18). In Zawati et al.'s study comparing AYA and adult HL patients, 62% of the AYA group received ABVD, 21% BEACOPP and 3% MOPP-ABVD as initial treatment. With a median follow-up of 51 months, the complete response (CR) rate with initial therapy was 74%. Mortality was 20%, and relapse and refractory disease occurred in 39% of patients. The study highlighted that adolescent patients presented with more advanced diseases at diagnosis, necessitating more intensive therapies (13). In our study, the complete response (CR) rate to initial treatment was approximately 90%, with 93% of patients receiving the ABVD regimen. Over a median follow-up of 47.5 months, 18.5% of patients were classified as having either primary refractory or relapsed disease. In comparison, Zawati et al. reported a primary refractory/relapsed disease rate of 39% in the 15–39-year age group based on data from Tunisia, with a median follow-up of 51 months (13). Meanwhile, Marr et al. observed a lower rate of 19.8% in the 18–25-year age group in a Canadian cohort, with a longer median follow-up of 67 months (18). Notably, this latter finding aligns more closely with the rate observed in our study. These discrepancies may be partly attributable to differences in patient demographics—particularly ethnic background—as well as variations in follow-up duration, age group classifications and treatment approach across studies.

Regarding mortality, the study by Kendel et al, which included a detailed analysis of chemotherapy agents, treatment complications, and supportive care, reported that approximately 70% of patients received alkylating agents, vinca alkaloids, and anthracyclines, while 55% were treated with bleomycin. However, no data on treatment outcomes were included, and the overall mortality rate was reported as 1%, without specifying the causes (14). A study using Surveillance, Epidemiology, and End Results (SEER) data of HL patients surviving five years after diagnosis reported a median follow-up of 9,4 years (15). In our study, the mean overall survival (OS) was 8.95 years, and the mortality rate was 3.7%. Among the two patients who died, one had achieved complete response but succumbed to complications of allo-HSCT two years after diagnosis, while the other, with primary refractory disease, died from an infection four years after diagnosis, despite partial disease control.

Additionally, we analyzed potential predictors of early complete response (CR) and progression-free survival (PFS). However, no significant predictive variables were identified in the multivariate analyses. To the best of our knowledge, there are currently no published data specifically addressing early predictors

of CR in this context, and our findings did not reveal any such factors. Data on predictors of event-free survival (EFS) and PFS in the adolescent and young adult (AYA) population also remain limited. Although the underlying mechanisms contributing to relapse in Hodgkin lymphoma (HL) are not fully understood, several well-established adverse prognostic factors—such as advanced stage at diagnosis, bulky disease, extranodal involvement, presence of B symptoms, and suboptimal early treatment response—are thought to increase the risk of relapse. In a study by Zawati et al. focusing on AYA patients, advanced stage was identified as the primary predictor of inferior EFS, while treatment with the ABVD regimen was associated with improved EFS (13). Similarly, in another study evaluating patients aged 6 to 25 years, Ann Arbor stage IV disease, presence of bulky disease, and B symptoms were identified as prognostic factors for PFS in univariate analysis (18). In contrast to these findings, our study identified the lymphocyte-depleted histological subtype and treatment with A-AVD as being associated with shorter PFS in univariate analysis; however, these variables did not retain statistical significance in the multivariate model. This discrepancy may be attributed to the specific age range of 18–39 years, potential ethnic variation, or the limited number of patients included in the study.

Limitations of our study include its retrospective nature, which may have resulted in incomplete assessment of B symptoms, and some patients discontinuing follow-up or transferring to other centers.

In conclusion, our study focused on the 18-39 age group, a cohort with limited data in the HL literature. The epidemiological distribution in our study is consistent with the existing literature. Furthermore, the response rates and mean survival observed in patients primarily treated with the ABVD protocol support its efficacy as a treatment. However, our analysis did not identify any predictors of prolonged PFS or early CR.

References

1. Medeiros LJ, Greiner TC. Hodgkin's disease. Cancer 1995;75:357-369.

2. Campo E, Jaffe ES, Cook JR, et al. The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee. Blood 2022;140:1229-1253.

3. Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia 2022;36:1720-1748.

4. Jachimowicz RD, Engert A. The challenging aspects of managing adolescents and young adults with Hodgkin's lymphoma. Acta Haematol 2014;132:274-278.

5. Henderson TO, Parsons SK, Wroblewski KE, et al. Outcomes in adolescents and young adults with Hodgkin lymphoma treated on US cooperative group protocols: An adult intergroup (E2496) and Children's Oncology Group (COG AHOD0031) comparative analysis. Cancer 2018;124:136-144.

6. Bhuller KS, Zhang Y, Li D, et al. Late mortality, secondary malignancy and hospitalisation in teenage and young adult survivors of Hodgkin lymphoma: report of the Childhood/Adolescent/Young Adult Cancer Survivors Research Program and the BC Cancer Agency Centre for Lymphoid Cancer. Br J Haematol 2016;172:757-768.

7. Akay OM, Birtaş Ateşoğlu E, Mehtap Ö, Salim O. Hodgkin Lenfoma. Türk Hematoloji Derneği Lenfoma Tanı ve Tedavi Kılavuzu içinde, Galenos Yayınevi, İstanbul 2020, 2-23.

8. Lister TA, Crowther D, Sutcliffe SB, et al. Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswolds meeting. J Clin Oncol 1989;7:1630-1636.

9. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014;32:3059-3068.

10. André MPE, Girinsky T, Federico M, et al. Early Positron Emission Tomography Response-Adapted Treatment in Stage I and II Hodgkin Lymphoma: Final Results of the Randomized EORTC/LYSA/FIL H10 Trial. J Clin Oncol 2017;35:1786-1794.

11. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med 1998;339:1506-1514.

12. https:// www.seer.cancer.gov. Cancer stat facts/Hodgkin lymphoma (Last access: 18.03.2025)

13. Zawati I, Adouni O, Finetti P, et al. Adolescents and young adults with classical Hodgkin lymphoma in northern Tunisia: insights from an adult single-institutional study. Cancer Radiother 2020;24:206-214.

14. Kendel NE, Stanek JR, Willen FK, Audino AN. Characterizing age-related differences in Hodgkin lymphoma in children, adolescents and young adults. Pediatr Hematol Oncol

2024;41:336-345.
15. Berkman AM, Andersen CR, Puthenpura V, et al. Impact of Race, Ethnicity, and Socioeconomic Status over Time on the Long-term Survival of Adolescent and Young Adult Hodgkin Lymphoma Survivors. Cancer Epidemiol Biomarkers Prev 2021;30:1717-1725.
16. Foltz LM, Song KW, Connors JM. Hodgkin's lymphoma in adolescents. J Clin Oncol 2006;24:2520-2526.
17. Eichenauer DA, Bredenfeld H, Haverkamp H, et al. Hodgkin's lymphoma in adolescents treated with adult protocols: a report from the German Hodgkin study group. J Clin Oncol 2009;27:6079-6085.
18. Marr KC, Connors JM, Savage KJ, Goddard KJ, Deyell RJ. ABVD chemotherapy with reduced radiation therapy rates in children, adolescents and young adults with all stages of Hodgkin lymphoma. Ann Oncol 2017;28:849-854.

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Evaluating Postpartum Attachment, Anxiety, and Depression Following Covid-19 Infection During Pregnancy Among a Turkish Cohort

Türkiye'de Gebelikte COVID-19 Enfeksiyonu Geçiren Annelerde Doğum Sonrası Bağlanma, Anksiyete ve Depresyonun Değerlendirilmesi

Eda Üreyen Özdemir[1] | Merve Aldıkaçtıoğlu Talmaç[2] | Cihan Kaya[3]
Nura Fitnat Topbaş Selçuki[4] | Ecem Atak Mutlu[5] | Pınar Yalçın Bahat[6]

[1]Ministry of Health Ankara City Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye
[2]Basaksehir Cam and Sakura City Hospital, Department of Gynecological Oncology Clinic, İstanbul, Türkiye
[3]Istanbul Aydın University Faculty of Medicine, Department of Obstetrics and Gynecology, Istanbul, Türkiye
[4]University of Health Sciences Turkey, Istanbul Sisli Hamidiye Etfal Training and Research Hospital, Department of Obstetrics and Gynecology, İstanbul, Türkiye
[5]University of Health Sciences Turkey, Istanbul Kanuni Sultan Suleyman Training and Research Hospital, Department of Obstetrics and Gynecology, İstanbul, Türkiye
[6]Istanbul Yeni Yuzyil University, Department of Obstetrics and Gynecology, İstanbul, Türkiye

Sorumlu Yazar | Correspondence Author
Eda Üreyen Özdemir
eda.ureyen@gmail.com
Address for Correspondence: Ministry of Health Ankara City Hospital, Department of Obstetrics and Gynecology, Ankara/Türkiye.

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Evaluating Postpartum Attachment, Anxiety, and Depression Following Covid-19 Infection During Pregnancy Among a Turkish Cohort

ABSTRACT

Objective: To evaluate the effects of COVID-19 on mother-infant bonding by using the Maternal Attachment Inventory, Edinburgh Postnatal Depression Scale, and Postpartum Specific Anxiety Scale on postpartum women who had COVID-19 during their pregnancies in Türkiye.

Material and Method: This study was conducted on 180 patients using the Maternal Attachment Inventory, Edinburgh Postnatal Depression Scale, and Postpartum Specific Anxiety Scale.

Results: There was no significant difference in terms of the Maternal Attachment Inventory, Edinburgh Postnatal Depression Scale, and Postpartum Specific Anxiety Scale scores in groups. There was a significant difference regarding the gestational week in which the disease was diagnosed, which was significantly higher in the asymptomatic group (*p=0.04*) and there was a significant difference in the symptomatic group in terms of thoracic involvement visualized with computer tomography scan (*p<0.001*). An increase in depression symptoms was observed in only 1.6% of all patients. Moderately increased anxiety symptoms were observed in 44.4% of the patients.

Conclusion: The COVID-19 pandemic has been a stress factor on all individuals causing a psychological burden on many aspects. According to our results, pandemic moderately increased anxiety levels among the pregnant population and it affected mother-infant bonding significantly in a negative manner.

Keywords: Anxiety, COVID-19, Depression, Maternal attachment.

ÖZET

Amaç: Türkiye'de gebelikleri sırasında COVID-19 geçiren annelere doğum sonrası Maternal Bağlanma Ölçeği, Edinburgh Doğum Sonrası Depresyon Ölçeği ve Doğum Sonrası Spesifik Anksiyete Ölçeği kullanılarak COVID-19'un anne bebek bağlanmasına etkilerini değerlendirmeyi amaçladık.

Gereç ve Yöntem: 180 hasta üzerinde Maternal Bağlanma Ölçeği, Edinburgh Doğum Sonrası Depresyon Ölçeği ve Doğum Sonrası Spesifik Anksiyete Ölçeği kullanılarak yapılmıştır.

Bulgular: Maternal Bağlanma Ölçeği, Edinburgh Doğum Sonrası Depresyon Ölçeği ve Doğum Sonrası Spesifik Anksiyete Ölçeği puanları açısından gruplar arasında anlamlı fark yoktu. Asemptomatik grupta hastalığın tanı konulduğu gebelik haftası anlamlı olarak daha yüksek izlendi (*p=0,04*) ve semptomatik grupta bilgisayarlı tomografi ile görüntülenen toraks tutulumu açısından anlamlı fark vardı (*p<0.001*). Tüm hastaların sadece %1,6'sında depresyon semptomlarında artış gözlendi. Hastaların %44,4'ünde orta derecede artmış anksiyete belirtileri gözlendi.

Sonuç: COVID-19 pandemisi tüm bireyler üzerinde birçok açıdan psikolojik yük oluşturan stres faktörü olmuştur. Bulgularımıza göre pandemi, gebe nüfusta kaygı düzeylerini orta düzeyde artırdı ve anne bebek bağlanmasını önemli ölçüde olumsuz yönde etkiledi.

Anahtar Sözcükler: Anksiyete, COVID-19, Depresyon, Maternal bağlanma.

Introduction

Mother-infant bonding (MIB) is defined as the development of the first and most basic relationship between the mother and the newborn, and this bond establishes a sense of trust in the newborn (1). Postpartum MIB disorders are seen in approximately 7-11.3% of the general population (2). According to the bonding theory, the failure of the proper development of MIB in early childhood can cause personality disorders and emotional distress in adulthood (3). It has been shown in several studies that MIB disorders have negative effects on the child's cognitive development such as brain development and language skills development (4, 5). Risk factors that may disrupt the healthy development of MIB should be determined and expectant mothers should be supported during and after pregnancy.

Several studies have shown that postpartum depression and/or anxiety are associated with impaired MIB (6-9). Better MIB assessment scores have been reported in patients who have received anxiety treatment during the postpartum period (10). The frequency of major or minor depression in the first 3 months following birth has been estimated to be 19.2%, and the frequency of anxiety disorders has been reported to be 8-13% (11,12). Higher frequency rates of 6.1-27% have also been reported for postpartum anxiety (13). Factors such as negative experiences during pregnancy or postpartum period, mode of delivery, number of children, and maternal age are known to have an effect on MIB (14). In addition, in mothers who tested positive for COVID-19 during pregnancy, anxiety, and depression symptoms frequency can increase and cause bonding problems between mother and the baby in the postpartum period. Although there are studies conducted among pregnant women reporting no risk to the fetus during pregnancy, there are several cases suggesting vertical transmission (15,16). This uncertainty regarding the effects of COVID-19 during pregnancy especially on the fetus can cause extra psychological burden during the postpartum period and increase anxiety, risk of postpartum depression, and attachment problems.

This study aimed to evaluate the effects of COVID-19 on MIB by using the Maternal Attachment Inventory (MAI), Edinburgh Postnatal Depression Scale (EPDS), and Postpartum Specific Anxiety Scale (PSAS) on postpartum women who had COVID-19 during their pregnancies in Türkiye.

Material and Method

This prospective observational study was conducted at the University of Health Sciences, Istanbul Kanuni Sultan Suleyman Training and Research Hospital Department of Obstetrics and Gynecology between 30 June 2020- 30 June 2021. The study protocol was approved by the institution's ethics committee on 29/06/2020 (the number: 2020.06.111). Written informed consent was obtained from all subjects. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

180 patients who had positive PCR-test results for COVID-19 during pregnancy or who were considered positive according to their thoracic computer tomography (CT) findings were included in the study. Pregnant women were divided into 3 groups according to the trimesters in which they tested positive and 2 groups according to whether they had symptoms or not. Pregnant women aged between 18-47 years, who conceived spontaneously, with no obstetrical complications, who gave birth at term, and who did not have preexisting psychiatric conditions or who did not receive any psychiatric treatments were included in the study. Patients who had baby blues or postpartum depression in their previous pregnancies, had gynecological malignancies, developed complications during pregnancy or who did not complete the questionnaires (scales), who had a family history of violence or abuse, adolescent pregnancies, and patients with fetal anomalies diagnosed during pregnancy were excluded from the study.

The data of the patients included age, gravidity, parity, weeks of gestation at which COVID-19 was diagnosed, birth weight of babies, 1st and 5th minute APGAR scores, COVID-19 related symptoms, history of contact, chronic diseases, CT findings and PCR test results. All patients were asked to complete the MAI, EPDS and PSAS scales at their 3-month postpartum controls.

The Edinburgh Postpartum Depression Scale (EPDS) was created to screen for postpartum maternal depression symptoms (17). It is a self-assessment scale consisting of 10 items, which includes the psychological state of the individual. Each item is scored on a 4-point Likert scale rated 0-3. The total score can range from 0-30, and high scores are associated with depression. The Turkish version of EPDS was used in this study (18). The cutoff value is determined to be 13, and the risk of developing major depression increases in patients with scores of ≥13 (17). The sensitivity for the cutoff value varies between 38-43% and specificity between 98-99% depending on the trimester of the patient (19).

The Postpartum Specific Anxiety Scale (PSAS) was developed to evaluate anxiety symptoms in the postpartum period. The scale, first created by Fallon et al, has 51 items and has four subtypes: maternal competence and attachment anxieties (Items 1-15), infant safety and welfare anxieties (Items 16-26), practical infant care anxieties (Items 27-33), and psychosocial adjustment to motherhood (Items 34-51) (20). Responses to the items are rated on a 4-point Likert scale ranging from 1 to 4 (1 = never, 2 = sometimes, 3 = often, 4 = almost always) (20). The Turkish validation PSAS was conducted by Duran and the Cronbach's alpha coefficient was found to be 0.91(21). It is revealed that those who score 73 and below on the scale have low postpartum anxiety levels, those who score 74-100 have moderate anxiety, and those who score 101 and above have high levels of anxiety.

The Maternal Attachment Inventory (MAI) was developed by Mary E. Muller in 1994 to measure attachment with maternal love (22). The reliability coefficient of the MAI was found to be Cronbach alpha 0.85. Each item of the inventory is evaluated by a 4-way to 26-point Likert-type scale ranging from "always" to "never". Always has 4 points, often 3 points, sometimes 2 points, and never has 1 point. The lowest score, which can be obtained from the scale is 26, and the highest score is 104. A high score indicates a high maternal attachment (23). The Turkish version of the MAI was used in this study (23).

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 20.0 software (IBM Corporation, Armonk, NY, USA). The distributions of continuous variables were determined by Kolmogorov-Smirnov test. Descriptive statistics for continuous variables were expressed as mean and standard deviation (SD). Frequency distribution was shown for categorical data. The continuous variables, which were not normally distributed were evaluated by Mann-Whitney U or Kruskal-Wallis tests depending on a number of independent groups. Categorical data were analyzed by Pearson's $\chi 2$ test. A *p-value less than 0.05* was considered statistically significant.

Results

All patients were grouped according to the trimester in which they were diagnosed with COVID-19 and their sociodemographic data and EPDS, PSAS, and MAI scores are listed in Table I. A mean age of 25.69 ± 7.44, a mean gravidity of 2 ± 0.7, and a mean parity of 0.9 ± 0.7 were calculated for the 1st trimester. The mean gestational week at diagnosis was 11.15 ± 2.8, the mean birth weight of the newborns was 3131.15 ± 291, the mean 1st minute Apgar score was 7.1 ± 0.3, and the mean 5th minute Apgar score was 9. 53.8% of the patients reported having a positive contact with a COVID-19 patient. 7.7% had a history of chronic disease. COVID-19 PCR test was positive in 92.3% of the patients. 23.1% of the patients were asymptomatic. 92.3% of the patients refused to have a CT scan, and 7.7% of them had thoracic involvement with different intensities. EPDS was calculated to be 7.3±2.6, PSAS 72.1±15.1, and MAI 86.5±11.9 for the patients in the 1st trimester group.

In the 2nd trimester group, the mean age was 26.85 ± 5.64, the mean gravidity was 2.4 ± 1.4, and the mean parity was 1.1 ± 1.2. The mean weeks of gestation at diagnosis was calculated to be 20.92 ± 4.3, and the mean birth weight of the newborns was 2984.2 ± 451.8 grams. 1st and 5th minute Apgar scores were 7 ± 0.3 and 9 respectively. Among the patients, 51.8% of them had a history of contact with a COVID-19 positive patient and 3.6% had a history of chronic disease. The PCR test was positive in 98.2% of the patients. Among the patients, 30.4% of them were asymptomatic, 62.5% of the patients refused to have a CT scan, and 16.1% did not show up to their CT scan appointments. Patients of 21.4%

had positive CT findings. EPDS was determined to be 7.1 ± 2.3, PSAS was 74.8 ± 11.1 and MAI was 84.5 ± 8.5 in this group.

Table I. Comparison of Data Between Trimesters

		1st trimester	2nd trimester	3rd trimester	*p value*
Age (years)		25.69± 7.44	26.85± 5.64	28.21± 6.42	*0.179*
Gravidity		2± 0.7	2.4± 1.4	2.5± 1.4	*0.532*
Parity		0.9± 0.7	1.1± 1.2	1.2± 1.2	*0.487*
Weeks of gestation		11.15± 2.8	20.92± 4.3	34.82± 3.4	***<0.001***
Birth weight (gr)		3131.15± 291	2984.2± 451.8	2963.82 507.9	*0.470*
APGAR 0 min		7.1± 0.3	7± 0.3	7± 0.7	*0.825*
APGAR 5 min		9	9	8.9± 0.4	*0.147*
EPDS		7.3± 2.6	7.1± 2.3	7.1± 2.1	*0.886*
PSAS		72.1± 15.1	74.8± 11.1	73± 11	*0.589*
MAI		86.5± 11.9	84.5± 8.5	84.5± 9.6	*0.324*
Symptoms	None	3 (23.1%)	17(30.4%)	37(33.3%)	*0.544*
	Cough	2 (15.4%)	15(26.8%)	25(22.5%)	
	Cough+Fever	4 (30.8%)	11(19.6%)	24(21.6%)	
	Cough+Fever+ Shortness of breath	3(23.1%)	4(7.1%)	15(13.5%)	
	Cough+Fever+ Sore throat	0(0)	2(3.6%)	2(1.8%)	
	Diarrhea	1(7.7%)	0(0)	1(0.9%)	
	Myalgia	0(0)	5(8.9%)	4(3.6%)	
	Anosmia	0(0)	2(3.6%)	3(2.7%)	
Contact	No	6 (46.2%)	27(48.2%)	63(56.8%)	*0.501*
	Yes	7(53.8%)	29(51.8%)	48(43.2%)	
Chronic disease	No	12 (92.3%)	54(96.4%)	109(98.2%)	*0.507*
	Yes	1(7.7%)	2(3.6%)	2(1.8%)	
PCR	Negative	1(7.7%)	1(1.8%)	12(10.8%)	*0.07*
	Positive	12(92.3%)	55(98.2%)	99(89.2%)	
CT	Negative	0(0)	9(16.1%)	19(17.1%)	***<0.001***
	Mild	0(0)	4(7.1%)	17(15.3%)	
	Moderate	0(0)	5(8.9%)	27(24.3%)	
	Severe	1(7.7%)	3(5.4%)	9(8.1%)	
	Suspicious	0(0)	0(0)	6(5.4%)	
	Patient did not want to have CT	12(92.3%)	35(62.5%)	33(29.7)	

Significant results (p<0.05) are shown in bold. EPDS: The Edinburgh Postpartum Depression Scale. PSAS: The Postpartum Specific Anxiety Scale. MAI: The Maternal Attachment Inventory. CT: Patients with atypical involvement in thorax computed tomography were evaluated as negative. Patients with typical involvement in thorax computed tomography were evaluated as mild, moderate, and severe.

The third trimester group had a mean age of 28.21 ± 6.42, mean gravidity of 2.5 ± 1.4, and mean parity of 1.2 ± 1.2. The mean weeks of gestation at diagnosis was determined to be 34.82 ± 3.4. The mean birth weight of the newborns was 2963.82 ± 507.9 grams. First minute Apgar score was 7 ± 0.7 and 5th minute Apgar score was 8.9 ± 0.4. Among patients, 43.2% of them had contact with a COVID-19 positive patient and 1.8% had a history of chronic disease. The PCR test was positive in 89.2% of the patients. Among the patients 33.3% of them were asymptomatic, 29.7% of the patients refused to have CT scan and 17.1% failed to be present at their CT appointments, 5.4% had suspicious areas of involvement on CT and 47.7% had positive thoracic involvement. EPDS was determined as 7.1 ± 2.1, PSAS was 73 ± 11, and MAI was 84.5 ± 9.6 in the third trimester.

When these 3 trimester groups were compared with each other, there was no significant difference in terms of EPDS, PSAS, and MAI scores, with p-values of *0.886, 0.589, and 0.324*, respectively. On the other hand, a significantly higher percentage of patients refused a CT scan in the 1st and 2nd trimester compared to the 3rd trimester (*p<0.001*).

Following the analysis according to trimesters patients were divided into 2 groups based on being symptomatic or asymptomatic. Sociodemographic data and EPDS, PSAS, and MAI scores are listed in Table II. In asymptomatic patients, the mean age was 26.43 ± 4.95 years, gravidity was 2.2 ± 1.2, and parity was 1.1 ± 1.1. Means weeks of gestation at diagnosis was 30.4 ± 8.6. The mean birth weight of the newborns was determined to be 3035.8 ± 430.8. The 1st and 5th minute Apgar scores were 7.1 ± 0.3 and 9, respectively. Among the patients, 54.4% of them had a positive contact history and none of the patients had a history of chronic disease. COVID-19 PCR test was positive in 94.7% of the patients. Patients of 43.9% refused CT scan, 29.8% did not show up to their CT appointments, and 3.5% of the CT findings showed suspicious areas on the scan and 22.8% had thoracic involvement. In asymptomatic patients, EPDS was 7 ± 1.9, PSAS was 73.4 ± 10.3, and MAI was 84.8 ± 8.2.

In symptomatic patients, the mean age was 28.14 ± 6.76, the mean gravidity was 2.5 ± 1.4, and the mean parity was 1.2 ± 1.3. The mean gestational week at diagnosis was reported to be 28.1 ± 8.8. The mean birth weight of the newborns was calculated to be 2958.1 ± 497.9 grams. The 1st minute Apgar score was 7 ± 0.7 and the 5th minute Apgar score was 8.4

± 0.4. In 43.1% of the patients, a history of positive contact was reported. Among the patients 4.1% of them had a history of chronic disease. The PCR test was positive in 91.1% of the patients. Patients of 44.7% did not want to have a CT scan, 8.9% failed to show up to their CT appointments, 3.3% had suspicious findings on CT and 43.1% had thoracic involvement. In symptomatic patients, EPDS was 7.2 ± 2.3, PSAS was 73.5 ± 11.1, and MAI was 84.6 ± 9.9.

Table II. Comparison of Data Based on the Presence of Symptoms

		Symptom -	Symptom +	*p-value*
Age (years)		26.43± 4.95	28.14± 6.76	*0.172*
Gravidity		2.2± 1.2	2.5± 1.4	*0.326*
Parity		1.1± 1.1	1.2± 1.3	*0.573*
Weeks of gestation		30.4± 8.6	28.1± 8.8	***0.040***
Birth weight (gr)		3035.8± 430.8	2958.1± 497.9	*0.255*
APGAR 0 min		7.1± 0.3	7± 0.7	*0.607*
APGAR 5 min		9	8.9± 0.4	*0.09*
EPDS		7± 1.9	7.2± 2.3	*0.748*
PSAS		73.4± 10.3	73.5± 11.1	*0.898*
MAI		84.8± 8.2	84.6± 9.9	*0.618*
Symptoms	None	57(100%)	0(0)	***<0.001***
	Cough	0(0)	42(34.1%)	
	Cough+Fever	0(0)	39(31.7%)	
	Cough+Fever+ Shortness of breath	0(0)	22(17.9%)	
	Cough+Fever+ Sore throat	0(0)	4(3.3%)	
	Diarrhea	0(0)	2(1.6%)	
	Myalgia	0(0)	9(7.3%)	
	Anosmia	0(0)	5(4.1%)	
Contact	No	26(45.6%)	70(56.9%)	*0.158*
	Yes	31(54.4%)	53(43.1%)	
Chronic disease	No	57(100%)	118(95.9%)	*0.181*
	Yes	0(0)	5(4.1%)	
PCR	Negative	3(5.3%)	11(8.9%)	*0.553*
	Positive	54(94.7%)	112(91.1%)	
CT	Negative	17(29.8%)	11(8.9%)	***<0.001***
	Mild	7(12.3%)	14(11.4%)	
	Moderate	6(10.5%)	26(21.1%)	
	Severe	0(0)	13(10.6%)	
	Suspicious	2(3.5%)	4(3.3%)	
	Patient did not want to have CT	25(43.9%)	55(44.7%)	

Significant results (*p<0.05*) are shown in bold. EPDS: The Edinburgh Postpartum Depression Scale. PSAS: The Postpartum Specific Anxiety Scale. MAI: The Maternal Attachment Inventory. CT: Patients with atypical involvement in thorax computed tomography were evaluated as negative. Patients with typical involvement in thorax computed tomography were evaluated as mild, moderate, and severe.

When the patients were analyzed by dividing them into two groups according to their symptomatology, there was no significant difference in terms of EPDS, PSAS, and MAI scores (*p values of 0.748, 0.898, and 0.618,* respectively). One of the significant differences was observed at the gestational week at which the disease was diagnosed, which was found to be significantly higher in the asymptomatic group (*p=0.04*). The other significant difference was that a significantly higher number of patients in the symptomatic group had thoracic involvement visualized with a CT scan (*p<0.001*).

When all pregnant patients were considered together, an increase in depression symptoms was observed in only 1.6% of all patients (EPDS≥13). Moderately increased anxiety symptoms were observed in 44.4% of the patients (PSAS scores between 74-100).

Discussion

The COVID-19 pandemic has taken the whole world under its influence since the beginning of 2020. The disease had serious psychological, economic, and health effects on people all over the world. In the postpartum period, MIB is affected by many factors such as social support, education level, number of children, income level, and psychological state (24). In this study, we investigated whether the COVID-19 pandemic had any effect on MIB, and the results indicated that the pandemic did not have a significant adverse effect. However, mild anxiety was detected in 44.4% of the study subjects.

It has already been shown that the COVID-19 pandemic increased the degree of anxiety in pregnant women (25). Mothers have concerns about the harmful effects of the virus on their babies and their own health (26). In a study conducted in China, this increase in anxiety was found to be due to the possible vertical transmission of the infection during pregnancy (27). Similarly, in different studies, a higher risk for developing anxiety and depression in pregnant women during the COVID-19 pandemic period was observed, and the risk of developing anxiety was reported to be between 63-68% (26,28). In a study by Yassa et al. during the COVID-19 pandemic period, anxiety and obsessive compulsion scores were found to be higher in pregnant women, but lower anxiety levels

were found in pregnant women compared to non-pregnant women (28). In a study conducted among pregnant women who were not infected during the pandemic, the risk of postpartum depression was reported in 14.7% of the subjects during the postpartum period, and MAI scores were found to be significantly lower in patients with depression compared to the healthy controls (29). In our study, moderately increased anxiety levels were found in 44.4% of the patients, but it was found that it had no effect on depression and MIB. The reason for this could be the easy access that pregnant women have to obstetricians and obstetrics clinics in Türkiye, regardless of the pandemic. Also, a selection bias regarding the study cohort could explain the results. All the patients who were recruited to the study were under pregnancy surveillance at our tertiary obstetrics clinic with adequate obstetricians, patient beds, and intensive care beds available. This might have provided a feeling of security to the patients, which reflected on their results.

In addition to depression and anxiety, we have also assessed secondary parameters related to COVID-19, such as diagnostic use of thoracic CT, weeks of gestation at diagnosis, and presence of thoracic involvement. A significantly higher number of patients in the 1st and 2nd trimester declined CT scan as a diagnostic tool compared to the patients in the 3rd trimester (*p<0.001*). Additionally, the weeks of gestation at diagnosis was found to be significantly higher in asymptomatic patients (*p=0.04*), and a significantly higher number of positive findings with CT scan was reported among symptomatic patients (*p<0.001*).

One of the most important limitations of the study is the lack of comparable data before and during the pandemic. In addition, the absence of a control group and unknown EPDS, PSAS, and MAI values of patients who were not infected during the pandemic period are also limitations. The illiteracy of some patients required the questions to be read and filled out by research assistants. The presence of a third person could have influenced the answers of some of the study subjects. MIB is multifactorial and there are many factors that affect this process before and after birth. In order to comment on MIB disorders and the effect of the pandemic on MIB multicenter studies with larger numbers and control groups are needed.

The COVID-19 pandemic has been a stress factor on all individuals causing a psychological burden on many levels. According to our results, the pandemic moderately increased the anxiety levels among the pregnant population, and it affected MIB significantly in a negative manner. Nonetheless, more studies are needed to drive a conclusion on the long-term effects of the pandemic on the postpartum period and the bonding between mother and infant.

References

1. Nath S, Pearson RM, Moran P, et al. The association between prenatal maternal anxiety disorders and postpartum perceived and observed mother-infant relationship quality. J Anxiety Disord 2019;68:102148.

2. Edhborg M, Nasreen HE, Kabir ZN. Impact of postpartum depressive and anxiety symptoms on mothers' emotional tie to their infants 2-3 months postpartum: a population-based study from rural Bangladesh. Arch Womens Ment Health 2011;14(4):307-316.

3. Bowlby J. The making and breaking of affectional bonds. I. Aetiology and psychopathology in the light of attachment theory. An expanded version of the Fiftieth Maudsley Lecture, delivered before the Royal College of Psychiatrists, 19 November 1976. Br J Psychiatry 1977;130:201-210.

4. Tolja R, Nakić Radoš S, Anđelinović M. The role of maternal mental health, infant temperament, and couple's relationship quality for mother-infant bonding. J Reprod Infant Psychol 2020;38(4):395-407.

5. Farré-Sender B, Torres A, Gelabert E, et al. Mother-infant bonding in the postpartum period: assessment of the impact of pre-delivery factors in a clinical sample. Arch Womens Ment Health 2018;21(3):287-297.

6. Kerstis B, Aarts C, Tillman C, et al. Association between parental depressive symptoms and impaired bonding with the infant. Arch Womens Ment Health 2016;19(1):87-94.

7. Dubber S, Reck C, Müller M, Gawlik S. Postpartum bonding: the role of perinatal depression, anxiety and maternal-fetal bonding during pregnancy. Arch Womens Ment Health 2015;18(2):187-195.

8. Kinsey CB, Baptiste-Roberts K, Zhu J, Kjerulff KH. Birth-related, psychosocial, and emotional correlates of positive maternal-infant bonding in a cohort of first-time mothers. Midwifery 2014;30(5):e188-194.

9. Tietz A, Zietlow AL, Reck C. Maternal bonding in mothers

with postpartum anxiety disorder: the crucial role of subclinical depressive symptoms and maternal avoidance behaviour. Arch Womens Ment Health 2014;17(5):433-442.
10. Hopkins J, Miller JL, Butler K, Gibson L, Hedrick L, Boyle DA. The relation between social support, anxiety and distress symptoms and maternal fetal attachment. J Reprod Infant Psychol 2018;36(4):381-392.
11. Andersson L, Sundström-Poromaa I, Wulff M, Aström M, Bixo M. Depression and anxiety during pregnancy and six months postpartum: a follow-up study. Acta Obstet Gynecol Scand 2006;85(8):937-944.
12. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol 2005;106(5 Pt 1):1071-1083.
13. Ali E. Women's experiences with postpartum anxiety disorders: a narrative literature review. Int J Womens Health 2018;10:237-249.
14. Pereira PK, Lima LA, Legay LF, de Cintra Santos JF, Lovisi GM. Maternal mental disorders in pregnancy and the puerperium and risks to infant health. World J Clin Pediatr 2012;1(4):20-23.
15. Schwartz DA. An Analysis of 38 Pregnant Women With COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. Arch Pathol Lab Med 2020;144(7):799-805.
16. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet 2020;395(10226):809-815.
17. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987;150:782-786.
18. Aydin N, Inandi T, Yigit A, Hodoglugil NN. Validation of the Turkish version of the Edinburgh Postnatal Depression Scale among women within their first postpartum year. Soc Psychiatry Psychiatr Epidemiol 2004;39(6):483-486.
19. Bergink V, Kooistra L, Lambregtse-van den Berg MP, et al. Validation of the Edinburgh Depression Scale during pregnancy. J Psychosom Res 2011;70(4):385-389.
20. Fallon V, Halford JCG, Bennett KM, Harrold JA. The Postpartum Specific Anxiety Scale: development and preliminary validation. Arch Womens Ment Health 2016;19(6):1079-1090.
21. Duran S. Postpartum Specific Anxiety Scale (PSAS): Reliability and validity of the Turkish version. Perspect Psychiatr Care 2020;56(1):95-101.
22. Müller ME. A questionnaire to measure mother-to-infant attachment. J Nurs Meas 1994;2(2):129-41.
23. Kavlak O, Şirin A. The Turkish version of maternal attachment inventory. Journal of Human Sciences 2009;6(1):188-202.
24. Gao S, Su S, Zhang E, et al. Psychological health status in postpartum women during COVID-19 pandemic: A systematic review and meta-analysis. J Affect Disord 2022;319:99-111.
25. Taubman-Ben-Ari O, Chasson M, Abu Sharkia S, Weiss E. Distress and anxiety associated with COVID-19 among Jewish and Arab pregnant women in Israel. J Reprod Infant Psychol 2020;38(3):340-348.
26. Saccone G, Florio A, Aiello F, et al. Psychological impact of coronavirus disease 2019 in pregnant women. Am J Obstet Gynecol 2020;223(2):293-295.
27. Wu Y, Zhang C, Liu H, et al. Perinatal depressive and anxiety symptoms of pregnant women during the coronavirus disease 2019 outbreak in China. Am J Obstet Gynecol 2020;223(2):240.e1-.e9.
28. Yassa M, Yassa A, Yirmibeş C, et al. Anxiety levels and obsessive compulsion symptoms of pregnant women during the COVID-19 pandemic. Turk J Obstet Gynecol 2020;17(3):155-160.
29. Oskovi-Kaplan ZA, Buyuk GN, Ozgu-Erdinc AS, Keskin HL, Ozbas A, Moraloglu Tekin O. The Effect of COVID-19 Pandemic and Social Restrictions on Depression Rates and Maternal Attachment in Immediate Postpartum Women: a Preliminary Study. Psychiatr Q 2021;92(2):675-682.

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Prospective Comparative Evaluation of Wagner, PEDIS, and Texas Classification Systems in Predicting Outcomes of Diabetic Foot Ulcers

Diyabetik Ayak Ülserlerinin Sonuçlarını Tahmin Etmede Wagner, PEDIS ve Texas Sınıflandırma Sistemlerinin Prospektif Karşılaştırmalı Değerlendirmesi

İsmail Sezikli[1] | Ramazan Topcu[1] | Emre Demir[2] | Murat Kendirci[1]

[1]Hitit University Faculty of Medicine, Department of General Surgery, Çorum, Türkiye
[2]Hitit University, Faculty of Medicine, Department of Biostatistics, Çorum, Türkiye

Sorumlu Yazar | Correspondence Author
Ramazan Topcu
topcur58@gmail.com
Address for Correspondence: Hitit University Faculty of Medicine, Department of Surgery, Çorum, Türkiye.

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Prospective Comparative Evaluation of Wagner, PEDIS, and Texas Classification Systems in Predicting Outcomes of Diabetic Foot Ulcers

ABSTRACT

Objective: This study aims to compare the effectiveness of three classification systems—Wagner, PEDIS, and Texas—in predicting treatment outcomes and amputation risk in patients with diabetic foot ulcers (DFUs). Given the high morbidity and mortality associated with DFUs, accurate prognostic tools are essential for guiding management and reducing limb loss.

Material and Method: A total of 121 patients diagnosed with DFUs between 2018 and 2020 at Hitit University Faculty of Medicine were enrolled in a prospective observational cohort study. Data collected included demographics, wound characteristics, ankle-brachial index (ABI), radiological findings, neuropathy status, and laboratory results. Patients were classified according to Wagner, PEDIS, and Texas systems. The relationship between classification results and clinical outcomes, such as healing and amputation, was analyzed using statistical methods, with significance set at $p<0.05$.

Results: The PEDIS system with a cutoff value of 7.5 effectively distinguished between healing and amputation cases. Wagner grade 4 and above significantly predicted higher amputation risk (AUC=0.728; $p<0.001$). Patients with ABI <0.9 showed a 50.9% amputation rate, compared to 23.5% in those with ABI ≥0.9. The neutrophil-to-lymphocyte ratio correlated with infection and higher amputation risk. Male gender, advanced age, and elevated neutrophil-to-lymphocyte ratios increased the likelihood of limb loss.

Conclusion: While PEDIS was more effective in differentiating healing from amputation, Wagner better predicted amputation risk. A lower ABI and high neutrophil-to-lymphocyte ratio were associated with worse outcomes. The study highlights the need for a comprehensive, universally applicable classification system that incorporates clinical and laboratory parameters to optimize patient management and reduce amputations.

Keywords: Amputation, Classification, Diabetic Foot Ulcer.

ÖZET

Amaç: Bu çalışma, diyabetik ayak ülseri (DAÜ) hastalarında tedavi sonuçlarını ve ampütasyon riskini öngörmede Wagner, PEDIS ve Texas sistemlerinin etkinliğini karşılaştırmayı amaçlamaktadır. DAÜ ile ilişkili yüksek morbidite ve mortalitenin göz önüne alındığında, doğru prognostik araçlar yönetimi yönlendirmek ve uzuv kaybını azaltmak için hayati öneme sahiptir.

Materyal ve Yöntem: 2018-2020 yılları arasında Hitit Üniversitesi Tıp Fakültesi'nde DAÜ tanısı konmuş toplam 121 hasta prospektif gözlemsel kohort çalışması olarak dahil edildi. Toplanan veriler arasında demografik bilgiler, yara özellikleri, ayak bilek-brakiyal indeks (ABI), radyolojik bulgular, nöropati durumu ve laboratuvar sonuçları bulunuyordu. Hastalar Wagner, PEDIS ve Texas sistemlerine göre sınıflandırıldı. Sınıflandırma sonuçları ile iyileşme ve ampütasyon gibi klinik sonuçlar arasındaki ilişki istatistiksel yöntemlerle analiz edildi ve anlamlılık $p<0,05$ olarak kabul edildi.

Bulgular: PEDİS sistemi, 7.5 eşik değeriyle iyileşme ve ampütasyon durumlarını etkili şekilde ayırt etti. Wagner sınıf 4 ve üzeri, anlamlı şekilde daha yüksek ampütasyon riskini öngördü (AUC=0.728; $p<0.001$). ABI <0.9 olan hastalarda ampütasyon oranı %50,9 iken, ABI ≥0.9 olanlarda bu oran %23,5 olarak bulundu. Nötrofil-lenfosit oranı enfeksiyon ve daha yüksek ampütasyon riski ile ilişkiliydi. Erkek cinsiyet, ileri yaş ve yüksek nötrofil-lenfosit oranları, uzuv kaybı olasılığını artırdı.

Sonuç: PEDIS, iyileşme ile ampütasyon arasındaki ayrımı daha iyi yaparken, Wagner ampütasyon riskini daha iyi öngördü. Düşük ABI ve yüksek nötrofil-lenfosit oranı kötü sonuçlarla ilişkiliydi. Çalışma, klinik ve laboratuvar parametrelerini içeren, uluslararası geçerliliği olan kapsamlı bir sınıflandırma sistemine ihtiyaç olduğunu vurgulamaktadır; böylece hasta yönetimi optimize edilip amputasyon oranları azaltılabilir.

Anahtar Sözcükler: Amputasyon, Sınıflandırma, Diyabetik Ayak Ülseri.

Introduction

The prevalence of diabetic foot ulcers (DFUs) continues to rise worldwide (1). DFUs are complex, chronic wounds with significant long-term impacts on morbidity, mortality, and quality of life (2,3). Unlike other chronic wounds, their development and progression are often complicated by diabetes-related alterations, such as neuropathy and vascular disease, which impair neutrophil function, reduce tissue perfusion, and hinder protein synthesis, creating unique management challenges in clinical practice (2).

Epidemiological studies indicate that the prevalence of DFUs ranges from 4% to 27%, with marked differences among countries (4–6). In the United States, prevalence is reported to be 15–20%, and the risk of amputation is 15–46 times higher in diabetic patients compared with non-diabetic individuals (7). Among individuals with type 2 diabetes, 12–15% develop DFUs, and approximately 14–24% of these cases result in amputation (8,9). Globally, it is estimated that one lower extremity is amputated due to diabetes every 20–30 seconds (1,10). The lifetime risk of ulcer development in diabetic patients has been estimated to reach up to 25% (8,9).

With an effective care plan, up to 85% of amputations can be prevented (11). However, inadequate education, insufficient assessment, inappropriate treatment methods, delayed referral, and limited access to multidisciplinary foot care teams reduce the chances of achieving optimal outcomes (12,13). DFUs therefore represent a major public health concern due to their high morbidity and mortality rates, prolonged hospital stays, and significant healthcare costs.

Accurate and practical classification systems are critical in guiding prognosis, treatment decisions, and communication among clinicians. Several systems have been developed for this purpose, including Wagner, PEDIS, and the University of Texas (UT) classification systems (14,15). Each emphasizes different dimensions of ulcer pathology: Wagner focuses on depth and gangrene, UT incorporates infection and ischemia in a stage–grade format, and PEDIS provides a numeric severity score based on perfusion, extent, depth, infection, and sensation (16). Although these systems are widely used, there is currently no universally accepted standard, and comparative evidence on their predictive validity remains limited (14–16).

In addition to ulcer-specific classification, systemic markers such as the ankle–brachial index (ABI) and neutrophil-to-lymphocyte ratio (NLR) have been identified as potential prognostic indicators. ABI, a non-invasive measure of arterial perfusion, is frequently abnormal in patients with DFUs and has been linked to poor healing and higher amputation rates (17). Elevated NLR, a marker of systemic inflammation, has also emerged as a simple but powerful predictor of adverse outcomes in diabetic wounds (18).

This study, therefore, aims to compare the predictive performance of the Wagner, PEDIS, and Texas classification systems in hospitalized patients with DFUs. Our primary objective is to evaluate their ability to predict clinical outcomes, specifically wound healing versus amputation. As secondary aims, we assess the prognostic value of ABI and NLR in risk stratification and treatment guidance. By integrating prospective clinical data with robust statistical analysis, we aim to contribute to the development of a more comprehensive, multidimensional classification model that can optimize limb preservation in diabetic patients.

Material and Method

The study was initiated after obtaining approval from the Clinical Research Ethics Committee of Hitit University Faculty of Medicine (date: 08.01.2020, decision number: 189). The protocol and informed consent form were reviewed and approved by the Ethics Committee. This clinical investigation was conducted in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. All patients included in the study were informed about the tests to be performed and the methods to be used. Written informed consent was obtained from each participant to allow for the administration of tests and physical examinations. Consent for publication was obtained from all patients prior to participation.

In this prospective, observational cohort study, participants aged between 18 and 85 years, who were being monitored at the Diabetic Foot Clinic of Hitit University Faculty of Medicine, were included. For every hospitalized patient, all parameters defined

in the Diabetic Foot Ulcer Assessment Form were documented and verified by a healthcare team actively involved in diabetic foot ulcer management. During hospitalization, the patient group was monitored, and the following information from the Diabetic Foot Assessment Form was evaluated. Based on this information, patient data flow was ensured and recorded. The collected data included the patients' full name, age, gender, and other demographic characteristics; type of diabetes mellitus (DM); history of alcohol, smoking, or substance use; comorbid conditions associated with diabetic foot ulcers (neuropathy, nephropathy, and retinopathy); level of education regarding DM and diabetic foot ulcers; adherence to diabetes treatment with insulin and/or oral antidiabetic medications; history of prior amputations, including the level and laterality, if applicable; history of revascularization procedures, specifying whether angioplasty, bypass, or reperfusion was performed; radiological findings, including the presence of osteomyelitis or soft tissue infection; ulcer type, location, and duration; classification of the ulcer according to the Wagner classification, University of Texas classification, and PEDIS scoring system; ankle-brachial index (ABI) value, if available at admission; estimated treatment duration and outcome; final treatment outcome; and categorization of whether healing was achieved with other treatment modalities or amputation. Laboratory data were also assessed, including blood glucose, HbA1c, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), blood urea nitrogen (BUN), urea, creatinine, total cholesterol, hemoglobin, white blood cell (WBC) count, and neutrophil-to-lymphocyte ratio.

Patients included in the study underwent daily foot dressing changes, during which wound cultures were collected after foot cleansing. Photographs of all wounds were taken at hospital admission and recorded in the computerized patient files. The wounds were categorized and documented according to the Wagner classification, the University of Texas classification, and the PEDIS scoring system. For blood glucose regulation, all patients were consulted with the endocrinology or internal medicine departments to ensure proper glycemic control. In cases of infection, the infectious diseases department was consulted for antibiotic therapy and clinical evaluation. For revascularization assessment, patients were evaluated by the cardiology department, and when necessary, interventional peripheral angiography was performed, followed by revascularization if deemed appropriate. In cases of vascular occlusion, patients were referred to the cardiovascular surgery department, where revascularization or additional treatment recommendations were implemented as needed. Consultations with other specialties were conducted when required, contributing to diagnosis and treatment. During standard clinical care, all appropriate treatments administered to patients were systematically recorded.

Ulcer classification was performed using three validated systems: Wagner, PEDIS, and the University of Texas (UT) classification. Each patient was independently assessed by two clinicians with a minimum of five years of experience in diabetic foot care. To reduce observer bias, both clinicians were blinded to the patients' clinical outcomes at the time of scoring. A standardized case evaluation form was used to ensure uniform data capture, including ulcer location, depth, presence of infection, perfusion status, and neuropathy. Classification scoring was completed within the first 24 hours of hospital admission and prior to any surgical or antimicrobial interventions. In cases of inter-rater disagreement, a third independent clinician reviewed the case, and the final classification was determined by consensus.

Patients with a confirmed clinical diagnosis of diabetic foot ulcer were included based on documented findings from physical examination and wound assessment by two independent clinicians. The study encompassed a patient population aged between 18 and 85 years. Patients with diabetic foot ulcers of any severity were included, regardless of age or gender. Strict measures were implemented to protect patient confidentiality, ensuring that access to personally identifiable information was restricted to authorized personnel, preventing unauthorized access. Patients who died during the study period or discontinued treatment by refusing further medical care were excluded. Furthermore, patients were not included if, upon admission and during the anamnesis process, they were identified as having autoimmune disorders, immunological diseases, oncological conditions, dementia, vasculitis,

or if they were deemed medically unfit to provide informed responses to health-related inquiries on the patient profile form.

The primary outcome measures were healing and amputation, both assessed at hospital discharge. Healing was defined as complete epithelialization of the ulcer without the need for surgical intervention, confirmed by clinical examination. Amputation was defined as any surgical removal of tissue performed during hospitalization due to persistent infection, ischemia, or failure to heal, and was categorized as minor (below the ankle) or major (above the ankle). These standardized definitions were applied consistently for all patients.

Statistical Analysis

Statistical analyses were conducted using the SPSS software package (version 22, SPSS Inc., Chicago, IL, USA). Descriptive statistics for continuous variables obtained through measurement were expressed as mean ± standard deviation or median ± interquartile range (IQR), depending on the data distribution. Categorical variables were presented as frequency (n) and percentage (%). The normality of data distribution was assessed via the Shapiro-Wilk test. For comparisons between two independent groups, Student's t-test was used for normally distributed variables, and the Mann-Whitney U test for non-normal distributions. Relationships between categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate. To evaluate whether PEDIS and Wagner scores could serve as diagnostic and prognostic markers for healing and amputation, receiver operating characteristic (ROC) analysis was performed. ROC curves were generated, and the area under the curve (AUC) with 95% confidence intervals (CIs) was calculated. The AUC was classified as follows: 0.9–1.0 (excellent), 0.8–0.9 (good), 0.7–0.8 (moderate), 0.6–0.7 (poor), and 0.5–0.6 (failed diagnostic performance). The optimal cut-off point for ROC analysis was determined using Youden's index (maximum sensitivity and specificity). Based on these cut-off points, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and positive likelihood ratios (+LR) were calculated to assess the discriminative power of the parameters used in diagnosing healing and amputation. To identify potential risk factors influencing healing and amputation, univariate and multivariate logistic regression analyses were performed. Parameters with $p<0.10$ in the univariate logistic regression analysis were incorporated into the multivariate model, with odds ratios (ORs) and confidence intervals calculated. For all fundamental statistical tests, a significance level of $p<0.05$ was considered statistically significant.

Results

In this prospective and observational study, a total of 121 participants aged between 18 and 85 years, diagnosed with diabetic foot ulcers at varying levels and without any gender discrimination, were included. When the demographic characteristics of these patients were evaluated, two groups were formed: the healed group, consisting of 78 patients (64.5%), and the amputation group, comprising 43 patients (35.5%).

Of the 121 patients, 94 (77.7%) were male and 27 (22.3%) were female. The mean age of the patients was 64.88 ± 11.66 years. The gender distribution between the study groups was statistically significant ($p=0.036$). The mean age of patients in the healed group was 62.51 ± 10.91, whereas the mean age in the amputation group was 69.16 ± 11.86, demonstrating a statistically significant difference between the groups ($p=0.002$). The comparison of demographic characteristics, clinical features, and blood parameters among the study groups is presented in Table I. Among the blood parameters, only lymphocyte count and neutrophil-to-lymphocyte ratio (NLR) values showed statistically significant differences between the groups ($p=0.027$ and $p=0.012$, respectively). Other blood parameters were similar between the groups ($p>0.05$).

A statistically significant relationship was found between the Texas-ABCD classification and the study groups ($p=0.008$). It was observed that as the letter grade increased, the rate of amputation also increased. However, no statistically significant relationship was found between the Texas-123 classification and the study groups ($p=0.593$). Overall, a statistically significant association was identified between the Texas classification system and the study groups ($p=0.047$, Table II).

Table I. Comparison of Demographic Characteristics and Blood Parameters of Patients According to Groups

Variables	Group	Healed (n=78)	Amputation (n=43)	All Patients (n=121)	*p-value*
Gender n(%)	Male	56 (59.6)	38 (40.4)	94 (77.7)	*0.036*[c]
	Female	22 (81.5)	5 (18.5)	27 (22.3)	
BMI n(%)	18.5–24.9 (Normal Weight)	19 (59.4)	13 (40.6)	32 (26.4)	*0.462*[d]
	25–29.9 (Overweight)	43 (68.3)	20 (31.7)	63 (52.1)	
	30–34.9 (Obese Class 1)	8 (50)	8 (50)	16 (13.2)	
	35–39.9 (Obese Class 2)	5 (71.4)	2 (28.6)	7 (5.8)	
	>40 (Obese Class 3)	3 (100)	0 (0)	3 (2.5)	
Side n(%)	Right	39 (60)	26 (40)	65 (53.7)	*0.269*[c]
	Left	39 (69.6)	17 (30.4)	56 (46.3)	
DM, n(%)	Tip 1	1 (33.3)	2 (66.7)	3 (2.5)	*0.287*[d]
	Tip 2	77 (65.3)	41 (34.7)	118 (97.5)	
HT, n(%)	Yok	31 (73.8)	11 (26.2)	42 (34.7)	*0.117*[c]
	Var	47 (59.5)	32 (40.5)	79 (65.3)	
Nephropathy, n(%)	Yok	59 (67.8)	28 (32.2)	87 (71.9)	*0.218*[c]
	Var	19 (55.9)	15 (44.1)	34 (28.1)	
Retinopathy, n(%)	Yok	68 (63)	40 (37)	108 (89.3)	*0.377*[d]
	Var	10 (76.9)	3 (23.1)	13 (10.7)	
Neuropathy, n(%)	Yok	19 (73.1)	7 (26.9)	26 (21.5)	*0.300*[c]
	Var	59 (62.1)	36 (37.9)	95 (78.5)	
Alcohol, n(%)	Yok	72 (65.5)	38 (34.5)	110 (90.9)	*0.518*[d]
	Var	6 (54.5)	5 (45.5)	11 (9.1)	
Smoking, n(%)	Yok	62 (66)	32 (34)	94 (77.7)	*0.522*[c]
	Var	16 (59.3)	11 (40.7)	27 (22.3)	
Drug abuse, n(%)	Yok	75 (64.1)	42 (35.9)	117 (96.7)	*1.000*[d]
	Var	3 (75)	1 (25)	4 (3.3)	
Age, Mean±SD		62.51±10.91	69.16±11.86	64.88±11.66	***0.002***[a]
DM duration, Median±IQR		12±9	13±9	12±9	*0.778*[b]
Ulcer duration, Median±IQR		75±58	85±70	75±55	*0.086*[b]
Fasting Blood Glucose, Median±IQR		191.5±140	169±128	185±131	*0.150*[b]
Creatinine, Median±IQR		1.1±0.7	1.1±0.9	1.1±0.6	*0.325*[b]
Urea, Median±IQR		50.5±35	56±43	51±39	*0.404*[b]
Total Cholesterol, Mean.±SD		156.68±36.9	144.4±32.5	152.3±35.7	*0.070*[a]
Albumin, Mean±SD		31.69±5.37	32±4.77	31.80±5.15	*0.755*[a]
HbA1C, Median±IQR		8.5±1.9	8±3	8.4±2.4	*0.267*[b]
C-reactive protein (CRP), Median±IQR		39.5±81.5	78.6±105.2	48.6±99.2	*0.183*[b]
ESR, Median±IQR		37.5±29	38±29	38±29	*0.828*[b]
Hemoglobin, Mean±SD		11.24±1.85	10.63±1.75	11.02±1.83	*0.082*[a]
White blood cell count, Median±IQR		9.67±4.58	11.03±5.11	10.08±4.67	*0.211*[b]
Neutrophil, Median±IQR		7.26±4.38	8.54±4.99	7.71±4.72	*0.096*[b]
Lymphocyte, Median±IQR		1.84±1.24	1.42±0.54	1.62±1.11	***0.027***[b]
Neutrophil/lymphocyte ratio Median±IQR		3.77±4.54	6.12±4.93	4.41±4.75	***0.012***[b]

BMI: body mass index, DM: diabetes mellitus, HT: hypertension, IQR: interquartile range

SD: standard deviation,ESR: erythrocyte sedimentation rate, [a] Student's t test with mean±SD, [b] Mann Whitney U test with Median±IQR, [c] Chi-square test, [d] Fisher's Exact test

Table II. Statistical Findings Regarding the Comparison of PEDIS, Wagner, and Texas Classification Distributions Among the Study Groups

PEDIS SCORE SYSTEM	Healed N (%)	Amputation N (%)	Total N (%)	*p-value*
Perfusion 0	25 (89.3%)	3 (10.7%)	28 (100%)	*0.002*[c]
Perfusion 1	38 (63.3%)	22 (36.7%)	60 (100%)	
Perfusion 2	15 (45.5%)	18 (54.5%)	33 (100%)	
Sensation 0	37 (77.1%)	11 (22.9%)	48 (100%)	***0.019***[c]
Sensation 1	41 (56.2%)	32 (43.8%)	73 (100%)	
Extension 0	1 (100.0%)	0 (0.0%)	1 (100%)	*0.862*[d]
Extension 1	2 (100.0%)	0 (0.0%)	2 (100%)	
Extension 2	25 (65.8%)	13 (34.2%)	38 (100%)	
Extension 3	50 (62.5%)	30 (37.5%)	80 (100%)	
Depth 0	1 (100.0%)	0 (0.0%)	1 (100%)	***0.001***[d]
Depth 1	30 (85.7%)	5 (14.3%)	35 (100%)	
Depth 2	34 (64.2%)	19 (35.8%)	53 (100%)	
Depth 3	13 (40.6%)	19 (59.4%)	32 (100%)	
Infection 0	6 (60.0%)	4 (40.0%)	10 (100%)	***0.006***[d]
Infection 1	38 (82.6%)	8 (17.4%)	46 (100%)	
Infection 2	32 (52.5%)	29 (47.5%)	61 (100%)	
Infection 3	2 (50.0%)	2 (50.0%)	4 (100%)	
WAGNER GRADE				
Grade 1	9 (81.8%)	2 (18.2%)	11 (100%)	***0.001***[d]
Grade 2	29 (87.9%)	4 (12.1%)	33 (100%)	
Grade 3	20 (64.5%)	11 (35.5%)	31 (100%)	
Grade 4	10 (50.0%)	10 (50.0%)	20 (100%)	
Grade 5	9 (42.9%)	12 (57.1%)	21 (100%)	
Grade 6	1 (20.0%)	4 (80.0%)	5 (100%)	
TEXAS CLASSIFICATION				
A0	1 (100.0%)	0 (0.0%)	1 (100.0%)	***0.047***[d]
A1	11 (91.7%)	1 (8.3%)	12 (100.0%)	
A2	4 (100.0%)	0 (0.0%)	4 (100.0%)	
A3	3 (60.0%)	2 (40.0%)	5 (100.0%)	
B0	1 (50.0%)	1 (50.0%)	2 (100.0%)	
B1	7 (100.0%)	0 (0.0%)	7 (100.0%)	
B2	11 (73.3%)	4 (26.7%)	15 (100.0%)	
B3	1 (100.0%)	0 (0.0%)	1 (100.0%)	
C1	2 (66.7%)	1 (33.3%)	3 (100.0%)	
C2	3 (33.3%)	6 (66.7%)	9 (100.0%)	
C3	9 (64.3%)	5 (35.7%)	14 (100.0%)	
D1	4 (36.4%)	7 (63.6%)	11 (100.0%)	
D2	12 (60.0%)	8 (40.0%)	20 (100.0%)	
D3	9 (52.9%)	8 (47.1%)	17 (100.0%)	
Total	**78 (64.5%)**	**43 (35.5%)**	**121 (100.0%)**	

a Student's t test with mean±SD, b Mann Whitney U test with Median±IQR, c Chi-square test, d Fisher's Exact test

A statistically significant relationship was found between perfusion within the PEDIS scoring system and the study groups (*p=0.002*). However, wound extent within the PEDIS scoring system did not show a statistically significant relationship with the study groups (*p=0.862*). A significant relationship was observed between wound depth and the study groups (*p=0.001*), as well as between infection status and the study groups (*p=0.006*). Additionally, sensory impairment was significantly associated with the study groups (*p=0.019*). The comparison of PEDIS scores between the groups is presented in Table II, where scores were significantly higher in the amputation group (*p<0.001*).

Table III. Sensitivity, Specificity, Positive-Negative Predictive Values, and Positive Likelihood Ratio (LR+) of PEDIS, Wagner, and ABI Parameters

	PEDIS	Wagner	ABI
Cut off value	≥7.5	≥3.5	≥0.9
Sensitivity	0.814 (0.661-0.911)	0.605 (0.445-0.746)	0.628 (0.467-0.766)
Specificity	0.564 (0.447-0.674)	0.744 (0.630-0.833)	0.667 (0.550-0.767)
PPV	0.507 (0.385-0.629)	0.565 (0.412-0.708)	0.509 (0.370-0.647)
NPV	0.846 (0.714-0.927)	0.773 (0.659-0.859)	0.765 (0.644-0.856)
LR+	1.87 (1.40-2.50)	2.36 (1.51-3.69)	1.88 (1.28-2.78)

PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, ABI: ankle-brachial index

To assess whether PEDIS scores could serve as a prognostic marker for predicting healing or amputation outcomes, ROC (Receiver Operating Characteristic) curve analysis was performed. The results, including sensitivity, specificity, positive and negative predictive values, and positive likelihood ratio (LR+), are presented in Table III. The ROC analysis demonstrated that the PEDIS score was significant in distinguishing between healing and amputation outcomes (AUC = 0.722, 95% CI: 0.629–0.816, *p<0.001*). The predictive performance of the PEDIS score is detailed in Table III.

When evaluating the relationship between the Wagner classification and study groups, a statistically significant association was found (*p=0.001*). It was observed that as the Wagner grade increased, the amputation rate also increased. ROC analysis for the Wagner classification showed it was significant in distinguishing between healing and amputation outcomes (AUC = 0.728, 95% CI: 0.633–0.822, *p<0.001*). The ROC curves for both PEDIS and Wagner classifications are shown in Figure I.

The optimal cut-off value for the Wagner classification was determined as 3.5. At this threshold, the classification performance was sensitivity = 60.5% (44.5–74.6%) and specificity = 74.4% (63.0–83.3%)

(Table III).

Patients with an ankle-brachial index (ABI) below 0.9 had a significantly higher amputation rate compared to those with an ABI of 0.9 or higher (*p=0.002*). The amputation rate was 23.5% in patients with ABI ≥ 0.9 and 50.9% in those with ABI < 0.9. The classification performance of ABI for predicting outcomes was sensitivity = 62.8% (46.7–76.6%) and specificity = 66.7% (55.0–76.7%) (Table III).

The results of univariate and multivariate binary logistic regression analyses, performed to identify factors influencing healing and amputation, are shown in Table IV. In the univariate analysis, significant parameters at *p<0.1* included gender, ulcer duration, age, diabetic foot care education (DMFCE), history of amputation, ulcer type, radiological findings, hemoglobin level, lymphocyte count, ABI, and diabetes mellitus education.

Table IV. Results of Univariate and Multivariate Binary Logistic Regression Analysis

	Univariate		Multivariate	
Variables	***p-values***	**Odds ratio (CI 95%)**	***p-values***	**Odds ratio (CI 95%)**
Gender (reference: female)	*0.042*	2.986 (1.040-8.573)	*0.011*	8.278 (1.628-42.093)
Age	*0.004*	1.055 (1.018-1.095)	*0.031*	1.060 (1.006-1.118)
Radiology: Soft tissue infection	*0.265*	0.560 (0.202-1.554)	*0.946*	0.953 (0.235-3.865)
Radiology: Osteomyelitis	*0.579*	0.667 (0.159-2.787)	*0.318*	0.398 (0.065-2.426)
Radiology: Soft tissue infection + osteomyelitis	*0.020*	3.200 (1.199-8.538)	*0.045*	4.386 (1.035-18.588)
ABI (Reference: ≥0.9)	*0.002*	3.375 (1.552-7.342)	*0.003*	5.385 (1.744-16.621)
PEDIS Prediction (reference: <7.5)	*<0.001*	5.662 (2.327-13.773)	*0.021*	3.930 (1.228-12.580)
Diabetic Foot Care Education (Reference: Diabetes education)	*<0.001*	10.956 (4.484-26.768)	*<0.001*	8.532 (2.770-26.275)
Ulcer duration	*0.061*	1.008 (1.000-1.016)	not included	
Hemoglobin	*0.085*	0.830 (0.671-1.026)	not included	
Lymphocyte count	*0.056*	0.576 (0.327-1.015)	not included	
Nagelkerke R Square: 0.595				

ABI: ankle-brachial index

The multivariate model, which incorporated these parameters, revealed that at *p<0.05*, the following factors were significant: gender (reference: female; OR = 8.28), age (OR = 1.06), radiological findings (soft tissue infection + osteomyelitis; OR = 4.39), ABI (reference: ≥ 0.9; OR = 5.39), PEDIS outcome prediction (<7.5; OR = 3.93), and diabetic foot care education (reference: diabetes education; OR=8.53). These results are summarized in Table IV.

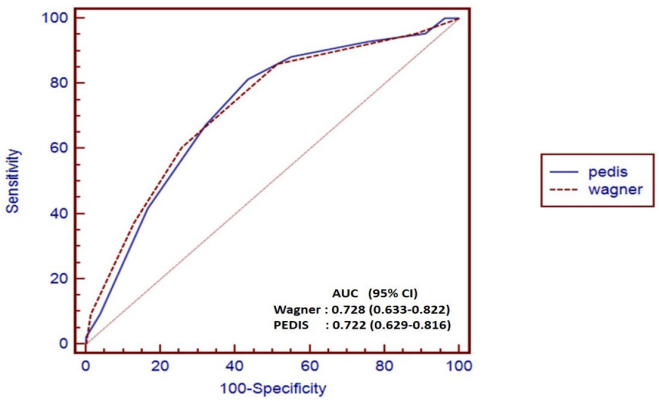

Figure I . ROC Curve Analysis for Outcome Prediction in the PEDIS and Wagner Classification Systems

Discussion

Diabetic foot ulcers (DFUs) have emerged as a significant public health problem in developing countries, paralleling the increasing prevalence of diabetes mellitus (DM). Resulting from neuropathy and/or peripheral vascular disease in an ischemic background, compounded by excessive pressure and infection, DFUs develop in approximately 15% of individuals with diabetes during their lifetime and require amputation in 7–20% of cases, representing a severe complication of diabetes (8). From a public health perspective, DFUs pose substantial concerns due to their high morbidity and mortality rates, prolonged hospital stays, and considerable healthcare costs. Therefore, early diagnosis and effective management are of critical importance for both patients and society. In this context, supportive tools for early detection and management, particularly classification and scoring systems—key prognostic assessment tools—play a crucial role in guiding clinical decision-making and improving patient outcomes. One of the widely utilized classification systems for DFU assessment is the Texas classification. It primarily grades ulcers based on depth and further

categorizes each grade using a staging system that differentiates between clean ulcers, infected ulcers, ischemic ulcers, and ulcers with both infection and ischemia (14,15). Due to its depth-based grading, the Texas system correlates well with the Wagner system in predicting major amputations and demonstrates superior performance in predicting wound healing compared to Wagner (14,15). Although it does not function as a scoring system, higher stages and grades are associated with worse clinical outcomes. Its complex practical application, however, remains a limitation.

In our study, both staging and grading within this classification were analyzed separately and in combination. We observed that as the stage (A, B, C, D) increased, the rate of amputation significantly rose between the groups. Conversely, when examining the grading (1-3) independently, no significant correlation was established. When evaluated together, a significant relationship was identified between the combined stage and grade and clinical outcomes. These findings support prior research indicating that the combined assessment of stage and grade offers prognostic value for healing and amputation. However, analyzing stage and grade separately did not yield the same predictive consistency. Thus, while the Texas classification demonstrates statistical significance in outcome prediction, it offers only moderate reliability.

An important aspect is the absence of neuropathy as a parameter within the Texas system, which is somewhat surprising. This omission is based on the premise that most patients with DFUs already have pre-existing neuropathy, rendering it a less useful differentiator once the ulcer has developed (14, 15). Our findings support this, as neuropathy evaluation did not significantly differ between groups. Although excluding neuropathy may be viewed as a limitation, the simplicity and clearly defined categories of the Texas system contribute to its widespread clinical use (15).

The PEDIS scoring system is another commonly employed classification tool. In this study, five parameters within PEDIS—perfusion, wound extent, wound depth, infection, and sensory function—were evaluated both individually and collectively. A significant relationship was found between perfusion status and clinical outcomes. Notably, the inclusion of ankle-brachial index (ABI) as a perfusion measure enhances the prognostic utility of PEDIS, as ABI values below 0.9 were significantly associated with higher amputation rates (*p=0.002*). This supports prior evidence that ABI is a valuable predictor of adverse outcomes in DFUs (17).

However, the wound extent parameter within PEDIS did not show a significant relationship with outcomes in our cohort, although other studies suggest that larger wound size correlates with poorer healing (16). Conversely, wound depth was significantly associated with outcomes, reinforcing the clinical relevance of this parameter. Sensory impairment also demonstrated a significant relationship, consistent with previous research highlighting its predictive importance. Infection severity, another critical component, was significantly linked to worse outcomes, aligning with literature indicating that increased infection severity prolongs hospitalization and raises amputation risk (19). Our ROC analysis confirmed that the PEDIS score is a significant prognostic marker, with a cut-off value of 7.5 providing moderate sensitivity and specificity.

The Meggitt-Wagner classification, characterized by its straightforward, six-grade structure, remains widely used due to its simplicity, despite limitations in data scope (10). In our study, most ulcers clustered around grades 2 and 3, consistent with prior findings. A significant association was found between Wagner grades and clinical outcomes (*p=0.001*), with higher grades correlating with increased amputation risk. The optimal cut-off was identified as 3.5, with moderate predictive accuracy—similar to previous studies (20,21). The consistency across literature supports the utility of Wagner grading in clinical practice, despite its limited scope.

Regarding vascular assessment, ABI proved to be a valuable predictor of amputation risk. Patients with ABI < 0.9 had significantly higher amputation rates, corroborating prior studies emphasizing ABI's sensitivity to lower extremity ischemia (17,22). Incorporating ABI into prognostic evaluation enhances predictive accuracy, underscoring its importance in comprehensive DFU assessment.

In summary, our findings indicate that the Texas, PEDIS, and Wagner classification systems hold varying degrees of prognostic value. The combined use of staging and scoring enhances predictive accuracy, while individual parameters such as perfusion and infection severity are crucial in outcome prediction. These tools, especially when used collectively, can guide clinicians toward more accurate prognosis and tailored management strategies, ultimately reducing morbidity and mortality associated with DFUs.

Conclusion

The PEDIS scoring system demonstrated the most significant capacity to distinguish between healing and amputation outcomes in diabetic foot ulcer (DFU) patients. Additionally, the Wagner classification effectively predicted the risk of amputation. The ankle-brachial index (ABI) also emerged as a crucial parameter in assessing amputation risk. Factors statistically significant in differentiating healing from amputation included male sex, advanced age, elevated neutrophil-to-lymphocyte ratio, absence of diabetic foot care education and general diabetes education, and the presence of soft tissue infection or osteomyelitis on radiological examination.

Current diabetic foot classification systems, despite their widespread use, are insufficient in guiding treatment and prognosis comprehensively. Notably, the Wagner classification, although easy to apply, lacks key prognostic factors such as neuropathy—an essential determinant of diabetic foot outcomes. Although neuropathy was not significantly associated with amputation risk in this study, the need for a new, comprehensive classification system is evident. Such a system should integrate clinically established prognostic factors, facilitate standardized treatment strategies, and be universally applicable across healthcare providers. Therefore, we advocate for the development and validation of a novel classification or scoring system that combines expert clinical experience with evidence-based prognostic factors, aiming to enhance treatment decision-making and improve patient outcomes.

References

1. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. Ann Med 2017;49(2):106–116.
2. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med 2017;376(24):2367–2375.
3. Abetz L, Sutton M, Brady L, McNulty P, Gagnon DD. The Diabetic Foot Ulcer Scale (DFS): a quality of life instrument for use in clinical trials. Pract Diab Int 2002;19:167–175.
4. Leone S, Pascale R, Vitale M, Esposito S. Epidemiologia del piede diabetico [Epidemiology of diabetic foot]. Infez Med 2012;20 Suppl 1:8–13.
5. Shahi SK, Kumar A, Kumar S et al. Prevalence of diabetic foot ulcer and associated risk factors in diabetic patients from North India. J Diabetic Foot Complications 2012;4:83–91.
6. Richard JL, Schuldiner S. Epidémiologie du pied diabétique [Epidemiology of diabetic foot problems]. Rev Med Interne 2008;2:S222–230.
7. Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons NB. Burden of diabetic foot ulcers for Medicare and private insurers. Diabetes Care 2014;37(3):651–658.
8. Singh S, Pai DR, Yuhhui C. Diabetic foot ulcer—diagnosis and management. Clin Res Foot Ankle 2013;1:120.
9. Lepäntalo M, Apelqvist J, Setacci C, et al. Chapter V: Diabetic foot. Eur J Vasc Endovasc Surg 2011;42:S60–74.
10. Game F. Classification of diabetic foot ulcers. Diabetes Metab Res Rev 2016;32:186–194.
11. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. Diabetes Care 1990;13:513–521.
12. Chadwick P, Jeffcoate W, McIntosh C. How can we improve the care of the diabetic foot? Wounds UK 2008;4:144–148.
13. McCardle J, Chadwick P, Leese G et al. Podiatry competency framework for integrated diabetic foot care: a user's guide. 2012;28:1-28.
14. Oyibo SO, Jude EB, Tarawneh I, Nguyen HC, Harkless LB, Boulton AJ. A comparison of two diabetic foot ulcer classification systems: the Wagner and the University of Texas wound classification systems. Diabetes Care 2001;24:84–88.
15. Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system. The contribution of depth, infection, and ischemia to risk of amputation. Diabetes Care 1998;21:855–859.
16. Chuan F, Tang K, Jiang P, Zhou B, He X. Reliability and validity of the PEDIS classification system and score in patients with diabetic foot ulcer. PLoS One 2015;10:e0124739.
17. Aerden D, Massaad D, von Kemp K, et al. The ankle–brachial

index and the diabetic foot: a troublesome marriage. Ann Vasc Surg 2011;25:770–777.
18. Li H, Lu X, Gao Y, Yang W, Dong P, Zheng J. Neutrophil-to-lymphocyte ratio is a risk factor for diabetic foot ulcer. J Diabetes Res 2020;2020:4217636.
19. Lavery LA, Armstrong DG, Murdoch DP, Peters EJ, Lipsky BA. Validation of the Infectious Diseases Society of America's diabetic foot infection classification system. Clin Infect Dis 2007;44:562-565.
20. Yekta Z, Pourali R, Nezhadrahim R, Ravanyar L, Ghasemi-Rad M. Clinical and behavioral factors associated with management outcome in hospitalized patients with diabetic foot ulcer. Diabetes Metab Syndr Obes 2011;4:371-375.
21. Sun JH, Tsai JS, Huang CH, et al. Risk factors for lower extremity amputation in diabetic foot disease categorized by Wagner classification. Diabetes Res Clin Pract 2012;95:358-363.
22. Jeon BJ, Choi HJ, Kang JS, Tak MS, Park ES. Comparison of five systems of classification of diabetic foot ulcers and predictive factors for amputation. Int Wound J 2017;14:537-545.

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Computed Tomography-guided Percutaneous Pelvic Bone Biopsy: Technical Success, Diagnostic Performance, and Safety

Bilgisayarlı Tomografi Kılavuzluğunda Perkütan Pelvik Kemik Biyopsisi: Teknik Başarı, Tanısal Performans ve Güvenilirlik

Kadir Han Alver | Muhammet Arslan

Pamukkale University Faculty of Medicine, Department of Radiology, Denizli, Türkiye

Sorumlu Yazar | Correspondence Author
Kadir Han Alver
kadirhanalver@gmail.com
Address for Correspondence: Pamukkale University Faculty of Medicine, Department of Radiology, Kınıklı, 20160 Pamukkale, Denizli, Türkiye.

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Computed Tomography-guided Percutaneous Pelvic Bone Biopsy: Technical Success, Diagnostic Performance, and Safety

ABSTRACT

Objective: To evaluate the technical success, diagnostic performance, and complications of CT-guided pelvic bone biopsies.

Material and Method: Fifty patients (32 women, 18 men; mean age: 57.5 ± 15.5 years; range: 20–91) who underwent CT-guided pelvic bone biopsy (sacrum, ilium, ischium, pubis, proximal femur) between 2017 and 2024 were included. Biopsies were performed by interventional radiologists with a minimum of five years of experience. Lesion size, location, type (lytic, sclerotic, or mixed), pathology results, technical success, diagnostic performance, and complications were recorded from patient files and the Picture Archiving and Communication System (PACS). Complications were classified as minor or major according to the Society of Interventional Radiology (SIR) guidelines.

Results: Technical success was 100% (50/50). Pathology revealed malignancy in 25 (50%) patients, benignity in 15 (30%), and nondiagnostic results in 10 (20%), yielding a diagnostic performance of 80%. Nondiagnostic lesions were significantly smaller than malignant (*p=0.002*) and benign (*p<0.001*) ones. Lesion types were lytic in 16 (32%), sclerotic in 17 (34%), and mixed in 17 (34%) cases. When pathology results were grouped as diagnostic (malignant or benign) vs. nondiagnostic, a significant association was found with lesion type (*p=0.025*); 70% of nondiagnostic lesions were sclerotic. Minor complications occurred in 5 (10%) patients, including moderate pain (n=2), transient hypotension (n=1), ecchymosis (n=1), and localized iliopsoas hematoma (n=1). No major complications were observed.

Conclusion: CT-guided pelvic bone biopsy is a safe procedure with high technical success and diagnostic yield. Smaller and sclerotic lesions are more likely to result in nondiagnostic outcomes.

Keywords: Complication, Image-Guided Biopsy, Multidetector Computed Tomography.

ÖZET

Amaç: BT kılavuzluğunda gerçekleştirilen pelvik kemik biyopsilerinin teknik başarısını, tanısal performansını ve komplikasyonlarını değerlendirmek.

Gereç ve Yöntem: 2017–2024 yılları arasında BT eşliğinde pelvik kemik (sakrum, ilium, iskium, pubis, femur proksimali) biyopsisi yapılan 50 hasta (32 kadın, 18 erkek; yaş ortalaması 57,5 ± 15,5; aralık 20–91) çalışmaya dahil edildi. Biyopsiler, en az 5 yıl deneyimli girişimsel radyologlar tarafından gerçekleştirildi. Lezyon boyutu, lokasyonu, tipi (litik, sklerotik, mikst), patoloji sonuçları, teknik başarı, tanısal performans ve komplikasyonlar hasta dosyalarından ve Picture Archiving and Communication System (PACS) üzerinden kaydedildi. Komplikasyonlar, Society of Interventional Radiology (SIR) rehberine göre minör veya majör olarak sınıflandırıldı.

Bulgular: Teknik başarı %100 (50/50) idi. Patoloji sonuçları 25 (%50) malign, 15 (%30) benign ve 10 (%20) nondiagnostik olarak raporlandı; tanısal performans %80 olarak hesaplandı. Nondiagnostik lezyonlar, malign (*p=0,002*) ve benign (*p<0,001*) lezyonlara kıyasla anlamlı derecede daha küçüktü. Lezyonların 16'sı litik (%32), 17'si sklerotik (%34) ve 17'si mikst (%34) tipteydi. Lezyon tipi ile tanısal sonuçlar (diagnostik vs. nondiagnostik) arasında anlamlı ilişki saptandı (*p=0,025*); nondiagnostik lezyonların %70'i sklerotikti. İki hastada ağrı, bir hastada geçici hipotansiyon, bir hastada cilt altı ekimoz ve bir hastada kendini sınırlayan iliopsoas hematomu olmak üzere toplam beş (%10) hastada minör komplikasyon izlenmiş olup, hiçbir hastada majör komplikasyon gelişmedi.

Sonuç: BT eşliğinde pelvik kemik biyopsisi, yüksek teknik başarı ve tanısal performans ile güvenli bir yöntemdir. Küçük ve sklerotik lezyonlarda nondiagnostik sonuç olasılığı daha yüksektir.

Anahtar Sözcükler: Çok Kesitli Bilgisayarlı Tomografi, Görüntüleme Eşliğinde Biyopsi, Komplikasyonlar.

Introduction

Despite significant advancements in modern imaging technologies, percutaneous image-guided or surgical biopsy remains the gold standard for establishing a definitive diagnosis in focal bone lesions that cannot be reliably characterized through imaging alone. Among these approaches, image-guided percutaneous bone biopsy has emerged as the preferred first-line diagnostic method, offering a minimally invasive alternative to open surgical biopsy for histopathological or microbiological analysis (1,2). Image-guided techniques provide several key advantages, including preservation of bone architecture, reduced trauma to adjacent soft tissues, avoidance of general anesthesia, shorter hospital stays, lower procedural costs, and reduced complication rates and tumor seeding risks (3–6).

Although magnetic resonance imaging (MRI) is superior in characterizing bone marrow pathology and musculoskeletal tumors, MRI-guided biopsy is rarely feasible in routine practice due to limited accessibility, logistical challenges, and difficulty in real-time needle guidance. Similarly, ultrasound guidance is primarily reserved for superficial bone lesions with prominent soft-tissue components. In contrast, many bone lesions—particularly those in the pelvis—lack a distinct soft-tissue component and are located in deep or complex anatomical regions. In such cases, computed tomography (CT) guidance provides clear advantages in terms of anatomical visualization, trajectory planning, and real-time confirmation of needle placement (7). Among the various image-guided modalities, CT-guided bone biopsy has become a cornerstone in interventional radiology practice. Its utility stems not only from its high spatial and contrast resolution, which facilitates accurate targeting even in small or sclerotic lesions, but also from its ability to navigate complex anatomy and safely access deep-seated regions such as the pelvis, spine, or posterior ribs. Unlike open surgical biopsy, CT guidance allows for real-time trajectory adjustment to avoid critical structures, minimizing patient risk while maximizing diagnostic yield. Moreover, it offers significant procedural flexibility, particularly in patients with comorbidities who are unsuitable for more invasive interventions. Owing to its reliability, safety, and wide applicability, CT-guided bone biopsy is now one of the most frequently performed procedures in interventional radiology, underscoring the expanding role of interventional radiologists in diagnosis, risk stratification, and multidisciplinary clinical decision-making.

Although CT-guided percutaneous bone biopsy is generally considered a safe procedure, reported complication rates range from 0% to 15.6% (4,8,9). Furthermore, despite its high diagnostic yield, nondiagnostic results have been observed in 2% to 31% of cases, often due to lesion characteristics or sampling limitations (10,11). Given the increasing frequency of these procedures in clinical practice, interventional radiologists must not only ensure technical proficiency but also be aware of the factors that may influence diagnostic success and complication risk. While several studies have evaluated bone biopsy in general, research specifically focusing on pelvic bone lesions remains relatively scarce—especially those examining the technical success, diagnostic performance, safety, and lesion-specific factors affecting diagnostic yield in this anatomically challenging region (12–14). Therefore, the aim of this study is to evaluate the technical success, diagnostic performance, associated complications, and potential predictors of nondiagnostic outcomes in CT-guided percutaneous pelvic bone biopsies performed at our institution between 2017 and 2024.

Material and Method

This study was initiated following approval from the Pamukkale University Non-Interventional Research Ethics Committee of our institution (Date: 24.04.2025, No: E-60116787-020-683857), and it was conducted in accordance with the principles of the Declaration of Helsinki. Although the requirement for informed consent was waived due to the retrospective design of the study, all patients had previously provided written informed consent as part of routine clinical practice after being thoroughly informed by the radiologist performing the biopsy about the procedure and its potential complications. Fifty patients (32 women, 18 men; mean age 57.5 ± 15.5 years, range 20–91) with lesions located in the pelvic bones that could not be definitively diagnosed through radiodiagnostic imaging, who were referred to our clinic for biopsy and underwent CT-guided bone lesion biopsy, were

included in the study. Biopsied lesion sizes, locations, and natures (lytic, sclerotic, and mixed), biopsy results, technical success, diagnostic performance, and procedure-related complications were reviewed and recorded from patient files and the PACS (Picture Archiving and Communication System). Based on the literature, the pelvic bones were defined as the ilium, ischium, pubis, sacrum, and proximal femur (15). Patients whose biopsy results were reported as nondiagnostic were further evaluated and categorized as those who underwent repeat biopsy, those referred for surgical biopsy, those followed up without any additional intervention, and those lost to follow-up. For these patients, the results of repeat CT-guided percutaneous pelvic bone biopsies, open surgical biopsy findings, and any changes in the nature or size of the lesions during follow-up were investigated through patient records and the PACS system.

Prebiopsy Preparation and Management

For all patients, a complete blood count and coagulation studies were conducted on the same day before the biopsy. Acceptable laboratory criteria before the procedure included platelets >50,000/ml and International Normalized Ratio (INR) < 1.5. Before the biopsy, patients' use of anticoagulant and antiplatelet medications was assessed, and necessary adjustments were made in accordance with the Society of Interventional Radiology (SIR) guidelines (16,17). Additionally, patients were assessed for prilocaine or lidocaine allergies, postural limitations affecting positioning, and infection or inflammation at the biopsy site. In cases of suspected sarcoma or planned surgery, a pre-procedural evaluation was conducted with the orthopedic team/physician to assess the risk of tumor seeding along the needle tract (3). In routine practice, the procedure was performed under local anesthesia; however, in patients with severe anxiety or when deemed necessary, the biopsy was performed under conscious sedation (Fentanyl, 25–50 µg [maximum 100 µg]; Midazolam, 0.5–1 mg [maximum 5 mg]) with the support of the anesthesia team (18,19). All biopsies were performed with two interventional radiologists with a minimum of five years of experience.

Biopsy Procedure

Patients were positioned on the CT table (Brilliance 16-slice CT scanner, Philips Healthcare, Amsterdam, Netherlands) in a supine, prone, or lateral decubitus position according to the biopsy plan. As a general principle, the biopsy trajectory was planned to pass through the fewest compartments and to reach the lesion via the shortest possible route. In patients with multiple lesions of similar nature, the largest or the safest lesion in terms of procedural risk was selected for biopsy. The procedure site was disinfected using a 10% povidone-iodine solution following standard sterilization protocols and was then covered with sterile drapes. Local anesthesia was administered using 10–20 cc of 2% prilocaine hydrochloride injected with a 21-gauge needle into the skin, subcutaneous fat, muscle tissue (if applicable), and down to the periosteum. Due to the high density of nerve fibers and significant pain sensitivity in the periosteum, the majority of the anesthetic was used for periosteal injection. In cases where the periosteum could not be reached with a standard needle, a 21-gauge spinal needle was used. A small skin incision was made with a scalpel at the entry point, and the biopsy needle was inserted. The needle tip position was confirmed via CT once it reached the lesion border. Subsequently, the inner stylet of an 11G bone biopsy needle (Bon-Core Trephine Bone Biopsy Needle, Egemen International, İzmir, Türkiye) was removed, and the needle was advanced manually or with the aid of a sterile surgical hammer in hard or sclerotic lesions. The obtained samples were placed in 10% formalin and sent to pathology along with a summary of relevant clinical information. In cases where the lesion had a soft tissue component, additional tissue samples were obtained using a 14G automated biopsy gun (Maxcore, Bard, Covington, GA, USA) with at least two passes (Figures I and II).

Following the procedure, CT imaging was performed to check for potential complications such as bleeding, and patients were monitored in our unit for 4–6 hours. Post-procedural complications were classified according to SIR guidelines. Complications that required no treatment or only nominal therapy were categorized as minor, while those necessitating hospitalization or major therapy, leading to permanent sequelae, resulting in death, prolonging hospital

stay, or causing an unplanned increase in patient care were classified as major complications (20).

Statistical Analysis

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 25.0. Continuous variables were presented as mean, standard deviation, minimum, and maximum values, while categorical variables were expressed as frequencies and percentages. The distribution of continuous variables was assessed using the Shapiro–Wilk test, and since normality was not observed across all groups, the Kruskal–Wallis test was used to compare continuous variables among the three pathology-based subgroups (malignant, benign, and nondiagnostic). Pairwise comparisons of significantly different variables were performed using the Mann–Whitney U test. The Chi-square test was used to analyze associations between categorical variables, including the relationship between lesion type (lytic, sclerotic, or mixed) and diagnostic outcome, which was regrouped as either "diagnostic" (malignant or benign) or "nondiagnostic." A *p-value of* ≤ 0.05 was considered statistically significant in all analyses.

Results

All targeted lesions were successfully accessed under imaging guidance, and tissue samples were obtained in all cases, resulting in a technical success rate of 100% (50/50).

Table I. Summary of Patient Age, Lesion Size, Type, and Location According to Histopathological Diagnosis

	Malign Group	Benign Group	Nondiagnostic Group	Total
Age	59.1 ± 16.7	56.4 ± 15.9	55.3 ± 13.4	57.5 ± 15.5
Average Lesion Size (mm)	33.1 ± 16.6	39.4 ± 12.8	16.4 ± 5.3	31.6 ± 15.9
Lesion Type				
Lytic	14 (28%)	1 (2%)	1 (2%)	16 (32%)
Sclerotic	4 (8%)	6 (12%)	7 (14%)	17 (34%)
Mixed	7 (14%)	8 (16%)	2 (4%)	17 (34%)
Lesion Location				
İlium	12 (24%)	6 (12%)	5 (10%)	23 (46%)
İschium	2 (4%)	1 (2%)	1 (2%)	4 (8%)
Pubis	1 (2%)	2 (4%)	0 (0%)	3 (6%)
Sacrum	5 (10%)	1 (2%)	3 (6%)	9 (18%)
Proximal femur	5 (10%)	5 (10%)	1 (2%)	11 (22%)
Total	25 (50%)	15 (30%)	10 (20%)	50 (100%)

There was no statistically significant difference in the mean ages of patients whose pathology results were reported as malignant (59.1 ± 16.7), benign (56.4 ± 15.9), or nondiagnostic (55.3 ± 13.4) (*p=0.662*). Among the biopsied lesions, pathology results revealed malignancy in 25 out of 50 cases (50%), benignity in 15 cases (30%), and were nondiagnostic in 10 cases (20%), yielding an overall diagnostic performance of 80%. The mean lesion sizes were 33.1 ± 16.6 mm in the malignant group, 39.4 ± 12.8 mm in the benign group, and 16.4 ± 5.3 mm in the nondiagnostic group. While there was no statistically significant difference in lesion size between the malignant and benign groups (*p=0.076*), the average size of lesions in the nondiagnostic group was significantly smaller compared to both the malignant (*p=0.002*) and benign (*p<0.001*) groups (Table I).

Table II. Histopathological Distribution of Malignant Biopsy Diagnoses

No.	Histopathological Diagnoses of Malignant Lesions	Number
1	Breast Carcinoma Metastasis	4
2	Prostate Adenocarcinoma Metastasis	3
3	Adenocarcinoma Metastasis (Primary Site Not Specified)	2
4	Malignant Epithelial Tumor Metastasis (Primary Site Not Specified)	2
5	Squamous Cell Carcinoma Metastasis (Primary Site Not Specified)	2
6	Chondrosarcoma	2
7	Lymphoma	2
8	Small Cell Lung Carcinoma Metastasis	1
9	Lung Squamous Cell Carcinoma Metastasis	1
10	Lung Adenocarcinoma Metastasis	1
11	Acute Myeloid Leukemia (AML) Infiltration	1
12	Gastric Adenocarcinoma Metastasis	1
13	Nasopharyngeal Carcinoma Metastasis	1
14	Solitary Plasmacytoma	1
15	Renal Cell Carcinoma Metastasis	1
Total		25

Of the biopsied lesions, 23/50 (46%) were located in the ilium, 11/50 (22%) in the proximal femur, 9/50 (18%) in the sacrum, 4/50 (8%) in the ischium, and 3/50 (6%) in the pubis. In terms of lesion type, 16/50 (32%) were lytic, 17/50 (34%) were sclerotic, and 17/50 (34%) were mixed (lytic–sclerotic). When pathology results were regrouped as diagnostic (malignant or benign) or nondiagnostic, lesion type was found to be significantly associated with diagnostic outcome

(*p=0.025*). While the majority of diagnostic cases involved lytic (15/16) or mixed-type (15/17) lesions, 7 of the 10 nondiagnostic lesions were sclerotic (Table I).

Table III. Histopathological Distribution of Benign Biopsy Diagnoses

No.	Histopathological Diagnoses of Benign Lesions	Number
1	Enchondroma	4
2	Fibrous Dysplasia	3
3	Degenerative Changes	2
4	Osteomyelitis	2
5	Non-ossifying Fibroma (NOF)	1
6	Paget's Disease	1
7	Osteonecrosis	1
8	Osteoid Osteoma	1
Total		15

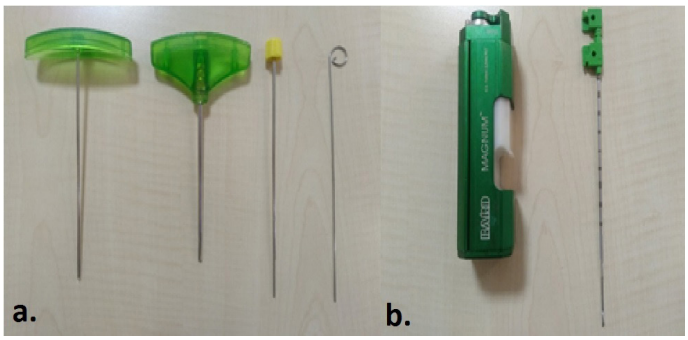

Figure I. (a) 11 Gauge Trephine needle set (Bon-Core Trephine Bone Biopsy Needle, Egemen International, İzmir, Turkey) used for bone biopsy. (b) Automatic biopsy gun (Maxcore, Bard, Covington, GA, USA) and 14 Gauge needle used for bone tumors with a soft tissue component.

Among the lesions reported as malignant (25/50), the most common pathology was metastasis, observed in 76% (19/25) of cases (Figures III and IV). In addition, lymphoma was detected in two patients, acute myeloid leukemia (AML) infiltration in one patient, and solitary plasmacytoma in one patient. Two patients were diagnosed with chondrosarcoma. The most frequent metastases were from the breast (4/19) and prostate (3/19), with two cases each of adenocarcinoma, malignant epithelial tumor, and squamous cell carcinoma metastases of unknown primary origin (Table II). Benign biopsy results included enchondroma (4/15), fibrous dysplasia (3/15), degenerative changes (2/15), osteomyelitis (2/15), and one case each of non-ossifying fibroma (NOF), Paget's disease, osteonecrosis, and osteoid osteoma (Table III).

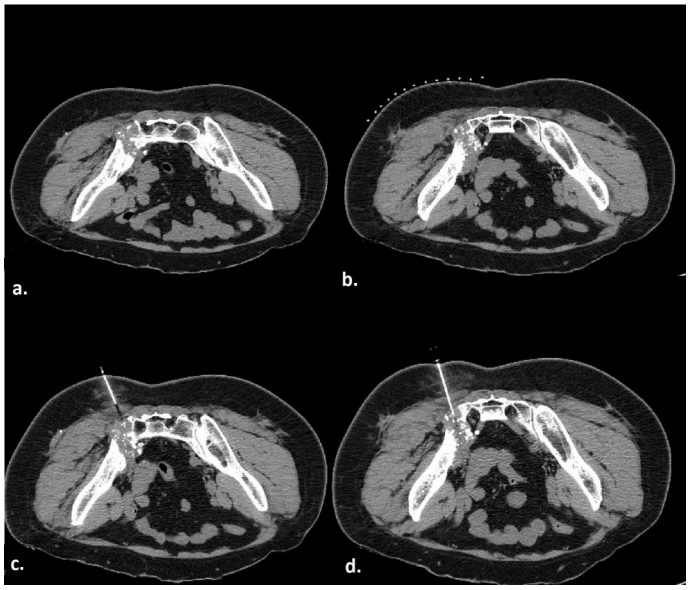

Figure II. Procedural steps of CT-guided bone biopsy. (a) An expansile lytic-sclerotic (mixed-type) mass lesion involving the joint space and causing bone destruction in the right sacroiliac junction. (b) A guide marker placed at the appropriate level in the prone position to determine the skin entry point corresponding to the lesion location. (c) Reference image obtained after injecting 2% prilocaine hydrochloride into the skin, subcutaneous tissue, adjacent soft tissue-muscle planes and periosteum. (d) Biopsy needle insertion into the lesion and sample collection. The pathological diagnosis of the lesion was reported as chondrosarcoma.

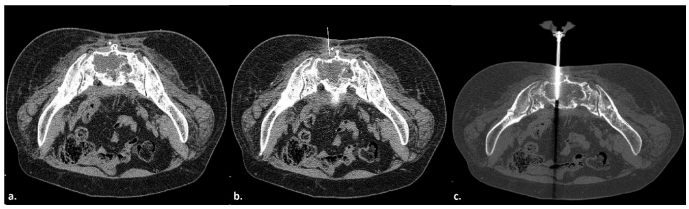

Figure III. a) In the prone position, a lytic lesion is observed in the midline of the sacrum in a follow-up patient with a history of nephrectomy due to renal cell carcinoma. b) Injection of 2% prilocaine hydrochloride into the skin, subcutaneous tissue, periosteum and adjacent soft tissues near the lesion. c) Entry into the lesion with a bone biopsy needle and sample collection. The pathological diagnosis of the lesion was reported as metastasis of renal cell carcinoma

Among the ten patients whose biopsy results were reported as nondiagnostic, four underwent repeat biopsy and two underwent surgical biopsy

during follow-up. Two patients were placed under surveillance, while no follow-up data were available in the system for the remaining two. Among the four patients who underwent repeat biopsy, one result remained nondiagnostic, one was reported as degenerative changes, one as prostate carcinoma metastasis, and one as low-grade chondrosarcoma/enchondroma. Of the two patients who underwent surgical biopsy, one was reported as showing necrosis, hemorrhage, and fibrous tissue, while the other was reported as having osteonecrosis, chronic active inflammation, and degeneration. Follow-up imaging was available for two patients under surveillance at 6 months and 2 years post-procedure, respectively, and in both cases, no significant changes were observed in lesion size or characteristics (Figure V).

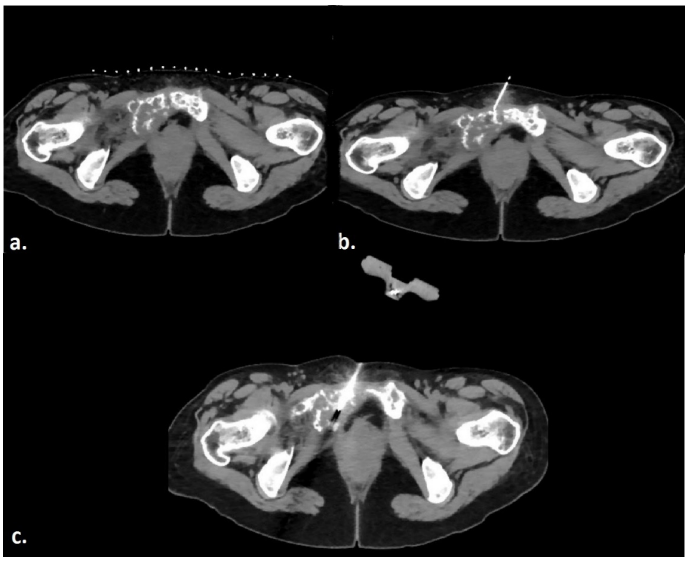

Figure IV. a) An expansile, lytic–sclerotic (mixed type) lesion observed in the right ischium on follow-up imaging of a patient diagnosed with lung adenocarcinoma, and a marker used for guidance to access the lesion in the supine position; b) Injection of 2% prilocaine hydrochloride into the skin, periosteum and subcutaneous tissue; c) Access to the lesion with a bone biopsy needle and tissue sampling. The lesion was reported as a metastasis on pathological examination.

During and after the procedure, minor complications were observed in 5 out of 50 patients (10%). These included moderate pain managed with oral analgesics in two patients, transient hypotension in one patient, and subcutaneous ecchymosis in one patient. Additionally, in one patient, a self-limiting intramuscular hematoma was detected in the iliopsoas muscle along the biopsy tract on imaging performed for unrelated reasons on the eighth day post-procedure. No major complications were observed in any patient.

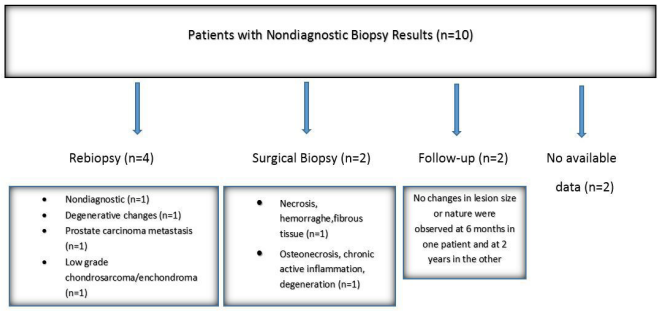

Figure V. Clinical Follow-up of Patients with Non diagnostic Biopsy Results

Discussion

Our study demonstrated that CT-guided pelvic bone biopsy is a highly effective and safe diagnostic procedure, with a technical success rate of 100% and a diagnostic yield of 80%. Importantly, nondiagnostic outcomes were significantly associated with smaller lesion size and sclerotic morphology—factors that may hinder adequate tissue sampling. The absence of major complications further supports the procedure's safety profile. These findings reinforce the utility of CT-guided biopsy as a first-line diagnostic tool for pelvic bone lesions, while also highlighting the challenges posed by specific lesion characteristics.

The overall diagnostic yield in our study was 80%, which falls within the broad range of 69% to 98% reported in prior studies of CT-guided musculoskeletal biopsies (10,11,21). For example, Wu et al. (2008) reported a diagnostic success rate of 88% in a large cohort including various skeletal sites, while Didolkar et al. (2013) found a lower rate of 76% specifically for pelvic and spinal lesions. Our results are comparable, especially considering the anatomical complexity of pelvic bone biopsies and the high proportion of sclerotic or small lesions in our sample. Among the 50 biopsied lesions, 10 (20%) yielded nondiagnostic histopathological results. These lesions were significantly smaller than both malignant ($p=0.002$) and benign ($p<0.001$) lesions, suggesting that lesion size plays a critical role in diagnostic success. When pathology results were

regrouped as diagnostic (malignant or benign) versus nondiagnostic, a statistically significant association was observed with lesion type (*p=0.025*). Notably, 70% of nondiagnostic lesions were sclerotic, whereas most diagnostic lesions were either lytic or mixed. These findings are consistent with previous studies identifying sclerotic morphology and small lesion size as major challenges in bone biopsy. In the study published by Spinnato et al. in 2023, lesion size was identified as the most critical factor influencing diagnostic yield (22). The authors reported that lesions larger than 3 cm had a significantly higher diagnostic yield compared to smaller lesions. Additionally, sclerotic or osteoblastic lesions were found to have a lower diagnostic accuracy than osteolytic or mixed lesions. Moreover, Cohen et al. (2016) emphasized that nondiagnostic rates are higher in sclerotic lesions due to sampling difficulty, and Sung et al. (2009) found lesion density and lack of soft tissue components to be independent risk factors for nondiagnostic outcomes. Additionally, in a study published by Donners et al. in 2022, the authors reported that targeting areas with predominantly mild sclerosis and lower CT attenuation in cancer patients with sclerotic bone disease can improve tumor tissue yield, suggesting that sampling from less dense, mildly sclerotic regions of the lesion has a positive impact on diagnostic outcomes (23). In line with our results, previous studies have reported that malignant bone lesions—particularly those that are lytic, demonstrate cortical destruction, or contain soft-tissue components—are generally more likely to yield diagnostic samples (24,25). Although the likelihood of nondiagnostic histopathological results increases with greater lesion density and sclerotic appearance, such bone lesions are also more likely to be non-malignant. In our study, among the eight nondiagnostic lesions with available follow-up or histopathological data, only two were ultimately confirmed as malignant—one prostate carcinoma metastasis and one low-grade chondrosarcoma/enchondroma—while the others were benign or stable. However, it is important to note that sclerotic bone lesions may be associated with malignancy, particularly in the context of prostate or breast cancer metastases, which are characteristically osteoblastic (26,27). Although coaxial battery-powered biopsy systems have been shown to improve tissue acquisition in sclerotic lesions, we used manual techniques exclusively in our study (25). The lack of drill-assisted systems may have contributed to the nondiagnostic results in some sclerotic cases. Nevertheless, we believe that the significantly smaller size of nondiagnostic lesions was the primary factor limiting diagnostic yield, likely more so than lesion type or biopsy method alone.

Minor complications were observed in 5 out of 50 patients (10%), including moderate pain in two patients, and transient hypotension, subcutaneous ecchymosis, and a self-limiting intramuscular hematoma in the iliopsoas muscle in one patient each. Consistent with our findings, previous studies have reported lower complication rates for percutaneous bone biopsy compared to surgical biopsy, with rates ranging from 0% to 15.6% (4,8,9,28). As in our study, pain is the most frequently observed minor complication, while others include bleeding, needle breakage, infection, neurological injury, pneumothorax, and tumor seeding along the needle tract. Notably, no major complications requiring hospitalization or significant intervention, as defined by the Society of Interventional Radiology (SIR) guidelines, occurred during or after the procedures. We believe that this favorable safety profile and the absence of major complications can be attributed to several key factors: the experience of the interventional radiologists performing the procedures; the use of CT guidance throughout all procedural steps; the adjustment of anticoagulant and antiplatelet therapy in accordance with current guidelines to reduce the risk of post-procedural hemorrhage and other complications; and the implementation of thorough pre-procedural clinical evaluation and questioning (e.g., assessment of postural limitations or presence of infection at the procedure site). Furthermore, meticulous procedural planning—including the selection of the shortest and safest access route to the lesion, and in cases of multiple lesions, targeting the one with the lowest risk of complications—likely contributed to the absence of major adverse events.

This study has several limitations. First, it was a retrospective, single-center study and is therefore subject to the inherent limitations of such study

designs. In addition, the patient population was relatively limited. Pathological evaluations performed at large, highly specialized centers dedicated to oncology or musculoskeletal tumors may offer higher diagnostic accuracy, and the lack of such specialization in our setting may have contributed to our nondiagnostic rate. Another limitation is the absence of follow-up data for some patients whose biopsy results were reported as nondiagnostic. Furthermore, for some lesions reported as benign, pre-procedural imaging was not performed at our institution, and the level of radiological assessment conducted at the referring centers is unknown. It is possible that if these lesions had been evaluated by experienced musculoskeletal radiologists at our center, a confident diagnosis might have been made without the need for biopsy. This, in turn, may have influenced the proportion of benign biopsy results in our study.

Conclusion

CT-guided bone biopsy is a safe, effective, and feasible diagnostic procedure with high technical success and diagnostic performance, and a low complication rate when performed by interventional radiologists. In our study, smaller lesion size was significantly associated with nondiagnostic biopsy outcomes. Most malignant lesions were lytic, benign lesions were predominantly of mixed type, and the majority of nondiagnostic lesions were sclerotic. These findings highlight the importance of considering lesion characteristics when planning the procedure. Interventional radiologists should be particularly cautious with small and sclerotic lesions, which carry a higher risk of nondiagnostic results, and adjust their approach accordingly to optimize diagnostic yield. Finally, close follow-up of biopsy results, re-biopsy when necessary, and referral to surgical biopsy for patients with inconclusive repeat procedures and high-risk lesions may help improve diagnostic accuracy and patient management.

References

1. Masood S, Mallinson PI, Sheikh A, Ouellette H, Munk PL. Percutaneous bone biopsy. Tech Vasc Interv Radiol 2022;25:100800.
2. Errani C, Traina F, Perna F, Calamelli C, Faldini C. Current concepts in the biopsy of musculoskeletal tumors. ScientificWorldJournal 2013;2013:538152.
3. Meek RD, Mills MK, Hanrahan CJ, et al. Pearls and pitfalls for soft-tissue and bone biopsies: A cross-institutional review. Radiographics 2020;40:266–290.
4. Espinosa LA, Jamadar DA, Jacobson JA, et al. CT-guided biopsy of bone: a radiologist's perspective. AJR Am J Roentgenol 2008;190:W283–W289.
5. McCarthy EF. CT-guided needle biopsies of bone and soft tissue tumors: a pathologist's perspective. Skeletal Radiol 2007;36:181–182.
6. Seeger LL. Revisiting tract seeding and compartmental anatomy for percutaneous image-guided musculoskeletal biopsies. Skeletal Radiol 2019;48:499–501.
7. Jelinek J, Buick M, Shmookler B. Image-guided percutaneous biopsies of musculoskeletal lesions. AJR Am J Roentgenol 1996;167:532–533.
8. Shif Y, Kung JW, McMahon CJ, et al. Safety of omitting routine bleeding tests prior to image-guided musculoskeletal core needle biopsy. Skeletal Radiol 2018;47:215–221.
9. Foremny GB, Pretell-Mazzini J, Jose J, Subhawong TK. Risk of bleeding associated with interventional musculoskeletal radiology procedures: A comprehensive review. Skeletal Radiol 2015;44:619–627.
10. Wu JS, Goldsmith JD, Horwich PJ, Shetty SK, Hochman MG. Bone and soft-tissue lesions: factors affecting diagnostic yield of image-guided core-needle biopsy. Radiology 2008;248:962–970.
11. Didolkar MM, Anderson ME, Hochman MG, et al. Image guided core needle biopsy of musculoskeletal lesions: are nondiagnostic results clinically useful? Clin Orthop Relat Res 2013;471:3601–3609.
12. Afonso PD, Weber MA, Isaac A, Bloem JL. Hip and pelvis bone tumors: can you make it simple? Semin Musculoskelet Radiol 2019;23:e37–e57.
13. Girish G, Finlay K, Fessell D, et al. Imaging review of skeletal tumors of the pelvis: malignant tumors and tumor mimics. ScientificWorldJournal 2012;2012:240281.
14. Girish G, Finlay K, Morag Y, et al. Imaging review of skeletal tumors of the pelvis—Part I: benign tumors of the pelvis. ScientificWorldJournal 2012;2012:290930.
15. Bloem JL, Reidsma II. Bone and soft tissue tumors of hip and pelvis. Eur J Radiol 2012;81:3793–3801.
16. Patel IJ, Rahim S, Davidson JC, et al. Society of Interventional Radiology consensus guidelines for the periprocedural management of thrombotic and bleeding risk in patients undergoing percutaneous image-guided interventions—Part II:

Recommendations. J Vasc Interv Radiol 2019;30:1168–1184.e1.
17. sDavidson JC, Rahim S, Hanks SE, et al. Society of Interventional Radiology consensus guidelines for the periprocedural management of thrombotic and bleeding risk in patients undergoing percutaneous image-guided interventions—Part I: Review of anticoagulation agents and clinical considerations. J Vasc Interv Radiol 2019;30:1155–1167.
18. Moran TC, Kaye AD, Mai AH, Bok LR. Sedation, analgesia, and local anesthesia: a review for general and interventional radiologists. Radiographics 2013;33:E47–E60.
19. Patatas K, Koukkoulli A. The use of sedation in the radiology department. Clin Radiol 2009;64:655–663.
20. Sacks D, McClenny TE, Cardella JF, Lewis CA. Society of Interventional Radiology clinical practice guidelines. J Vasc Interv Radiol 2003;14:S199–S202.
21. Chang IJ, Ilaslan H, Sundaram M, Schils J, Subhas N. CT-guided percutaneous biopsy of sclerotic bone lesions: diagnostic outcomes. Skeletal Radiol 2018;47:661–669.
22. Spinnato P, Colangeli M, Rinaldi R, Ponti F. Percutaneous CT-guided bone biopsies: indications, feasibility and diagnostic yield in the different skeletal sites—from the skull to the toe. Diagnostics (Basel) 2023;13:2350.
23. Donners R, Fotiadis N, Figueiredo I, et al. Optimising CT-guided biopsies of sclerotic bone lesions in cancer patients. Eur Radiol 2022;32:6820–6829.
24. Sung KS, Seo SW, Shon MS. The diagnostic value of needle biopsy for musculoskeletal lesions. Int Orthop 2009;33:1701–1706.
25. Cohen MG, McMahon CJ, Kung JW, Wu JS. Comparison of battery-powered and manual bone biopsy systems for core needle biopsy of sclerotic bone lesions. AJR Am J Roentgenol 2016;206:W83–W86.
26. Goode EA, Wang N, Munkley J. Prostate cancer bone metastases: biology and clinical management. Oncol Lett 2023;25:163.
27. O'Sullivan GJ, Carty FL, Cronin CG. Imaging of bone metastasis: an update. World J Radiol 2015;7:202–211.
28. Kattapuram SV, Rosenthal DI. Percutaneous biopsy of skeletal lesions. AJR Am J Roentgenol 1991;157:935–942.

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Association Between Weight-Adjusted Waist Index and Depressive Symptoms in Older Adults

Yaşlı Bireylerde Ağırlıkla Düzeltilmiş Bel Çevresi İndeksi ile Depresif Semptomlar Arasındaki İlişki

Ayşe Dikmeer[1] | Suna Bürkük[2]

[1]Ankara Bilkent City Hospital, Department of Internal Medicine, Division of Geriatrics, Ankara, Türkiye
[2]Hitit University Erol Olçok Education and Research Hospital, Department of Internal Medicine, Division of Geriatrics, Çorum, Türkiye

Sorumlu Yazar | Correspondence Author
Ayşe Dikmeer
adikmeer@yahoo.com
Address for Correspondence: Ankara Bilkent City Hospital, Geriatrics Clinic, 06800, Ankara, Türkiye.

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Association Between Weight-Adjusted Waist Index and Depressive Symptoms in Older Adults

ABSTRACT

Objective: Depression is a common and disabling condition in older adults. Identifying simple, non-invasive predictors of depression risk is essential for early intervention. The Weight-Adjusted Waist Index (WWI), a novel anthropometric marker of central adiposity, may be associated with depressive symptoms in older populations. This study aims to investigate the association between WWI and depressive symptoms in adults aged 65 years and older.

Material and Method: This retrospective cross-sectional study included 150 patients aged ≥65 years attending a geriatrics outpatient clinic. Sociodemographic, functional, cognitive, nutritional, and anthropometric data were collected. Depressive symptoms were assessed using the Yesavage Geriatric Depression Scale (GDS), with scores ≥5 indicating depression. WWI was calculated as waist circumference (cm) divided by the square root of weight (kg). Binary logistic regression analysis was performed to identify factors independently associated with depressive symptoms.

Results: Depressive symptoms were present in 53 participants (35.3%). Patients with depressive symptoms had significantly higher WWI values (11.68 ± 0.73 vs. 11.28 ± 0.66, *p<0.001*). In the final regression model, female gender (OR: 3.17; 95% CI: 1.21–8.32; *p=0.019*), lower Standardized Mini-Mental State Examination (SMMSE) score (OR: 0.84; 95% CI: 0.75–0.95; *p=0.005*), higher WWI (OR: 1.66; 95% CI: 0.91–3.02; *p=0.097*), and lower MNA-SF score (OR: 0.76; 95% CI: 0.60–0.97; *p=0.027*) were associated with depressive symptoms.

Conclusion: Higher WWI may be linked to depressive symptoms in older adults. WWI could serve as a simple, non-invasive tool to help identify individuals at increased risk of depression. Longitudinal studies are needed to confirm these findings.

Keywords: Depression, Older adults, Weight-Adjusted Waist Index.

ÖZET

Amaç: Depresyon, yaşlı bireylerde yaygın ve işlevselliği bozan bir durumdur. Depresyon riskini öngörebilecek basit ve invaziv olmayan belirteçlerin tanımlanması, erken müdahale açısından büyük önem taşır. Ağırlıkla Düzeltilmiş Bel Çevresi İndeksi (WWI), santral obezitenin yeni bir antropometrik göstergesi olup yaşlı bireylerde depresif semptomlarla ilişkili olabilir. Bu çalışmanın amacı, WWI ile depresif semptomlar arasındaki ilişkiyi 65 yaş ve üzeri bireylerde incelemektir.

Gereç ve Yöntem: Bu retrospektif kesitsel çalışmaya, geriatri polikliniğine başvuran 65 yaş ve üzeri 150 hasta dâhil edilmiştir. Sosyodemografik, fonksiyonel, bilişsel, beslenme durumu ve antropometrik veriler toplanmıştır. Depresif semptomlar, Yesevage Geriatrik Depresyon Ölçeği (GDÖ) kullanılarak değerlendirilmiş; GDÖ skoru ≥5 olanlar depresyon olarak kabul edilmiştir. WWI, bel çevresinin (cm) vücut ağırlığının (kg) karekköküne bölünmesiyle hesaplanmıştır. Depresif semptomlarla bağımsız olarak ilişkili faktörleri belirlemek için ikili lojistik regresyon analizi uygulanmıştır.

Bulgular: Katılımcıların 53'ünde (%35,3) depresif semptomlar tespit edilmiştir. Depresif semptomları olan hastaların WWI değerleri anlamlı olarak daha yüksekti (11,68 ± 0,73 vs. 11,28 ± 0,66, *p<0,001*). Nihai regresyon modelinde; kadın olmak (OR: 3,17; %95 GA: 1,21–8,32; *p=0,019*), daha düşük Standardize Mini-Mental Durum Muayenesi (SMMSE) skoru (OR: 0,84; %95 GA: 0,75–0,95; *p=0,005*), daha yüksek WWI (OR: 1,66; %95 GA: 0,91–3,02; *p=0,097*) ve daha düşük MNA-SF skoru (OR: 0,76; %95 GA: 0,60–0,97; *p=0,027*) depresif semptomlarla ilişkili bulundu.

Sonuç: Yüksek WWI, yaşlı bireylerde depresif semptomlarla ilişkili olabilir. WWI, depresyon riski yüksek bireyleri belirlemek için kullanılabilecek basit ve invaziv olmayan bir araç olabilir. Bu bulguların doğrulanması için ileriye dönük çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Ağırlıkla Düzeltilmiş Bel Çevresi İndeksi, Depresyon, Yaşlı bireyler.

Introduction

Depression is one of the most common and disabling mental health conditions in older adults, affecting up to 20% of individuals aged 65 and above and often going underdiagnosed due to atypical presentations and overlapping symptoms with physical illnesses (1). Identifying novel, non-invasive biomarkers that may aid in early detection and risk stratification is critical for improving outcomes in this vulnerable population.

Traditional anthropometric measures such as Body Mass Index (BMI) have limitations in older adults, as they do not distinguish between fat and muscle mass and may underestimate the health risks associated with central adiposity. In contrast, the Weight-Adjusted Waist Index (WWI), calculated as waist circumference (cm) divided by the square root of body weight (kg), has emerged as a promising indicator that independently captures central fat accumulation regardless of overall body size (2). WWI has been shown to reflect fat and muscle mass in opposite directions, increasing with adiposity and decreasing with muscle mass, which is particularly relevant in aging populations prone to both sarcopenia and visceral fat accumulation.

Recent studies have begun to investigate the relationship between WWI and mental health outcomes. In several large-scale cross-sectional and cohort studies, higher WWI values were found to be significantly associated with elevated depressive symptoms, independent of confounding factors such as BMI and comorbidities (3-5). Additionally, hospitalized older patients with higher WWI values were more likely to exhibit depressive symptoms, supporting the utility of WWI in clinical geriatric settings (6). A recent study by Wang et al. further proposed that depressive symptoms may mediate the relationship between WWI and cognitive decline, highlighting the importance of understanding WWI's broader implications in geriatric mental and cognitive health (7).

Despite growing evidence, most studies to date have been conducted in Asian or US populations, with limited data available from diverse older adult populations in different sociocultural contexts. Furthermore, many existing studies rely on secondary data from population health surveys, with few specifically targeting individuals aged 65 and older as a primary focus.

The aim of this study is to investigate the association between WWI and depression in older adults aged 65 years and above in a clinical cohort. By examining this relationship in a population with distinct demographic and lifestyle characteristics, the study seeks to validate previous findings and contribute to the growing body of evidence on WWI as a practical, non-invasive screening tool for mental health risk in older adults.

Material and Method

Study Design and Participants

A retrospective screening was conducted on patients who consecutively applied to the Geriatrics outpatient clinic, and 150 patients aged 65 years and older were included. Exclusion criteria were acute illness, severe cognitive impairment, and incomplete data of anthropometric measurements.

Data Collection

Sociodemographic data, including age, gender, and education duration (categorized as ≤5 years or >5 years), were collected. Comprehensive geriatric assessments were noted, including measures of functionality, cognition, nutrition, comorbidity, and anthropometry. Activities of Daily Living (ADL) were assessed using the Katz Index, with scores ranging from 0 (completely dependent) to 6 (completely independent) (8,9). Instrumental Activities of Daily Living (IADL) were evaluated using the Lawton–Brody scale, ranging from 0 to 8 (10,11). Cognitive status was assessed with the Standardized Mini-Mental State Examination (SMMSE) (12). Frailty was assessed using the Clinical Frailty Scale (CFS, Version 2.0) (13,14) and nutritional status was evaluated using the Mini Nutritional Assessment-Short Form (MNA-SF) (15,16). Handgrip strength was measured using a calibrated handheld dynamometer (T.K.K.5401; Takei Scientific Instruments), with the highest value of three attempts from the dominant hand recorded. Comorbidities were assessed using the Charlson Comorbidity Index, which assigns weighted scores to a range of chronic diseases such as heart disease, diabetes, chronic pulmonary disease, malignancies, and others. The cumulative score reflects the overall

comorbidity burden, with higher scores indicating increased risk of mortality and more severe disease burden (17).

The study was conducted in compliance with the Declaration of Helsinki. Informed consent was not required, as the study was retrospective in design. Ethical approval was obtained from the Ankara Bilkent City Hospital Clinical Research Ethics committee with the reference number of TABED 2-25-1219.

Assessment of Depressive Symptoms

Depressive symptoms were evaluated using the Yesavage Geriatric Depression Scale (GDS) short form (18,19). A GDS score of 5 or higher was considered indicative of clinically relevant depressive symptoms.

Anthropometric Measurements

Height, weight, and waist circumference were measured using standard techniques. Body Mass Index (BMI) was calculated as weight (kg) divided by height squared (m^2). WWI was calculated by dividing waist circumference (cm) by the square root of weight (kg) (2).

Statistical Analysis

All analyses were performed using SPSS software (version 27.0, IBM Corp.). Normally distributed variables were presented as mean ± standard deviation, while non-normally distributed variables were reported as median (interquartile range). Categorical variables were presented as frequencies and percentages. Differences between groups (depressed vs. non-depressed) were compared using the t-test or Mann–Whitney U test for continuous variables and the chi-square test for categorical variables.

To identify factors independently associated with depressive symptoms, a multivariable logistic regression analysis with backward stepwise likelihood ratio method was performed. Variables included in the initial model were age, gender, education duration, ADL, IADL, SMMSE score, WWI, BMI, MNA-SF score, handgrip strength, CFS score, and Charlson Comorbidity Index. Odds ratios (OR) and 95% confidence intervals (CI) were reported. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test, and model performance was evaluated by Nagelkerke R^2 values. A p value <0.05 was considered statistically significant.

Table I. Patient Characteristics Based on Depressive Symptoms

	Depression (n=53)	No Depression (n=97)	*p*
Age	74 (70-79)	71 (68-78)	***0.020***
Gender Female Male	 45 (84.9%) 8 (15.1%)	 49 (50.5%) 48 (49.5%)	***<0.001***
Education duration ≤5 years >5 years	 49 (92.5%) 4 (7.5%)	 59 (60.8%) 38 (39.2%)	***<0.001***
ADL	5 (4-6)	6 (6-6)	***<0.001***
IADL	8 (4-8)	8 (8-8)	***<0.001***
CFS	4 (3-5)	3 (2-3)	***<0.001***
GDS	6 (5-8)	1 (1-3)	***<0.001***
SMMSE	24 (21-27)	28 (26-30)	***<0.001***
MNA-SF	12 (10-14)	14 (13-14)	***<0.001***
Handgrip strength (kg)	18.53 ± 6.52	24.15 ± 7.51	***<0.001***
Charlson comorbidity index	5 (3-6)	4 (3-5)	***0.040***
Height (cm)	156.6 ± 8.7	162.3 ± 8.5	***<0.001***
Weight (kg)	77.6 ± 14.8	77.3 ± 12.4	*0.910*
BMI (kg/m2)	29.7 (27.7-34.7)	28.3 (25.9-32.4)	***0.020***
Waist circumference (cm)	102.4 ± 10.8	98.9 ± 10.0	*0.052*
WWI	11.68 ± 0.73	11.28 ± 0.66	***<0.001***

ADL: Katz Index of Independence in Activities of Daily Living, IADL: Lawton-Brody Instrumental Activities of Daily Living, CFS: Clinical Frailty Scale, GDS: Yesevage Geriatric Depression Scale, SMMSE: Standardized Mini Mental State Examination, MNA-SF: Mini Nutritional Assessment Short Form, WWI: Weight-adjusted waist index

Results

A total of 150 patients aged 65 years and older (62.7% women) were included in the study. The median age of the study population was 73 years (68-78). Baseline characteristics of participants according to depressive symptom status are presented in Table I. Compared to those without depressive symptoms, participants with depressive symptoms were significantly older, and more likely to be women. Lower education duration (≤5 years) was significantly more common in the depression group (*p<0.001*). Functional and cognitive assessments revealed that participants with depressive symptoms had lower scores in ADL and IADL, lower SMMSE scores, and higher CFS scores. Nutritional assessment showed that participants with depressive symptoms had

lower MNA-SF scores and weaker handgrip strength. Anthropometric measurements revealed that although body weight and waist circumference were similar between groups, BMI was significantly higher in individuals with depressive symptoms (median 29.7 vs. 28.3 kg/m^2, *p=0.02*). Importantly, the WWI was significantly higher in participants with depressive symptoms compared to those without (11.68±0.73 vs. 11.28±0.66, *p<0.001*).

Table II. Logistic Regression Analysis of the Independent Factors Associated with depressive symptoms

Odds Ratio		Depression		
		95% CI	p-value	
Model 9 Nagelkerke R^2=0.388	Gender (female)	3.17	1.21-8.32	0.019
	SMMSE	0.84	0.75-0.95	0.005
	WWI	1.66	0.91-3.02	0.097
	MNA-SF	0.76	0.60-0.97	0.027

SMMSE: Standardized Mini-Mental State Examination, WWI: Weight-adjusted waist index, MNA-SF: Mini Nutritional Assessment Short Form, (Only the final step is presented due to the utilization of the backward method.)

In the logistic regression analysis using a backward stepwise likelihood ratio method, several variables were initially entered into the model, including age, gender, education duration, ADL, IADL, SMMSE score, WWI, BMI, MNA-SF score, handgrip strength, CFS score, and Charlson comorbidity index.

In the final model (Step 9), several factors were independently associated with depressive symptoms. Female gender was significantly associated with increased odds of depression (OR: 3.17; 95% CI: 1.21-8.32; *p=0.019*). Lower SMMSE scores were also linked to higher likelihood of depressive symptoms (OR: 0.84; 95% CI: 0.75-0.95; *p=0.005*). Although the association between higher WWI and depressive symptoms did not reach statistical significance (OR: 1.66; 95% CI: 0.91-3.02; *p=0.097*), it demonstrated a meaningful trend. Additionally, lower MNA-SF scores remained significantly associated with depressive symptoms (OR: 0.76; 95% CI: 0.60-0.97; *p=0.027*). The final model showed good fit according to the Hosmer–Lemeshow goodness-of-fit test (*p=0.656*) (Table II).

Discussion

In this cross-sectional study, we examined the association between the WWI and depressive symptoms among older adults aged 65 years and above. Our findings revealed that higher WWI values were associated with a greater likelihood of depressive symptoms, although the association did not reach conventional statistical significance. Additionally, female gender, lower cognitive performance as measured by the SMMSE, and poorer nutritional status were independently associated with depressive symptoms.

Our results are consistent with previous studies demonstrating a relationship between higher WWI and increased depressive symptoms. Li et al. and Shen et al. both reported significant associations between WWI and depression in large, nationally representative cohorts from the United States, independent of traditional obesity indices such as BMI (3,4). Similarly, Zeng et al. confirmed this association in a longitudinal study among middle-aged and older Chinese adults, suggesting that WWI may serve as a stable predictor of depressive symptomatology over time (5). These findings, together with our results, reinforce the emerging evidence that WWI may capture central adiposity and its related metabolic and inflammatory pathways, which could contribute to depression risk.

The biological plausibility linking WWI and depression may be explained through several mechanisms. Central adiposity, more accurately reflected by WWI than BMI, is associated with systemic inflammation, dysregulation of the hypothalamic-pituitary-adrenal axis, and altered neurotransmitter activity, all of which have been implicated in the pathophysiology of depression (2). Notably, WWI reflects fat and muscle mass changes in opposite directions, making it particularly relevant in geriatric populations where sarcopenia and visceral fat accumulation often coexist.

Interestingly, in our study, although the association between WWI and depressive symptoms was clinically meaningful, it did not reach statistical significance (*p=0.097*). Several factors may explain this finding. Our sample size was relatively modest compared to the larger population-based studies such as NHANES analyses (3,4). Furthermore, sociocultural differences in body composition and perception of weight status in older Turkish adults compared

to US and Chinese populations may influence the observed associations. Nevertheless, the direction and strength of the association in our study align with previous findings and suggest that WWI is a promising anthropometric marker worthy of further exploration in diverse populations.

Our findings regarding the association of female gender and depression are consistent with prior research indicating that older women are at higher risk of depression than men (1). Additionally, cognitive impairment and poor nutritional status were independently linked to depression, echoing findings from previous studies that emphasized the interconnected nature of physical, nutritional, and mental health in late life (7,20).

Beyond depression, previous studies have also linked higher WWI values to adverse cognitive outcomes (7,21) and even suicidal ideation (22), further supporting the clinical relevance of WWI as a holistic health risk indicator. In particular, mediation analyses have suggested that depression may serve as an intermediary between WWI and cognitive decline, highlighting the need for early identification and intervention in individuals with elevated WWI. In addition to the anthropometric, nutritional, and cognitive associations explored in this study, a broad range of psychosocial and biological factors contribute to depressive symptoms in older adults. Common risk factors include chronic medical conditions, multimorbidity, physical disability, sensory impairment, poor social support, bereavement, low socioeconomic status, and loneliness (1). Cognitive decline and frailty have also been consistently associated with increased depression risk, as reflected in our findings through lower SMMSE scores and MNA-SF scores among those with depressive symptoms (23).

On the other hand, several protective factors can buffer against depression in this age group. These include strong family and social networks, higher educational attainment, regular physical activity, engagement in meaningful activities, and adequate nutritional status (24). Early identification and intervention through comprehensive geriatric assessment, promotion of social connectedness, and integrated physical and mental health care models are essential in preventing and mitigating depressive symptoms in older populations (25-27). These broader contextual factors should be considered when interpreting the association between WWI and depressive symptoms, as they may mediate or moderate this relationship.

This study has several strengths. It is among the few investigations specifically focusing on the association between WWI and depressive symptoms in a clinical cohort of adults aged 65 years and older. Comprehensive geriatric assessments, including validated measures of cognitive function, nutritional status, physical performance, and depression, strengthen the robustness of our findings.

However, certain limitations should be considered. The cross-sectional design prevents the establishment of causality between WWI and depressive symptoms. The sample size, while adequate for preliminary investigation, may limit the generalizability and statistical power, particularly regarding associations that approached but did not reach conventional significance thresholds. Furthermore, unmeasured confounding factors such as inflammatory markers, physical activity levels, and psychosocial variables were not assessed and may have influenced the observed relationships. Finally, the study population was drawn from a single center, which may limit the external generalizability to broader populations.

Conclusion

Our findings contribute to the growing evidence suggesting that WWI is associated with depressive symptoms in older adults. Although further longitudinal and interventional studies are needed, WWI may offer a simple, non-invasive screening tool to identify individuals at increased risk for depression, enabling earlier interventions aimed at improving mental and physical health outcomes in the aging population.

References

1. Maier A, Riedel-Heller SG, Pabst A, Luppa M. Risk factors and protective factors of depression in older people 65+. A systematic review. PloS one 2021;16(5):e0251326.

2. Kim NH, Park Y, Kim NH, Kim SG. Weight-adjusted waist index reflects fat and muscle mass in the opposite direction in older adults. Age and ageing 2021;50(3):780-786.

3. Li M, Yu X, Zhang W, et al. The association between weight-adjusted-waist index and depression: Results from NHANES 2005-2018. Journal of affective disorders 2024;347:299-305.

4. Shen Y, Wu Y, Luo P, Fu M, Zhu K, Wang J. Association between weight-adjusted-waist index and depression in US adults: A cross-sectional study. Journal of affective disorders 2024;355:299-307.
5. Zeng P, Jiang C, Cao J, Li M, Lin F. Longitudinal relationship between weight-adjusted waist index and depressive symptoms in middle-aged and older Chinese adults: A prospective cohort study. Journal of affective disorders 2024;363:381-390.
6. Korycka-Bloch R, Balicki P, Guligowska A, Soltysik BK, Kostka T, Chrzastek Z. Weight-Adjusted Waist Index (WWI)-A Promising Anthropometric Indicator of Depressive Symptoms in Hospitalized Older Patients. Nutrients 2024;17(1).
7. Wang J, Wang Y, Li S, et al. Waist-to-weight index and cognitive impairment: Understanding the link through depression mediation in the NHANES. Journal of affective disorders 2024;365:313-320.
8. Arik G, Varan HD, Yavuz BB, et al. Validation of Katz index of independence in activities of daily living in Turkish older adults. Archives of gerontology and geriatrics 2015;61(3):344-350.
9. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the Aged. The Index of ADL: A Standardized Measure of Biological and Psychosocial Function. JAMA 1963;185:914-919.
10. Isik EI, Yilmaz S, Uysal I, Basar S. Adaptation of the Lawton Instrumental Activities of Daily Living Scale to Turkish: Validity and Reliability Study. Ann Geriatr Med Res 2020;24(1):35-40.
11. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9(3):179-186.
12. Molloy DW, Alemayehu E, Roberts R. Reliability of a Standardized Mini-Mental State Examination compared with the traditional Mini-Mental State Examination. Am J Psychiatry 1991;148(1):102-105.
13. Rockwood K, Theou O. Using the Clinical Frailty Scale in Allocating Scarce Health Care Resources. Canadian geriatrics journal: CGJ 2020;23(3):210-215.
14. Aşık Z, Kılınç Ş, Kurşun Ö, Özen M. Validation of the Clinical Frailty Scale version 2.0 in Turkish older patients. Geriatrics & gerontology international 2022;22(9):730-735.
15. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. Clin Geriatr Med 2002;18(4):737-757.
16. Sarikaya D, Halil M, Kuyumcu ME, et al. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. Archives of gerontology and geriatrics 2015;61(1):56-60.
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of chronic diseases 1987;40(5):373-383.
18. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17(1):37-49.
19. Durmaz B, Soysal P, Ellidokuz H, Isik AT. Validity and reliability of geriatric depression scale-15 (short form) in Turkish older adults. North Clin Istanb 2018;5(3):216-220.
20. Niu Y, Sun Y, Xie Y, Yu S. Association between weight-adjusted waist circumference index and depression in older patients with hypertension: a study based on NHANES 2007-2016. Frontiers in public health 2024;12:1461300.
21. Wang XL, Feng HL, Xu XZ, Liu J, Han X. Relationship between cognitive function and weight-adjusted waist index in people ≥ 60 years old in NHANES 2011-2014. Aging clinical and experimental research 2024;36(1):30.
22. Guo S, Qing G, Chen Q, Yang G. The relationship between weight-adjusted-waist index and suicidal ideation: evidence from NHANES. Eating and weight disorders: EWD 2024;29(1):37.
23. Hu C, Sun X, Li Z, et al. Multitrajectories of Frailty and Depression with Cognitive Function: Findings From the Health and Retirement Longitudinal Study. Journal of cachexia, sarcopenia and muscle 2025;16(2):e13795.
24. Cuijpers P, Smit F, Patel V, Dias A, Li J, Reynolds CF, 3rd. Prevention of depressive disorders in older adults: An overview. PsyCh journal. 2015;4(1):3-10.
25. Casey DA. Depression in Older Adults: A Treatable Medical Condition. Primary care 2017;44(3):499-510.
26. Kok RM, Reynolds CF, 3rd. Management of Depression in Older Adults: A Review. Jama 2017;317(20):2114-2122.
27. Weyerer S, Eifflaender-Gorfer S, Wiese B, et al. Incidence and predictors of depression in non-demented primary care attenders aged 75 years and older: results from a 3-year follow-up study. Age and ageing 2013;42(2):173-180.

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Influence of Lean Body Mass and Disease Etiology on Levothyroxine Requirements in Patients with Hypothyroidism

Hipotiroidili Hastalarda Yağsız Vücut Kütlesi ve Hastalık Etiyolojisinin Levotiroksin Gereksinimlerine Etkisi

Ülkem Şen Uzeli | Duygu Tutan

Hitit University Faculty of Medicine, Department of Internal Medicine, Çorum, Türkiye

Sorumlu Yazar | Correspondence Author
Ülkem Şen Uzeli
ulkem_sen@hotmail.com
Address for Correspondence: Hitit University Faculty of Medicine, Department of Internal Medicine, 19040, Çorum, Türkiye.

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Influence of Lean Body Mass and Disease Etiology on Levothyroxine Requirements in Patients with Hypothyroidism

ABSTRACT

Objective: It was aimed to evaluate the dose requirement depending on the etiology and to compare lean body mass and total body weight in the calculation of drug dose in patients receiving levothyroxine sodium replacement.

Material and Method: A total of 124 patients who were receiving levothyroxine sodium treatment for total thyroidectomy, hypothyroidism due to radioactive iodine therapy treatment, and autoimmune hypothyroidism were included in this cross-sectional study. Patients' drug doses, height, weight, thyroid-stimulating hormone, T4, and T3 values were recorded on the hospital documentation system. Lean Body Mass was calculated, and the doses of drugs were calculated based on total body weight and Lean Body Mass. Patients were separated into three groups as normal weight, overweight, and obese according to body mass index.

Results: Patients with Hashimoto's thyroiditis required lower daily levothyroxine doses compared to those who had undergone total thyroidectomy. Similarly, the daily levothyroxine dosage per kilogram of lean body mass and total body weight was significantly lower in the Hashimoto's group than in the total thyroidectomy group. While the RAI group showed intermediate values that did not differ significantly from either group

Conclusion: This study shows that the use of lean body mass is more significant than body mass index in determining the dose of levothyroxine in hypothyroid patients. The findings show that the dose of levothyroxine varies according to the etiology of hypothyroidism and that treatment doses should be determined accordingly.

Keywords: Hypothyroidism, Lean Body Mass, Levothyroxine Sodium.

ÖZET

Amaç: Levotiroksin sodyum replasmanı alan hastalarda etyolojiye bağlı doz gereksinimini değerlendirmek ve ilaç dozunun hesaplanmasında yağsız vücut kütlesi ile toplam vücut ağırlığını karşılaştırmak amaçlandı.

Gereç ve Yöntem: Total tiroidektomi, radyoaktif iyot tedavisine bağlı hipotiroidi ve otoimmün hipotiroidi nedeniyle levotiroksin sodyum tedavisi alan toplam 124 hasta kesitsel çalışmaya dahil edildi. Hastaların ilaç dozları, boy, kilo, tiroid uyarıcı hormon, T4 ve T3 değerleri hastane dokümantasyon sistemine kaydedildi. Yağsız Vücut Kütlesi hesaplandı ve ilaç dozları toplam vücut ağırlığı ve Yağsız Vücut Kütlesi değerlerine göre hesaplandı. Hastalar vücut kitle indeksine göre normal kilolu, kilolu ve obez olmak üzere 3 gruba ayrıldı.

Bulgular: Hashimoto tiroiditi olan hastaların, total tiroidektomi geçiren hastalara kıyasla daha düşük günlük levotiroksin dozlarına ihtiyaçları vardı. Benzer şekilde, yağsız vücut kütlesi ve toplam vücut ağırlığının kilogramı başına günlük levotiroksin dozu, Hashimoto grubunda total tiroidektomi grubuna göre anlamlı derecede düşüktü. RAI grubu ise her iki gruptan da anlamlı farklılık göstermeyen orta düzeyde değerler gösterdi.

Sonuç: Bu çalışma, hipotiroid hastalarında levotiroksin dozunun belirlenmesinde yağsız vücut kütlesi kullanımının vücut kitle indeksinden daha önemli olduğunu göstermektedir. Bulgular, levotiroksin dozunun hipotiroidizmin etyolojisine göre değiştiğini ve tedavi dozlarının buna göre belirlenmesi gerektiğini göstermektedir.

Anahtar Sözcükler: Hipotiroidizm, Levotiroksin Sodyum, Yağsız Vücut Kütlesi.

Introduction

Hypothyroidism is a common endocrine disorder worldwide characterized by inadequate regulation of thyroid hormones. In nearly all cases (99%), hypothyroidism is primary hypothyroidism and develops due to thyroid gland dysfunction. The most common etiologies of hypothyroidism are Hashimoto's thyroiditis, thyroid surgery, radioactive iodine therapy (RAI), and radiation therapy-induced hypothyroidism (1).

Thyroid hormone replacement therapy with levothyroxine (LT4) is recommended for all causes of hypothyroidism, whether primary hypothyroidism, central hypothyroidism, or, rarely, peripheral hypothyroidism. With its long elimination half-life (approximately one week), once-daily use of LT4 provides appropriate T4 and T3 blood levels and is sufficient as a standalone replacement (2). The dose of LT4 depends on the age, gender, and weight of the patient. Patients with hypothyroidism usually need an oral LT4 replacement dose of 1.6–1.8 mcg/kg actual body weight to achieve euthyroid status (3).

However, the literature shows that the necessity of using alternative methods to total body weight was discussed upon the detection of unexplained dose requirement differences in patients of similar age and body weight, and the observation that the dose required decreased in obese and elderly patients. Studies have suggested that actual body mass, ideal body mass, and lean body mass (LBM) may influence LT4 dose requirements (4). In these studies, LBM was considered the best predictor of daily requirements for LT4. It is known that the deiodination process, which converts T4 to T3, occurs mainly in muscle tissue rather than adipose tissue (5). Furthermore, most metabolic processes of T4 occur within the LBM, which include type 1 deiodinase, glucuronidation, and sulfation in the liver, and deiodinase type 3 in the skin (6). Although hypothyroid obese patients require higher absolute doses of LT4 than normal-weight individuals, obese patients require a lower dose of LT4 relative to body weight to maintain euthyroid status. It is suggested that a higher LT4 dose requirement in morbidly obese individuals may be associated with increased LBM and a higher volume of distribution (7,8). This study aimed to investigate whether lean body mass (LBM) provides a more accurate basis for levothyroxine dose adjustment compared to total body weight or body mass index, and to evaluate whether this relationship varies according to the underlying etiology of hypothyroidism.

Material and Method

This investigation received authorization from the Hitit University Clinical Research Ethics Committee (July 10, 2024, approval 2024-32), and all protocols undertaken in investigations involving human subjects were conducted in strict compliance with the ethical guidelines outlined by the institutional and/or national research governing body, the 1964 Declaration of Helsinki, and its subsequent revisions or analogous ethical criteria.

Patients with normal thyroid-stimulating hormone (TSH) values, who had undergone total thyroidectomy, hypothyroidism due to RAI treatment, or LT4 sodium treatment due to autoimmune hypothyroidism, and who applied to the Department of Internal Medicine of Hitit University Erol Olçok Training and Research Hospital between July 2024 and September 2024, were included in this cross-sectional study. Demographic characteristics of the patients, drug doses (LT4 dose [mcg]), height (cm), weight (kg), body mass index (BMI), TSH, T4, and T3 values were recorded. Patients included in the study were those whose LT4 sodium dose had not been changed for the last year. Patients with more than one cause of hypothyroidism, patients under the age of 18, patients who did not comply with treatment, patients with gastrointestinal absorption problems, patients using drugs that interact with LT4 sodium, patients whose TSH values were not within the expected range, and patients who were pregnant or breastfeeding were excluded from the study (Figure I). The patients were first divided into three separate groups according to their etiological causes: autoimmune hypothyroidism, hypothyroidism due to RAI treatment, and hypothyroidism due to total thyroidectomy. These three groups of patients were compared in terms of age, gender, height, weight, mean TSH value, daily LT4 sodium medication dose used per kg, daily medication dose used per LBM, and body mass index. The patients were divided

into three groups (18.5–24.9 kg/m^2, 25–29.9 kg/m^2, and 30 kg/m^2 and above) according to the World Health Organization classification of BMI (kg/m^2) values. The differences in LT4 medication doses were evaluated among groups categorized by etiology as well as groups classified by BMI. The Boer formula, an equation used for measuring lean body mass, was used for the LBM. It was calculated as (0.407 × weight) + (0.267 × height) − 19.2 for men and (0.252 × weight) + (0.473 × height) − 48.3 for women.

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized using descriptive statistics, presented as counts and percentages, while continuous variables were expressed as mean ± standard deviation or median (minimum–maximum), depending on the distribution pattern. The Shapiro–Wilks test was employed to assess the normality of the data distribution. Pearson or Spearman correlation coefficients were used to analyze the relationships between variables, depending on the distribution characteristics.

The ANOVA test was utilized to compare numeric variables, such as age and height, between groups, while other continuous variables were compared using the Kruskal–Wallis test due to their non-Gaussian distribution. For variables analyzed with ANOVA, Bonferroni-adjusted pairwise comparisons were performed. For variables analyzed with the Kruskal–Wallis test, where significant differences were found, pairwise group comparisons were performed using Mann–Whitney U tests with the Bonferroni correction for post-hoc comparisons. Categorical data comparisons between groups were conducted using the chi-square test. The patients were categorized into three groups based on the etiology of their hypothyroidism, and statistical analyses were performed to identify significant differences between these groups. The patients were also categorized into three additional groups based on BMI: normal, overweight, and obese, and the differences between these categories were similarly analyzed. A multivariate linear regression analysis was conducted to evaluate the effects of etiology, LBM, age, BMI, weight, and height on LT4 requirements. Statistical significance was defined as *p<0.05*.

Results

A total of 124 eligible patients were included in the study, with a mean age of 50.05 ± 13.35 years. The median BMI was 29.16 (range 16.53–51.89), and the median TSH level was 2.19 (range 0.21–4.3). The median LBM was 46.72 kg (range 35.5–66.25), while the median daily LT4 dosage requirement was 88.25 mcg (range 10–200 mcg). Among the participants, 36 patients (29%) had undergone total thyroidectomy as the etiology for hypothyroidism, 4 patients (3.3%) had received RAI therapy, and 84 patients (67.7%) were diagnosed with Hashimoto's thyroiditis

Table I. Characteristics of Patients and Comparison Between Etiology Groups

Variables	All Patients (n=124)	Total Thyroidectomy (n=36; 29%)	After RAI (n=4; 3.3%)	Hashimoto Thyroiditis (n=84; 67.7%)	*p Value*
Age	50.05±13.35	56.86±9.55	37±12.38	47.75±13.66	*<0.001*
Weight (kg)	75 (45-143)	78.5 (50-130)	63 (58-86)	73.5 (45-143)	*0.150*
Height (cm)	1.61±0.06	1.61±0.07	1.64±0.06	1.6±0.06	*0.473*
BMI (kg/m^2)	29.16 (16.53-51.89)	30.59 (20.81-46.61)	24.1 (20.55-31.59)	28.83 (16.53-51.89)	*0.117*
TSH (uU/ml)	2.19 (0.21-4.3)	1.73 (0.21-4.3)	2.95 (1.7-4.02)	2.41 (0.41-4.2)	*0.129*
fT3 (ng/dL)	2.55 (1.22-3.34)	2.36 (1.22-3.1)	2.58 (2.01-2.83)	2.61 (1.22-3.34)	*0.055*
fT4 (ng/dL)	1.32 (0.44-2.81)	1.4 (0.97-2.12)	1.27 (1.2-1.34)	1.3 (0.44-2.81)	*0.049*
LBM (kg)	46.72 (35.5-66.25)	46.83 (37.61-63.45)	46.41 (41.36-51.42)	46.72 (35.5-66.25)	*0.616*
Daily LT4 (mcg/day)	88.25 (10-200)	100 (10-100)	100 (57-132)	75 (25-200)	*<0.001*
Daily LT4 per LBM	1.90 (0.19-3.83)	2.32 (0.19-3.83)	2.06 (1.38-2.81)	1.57 (0.38-3.33)	*<0.001*
Daily LT4 per kg	1.10 (0.10-2.69)	1.47 (0.10-2.69)	1.44 (0.90-2.10)	0.98 (0.17-2.38)	*<0.001*

RAI: radioactive iodine therapy, BMI: Body Mass Index, TSH: thyroid-stimulating hormone, LBM: Lean body Mass, fT3: free T3 hormone, fT4: free T4 hormone, Daily LT4: daily levothyroxine T4

Patients in the total thyroidectomy group were significantly older than those in the other two groups (*p<0.001*). No significant differences were observed between the etiology groups concerning weight, height, BMI, TSH, fT3, or LBM (*p=0.150, p=0.473,*

p=0.117, p=0.129, p=0.055, and p=0.616, respectively). The fT4 levels were marginally higher in the total thyroidectomy group; this difference was statistically significant (*p=0.049*) but not considered clinically relevant.

Table II. Levothyroxine Dosage Comparison between BMI Groups

Variables	Normal Weight (n=32)	Overweight (n=37)	Obese (n=55)	*p value*
Daily LT4(mcg/day)	72.5 (25-175)	82 (25-167)	100 (10-200)	*0.119*
Daily LT4 per LBM	1.51 (0.52-3.83)	2.05 (0.52-3.33)	1.87 (0.19-3.47)	*0.300*
Daily LT4 per kg	1.06 (0.37-2.69)	1.28 (0.33-2.11)	1.07 (0.10-2.00)	*0.157*

BMI: Body Mass Index, Daily LT4: daily levothyroxine T4

Patients with Hashimoto's thyroiditis required lower daily LT4 doses compared to those who had undergone total thyroidectomy (median 75 mcg vs. 100 mcg, *p<0.001*). Similarly, the daily LT4 dosage per kilogram of LBM and total body weight was significantly lower in the Hashimoto's group than in the total thyroidectomy group (*p<0.001* for both; Table I).

Table III. Multivariate Regression Analysis for Estimation of Required LT4 Dosage

Coefficients	Unstandardized Coefficients		Standardized Coefficients			%95 Confidence Intervals
	B	Std. Error	Beta	t	Sig.	
(Constant)	7.230	28.102		0.257	0.797	-48.405 - -62,866
Hypothyroidism Etiology	-17.096	3.612	-0.374	-4.733	<0.001	-24.248 - -9.945
LBM (kg)	2.169	0.572	0.300	3.790	<0.001	1.036 – 3.302
Age	-0.020	0.082	-0.018	-0.219	0.827	-0.180 – 0.144
BMI (kg/m^2)	-0.031	0.104	-0.035	-0.335	0.738	-0.240 – 0.170
Weight (kg)	-0.027	0.160	-0.047	-0.293	0.770	-0.363 – 0.269
Height (cm)	0.027	0.099	0.029	0.293	0.770	-0.167 – 0.225

LT4: levothyroxine T4, LBM: Lean body Mass, BMI: Body Mass Index

The comparison of daily dosage requirements across BMI categories showed that normal-weight patients required a median of 72.5 mcg (range 25–175 mcg), overweight patients required 82 mcg (range 25-167mcg), and obese patients required 100 mcg (range 10-200 mcg) of LT4 daily. Although there was an observed increase in LT4 dose requirements with a higher BMI, this trend did not reach a statistically significant level (*p=0.300*). In addition, no significant differences were found in the median daily LT4 dosage per LBM or per kilogram across the BMI groups (*p=0.300 and p=0.157*, respectively; Table II).

Table IV. Univariate Linear Regression Results of LBM and LT4 in Subgroups (every row reports an analysis in a subgroup)

Model Summary and Parameter Estimates	Model Summary					Parameter Estimates	
Subgroups	R Square	F	df1	df2	Sig.	Constant	b1
Hashimoto	0.079	7.027	1	82	0.010	-13.950	1.888
RAI	0.385	1.252	1	2	0.379	-117.035	4.618
Thyroidectomy	0.160	6.471	1	34	0.016	-14.217	2.608
All Patients	0.111	15.301	1	122	<0.001	-28.188	2.417

RAI: radioactive iodine therapy, LBM: Lean Body Mass, LT4: levothyroxine T4

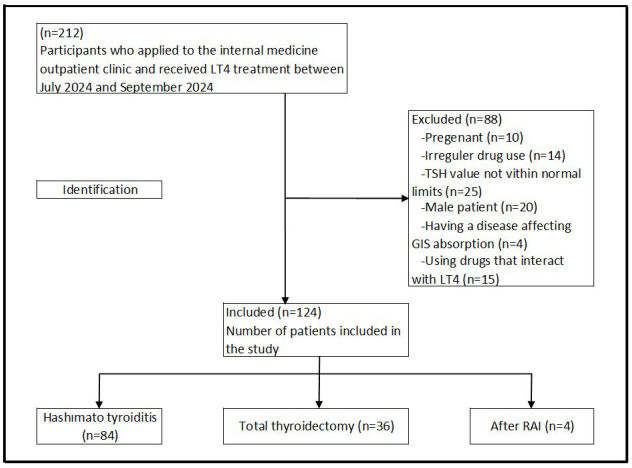

Figure I. STROBE Flow Chart

A multivariate linear regression analysis was conducted, incorporating hypothyroidism etiology, LBM, age, BMI, weight, and height as covariates to assess their predictive value for LT4 dosage requirements. The analysis revealed no significant effects of age, BMI, weight, or height between the groups (*p=0.827, p=0.738, p=0.770, and p=0.770*, respectively; Table III). The regression model was significant (*R^2=0.250, p<0.001*), with hypothyroidism etiology and LBM emerging as independent predictors of LT4 dosage even after adjusting for potential confounders (*β=−0.374, t=−4.733, p<0.001* for etiology and *β=0.300, t=3.790, p<0.001* for LBM). Univariate linear regression analysis and curve estimation

between LBM and LT4 dosage yielded the following predictive formula: [required LT4 dosage] = (2.42 * LBM) – 28.2 (*p<0.001*; Figure II).

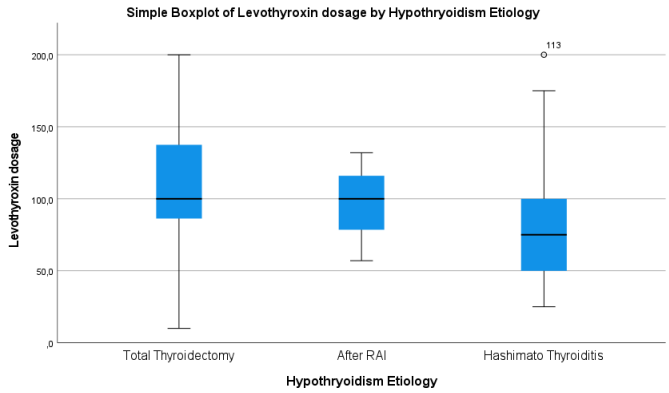

Figure II. Boxplot diagram of levothyroxine dosage requirements (µg/day) according to hypothyroidism etiology. The horizontal line within each box represents the median; the box edges represent the interquartile range (IQR); whiskers extend to the minimum and maximum values within 1.5 × IQR; circles indicate mild outliers. Numerical labels next to outliers (e.g., "113") correspond to case identifiers in the dataset.

Further linear regression analyses were performed to evaluate the predictive accuracy of LBM for LT4 requirements across different etiologies. In both the Hashimoto's thyroiditis and total thyroidectomy groups, LBM was a significant predictor of LT4 dosage (*p=0.010 and p=0.016,* respectively). However, in the RAI group, LBM demonstrated limited predictive capability (*p=0.379*; Table IV).

Discussion

This is the first study in Türkiye to show that LBM is more meaningful in determining the dose of L-thyroxine used in hypothyroidism treatment. The findings of this study may aid clinicians in optimizing LT4 dosing by prioritizing LBM over BMI.

The basis of hypothyroidism treatment is LT4, which is formed by the conversion of the biologically active hormone T3 from T4. A stable dose of LT4 is maintained when the amount of hormone entering the bloodstream equals the amount metabolized. As much as 80% of LT4 is absorbed, and serum T4 level reaches peak level in 2–4 hours and decreases to basal level in approximately 6 hours. The plasma half-life of T4 in euthyroid states is approximately 7 days, and clearance is mainly dependent on deiodination (9,10). The average daily LT4 replacement dose is 1.6 µg/kg to normalize serum TSH. The daily dose requirement for LT4 varies according to age, sex, and body weight. Since the therapeutic range of LT4 is not extensive, a minimal increase or decrease in the dose of LT4 may cause a significant change in the TSH value (11). With these changes, altered TSH levels may cause unexpected signs of hypothyroidism or hyperthyroidism. For this reason, it is crucial that the necessary dosage of LT4 therapy be regulated in patients with hypothyroidism, regardless of the etiology. There is a consensus in the literature that ideal body weight should be considered to calculate the amount of LT4 for each patient (12). Although total daily LT4 requirements are related to body mass, unexplained differences can occur between individuals of the same age and body size, even in the absence of functional thyroid tissue. Our study aimed to investigate whether normal body weight or lean body mass should be used to determine the LT4 dose in female hypothyroid patients.

In a previous study, the daily dose requirement between BMI groups was compared, and it was found that obese patients had a lower LT4 dose requirement per kilogram than normal-weight patients. Moreover, this study found that actual body weight and daily dose of LT4 were negatively correlated (13). Devdhar et al. found that age had no significant role in determining the dose of LT4 and was negatively correlated with body weight (14). It was found that body weight is not a variable parameter alone in determining the required dose of LT4 in patients with total thyroidectomy associated with thyroid cancer, but it decreases with increasing age and BMI (15). In our study, we observed an increase in LT4 dose requirements as BMI increased, but this was not statistically significant (*p=0.300*). We consider that this finding may be due to the fact that our study was conducted only on female patients and included patients who were already receiving treatment.

We think that although there was an increase in LT4 dose with increasing BMI in our study, it was not statistically significant and that BMI and LT4 dose were negatively correlated in studies in the literature, this may be related to the increase in

muscle mass of the patients. However, we believe that retrospective studies with many participants are needed, including patients who will start new treatment, to reveal these more clearly.

Currently, the LT4 dose required to achieve euthyroidism is based on the demand per total body weight. Previous studies have shown that different doses of LT4 are necessary in individuals of the same age, with the same etiologic cause, and with the same body mass index. For this reason, new studies are being performed on the use of lean body mass in determining the dose of LT4. Inspired by this, we evaluated the relationship between lean body mass and LT4 dose, and we compared LBM and total body weight between BMI groups. Most of the increase in total body weight when weight gain occurs is due to fat mass. Fat mass is not metabolically active, so when total weight is used as the basis for determining the dose of LT4, it may result in overdose exposure. The concept of LBM as a predictor of drug dosage has been applied to the sensitive assessment of body composition by dual-energy X-ray absorptiometry. In a retrospective study of 271 hypothyroid patients in Thailand, it was found that a lower dose of LT4 was needed compared to LBM (16). A retrospective study of 75 hypothyroid adults aged 24–88 years on full replacement therapy was conducted in another study. LBM was found to be a stronger predictor of LT4 requirements than age or weight for all gender subgroups over 51 years of age. A retrospective study including 200 patients showed that LBM was a better indicator for the calculation of an appropriate LT4 replacement dose than actual BM (17). In our study, we demonstrated that LMB was a more powerful parameter than BMI in determining LT4 dose (*p=0.010, p=0.016*). A previous study of 264 total thyroidectomy patients showed that patients with malignant pathology had a higher LT4 requirement despite having the same body weight (18). Some studies have reported that not only body weight but also medications and comorbidities are effective in determining the dose of LT4 (19). In a prospective study of 60 patients undergoing total thyroidectomy for benign causes, the daily dose of LT4 was correlated with body mass. However, to explain the correlation, it has been stated that other etiologic causes should also be investigated after the initiation of LT4 treatment (20). When the literature was reviewed, it was observed that parameters such as the etiology of hypothyroidism, age, gender, body mass index, and lean body mass of the patients were important in determining the dose of LT4. However, most of these studies were mainly performed on patients with total or subtotal thyroidectomy for malignant or benign etiologies. It was shown that Hashimoto's thyroiditis or ablative therapy-associated hypothyroidism required a lower dose of LT4 than patients with complete loss of thyroid tissue after total thyroidectomy (21,22). In a study by Gordon et al., it was stated that the dose of LT4 varied depending on the etiology of hypothyroidism (23). In contrast, the study which included patients using 75 mcg or more of LT4 , which included patients using 75 mcg or more of LT4, the required dose of LT4 was found to be 1.45 mcg/kg/day in hypothyroidism associated with Hashimoto's disease (70% of study patients) and 1.48 mcg/kg/day in hypothyroidism associated with total thyroidectomy and radioactive iodine; no statistical difference was observed between the groups (*p=0.56*). In our study, it was found that patients with Hashimoto's thyroiditis required lower daily doses of LT4 than patients with total thyroidectomy (*p<0.001*).

Our findings contribute to the growing body of evidence supporting the use of LBM over BMI in LT4 dose determination. Furthermore, we found that there was a significant difference in the dose of LT4 between patients with Hashimoto's disease and patients with total thyroidectomy, even if they had the same BMI.

The limitations of our study include the fact that it was performed on patients who had previously started LT4 treatment, that it included patients of a single ethnic group, calculating LMB with the formulation, is limited due to the limited number of patients receiving RAI treatment in the patient population and that it was performed in a single center. We recommend that large population, multicenter, randomized controlled trials with strong and robust evidence to determine the dose of LT4 based on LMB and not BMI in hypothyroid patients should be conducted to clarify this issue in the future.

Conclusion

This study demonstrates that lean body mass (LBM) is a stronger and more reliable predictor of levothyroxine (LT4) dose requirements than body mass index (BMI). Furthermore, the underlying etiology significantly influences LT4 needs and should be considered when titrating therapy. These findings highlight the importance of individualized dosing strategies in hypothyroidism management.

References

1. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Publisher Correction: Hypothyroidism. Nat Rev Dis Primers 2022;8(1):39.
2. Almandoz JP, Gharib H. Hypothyroidism: etiology, diagnosis, and management. Med Clin North Am 2012;96(2):203-221.
3. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. Thyroid 2014;24(12):1670-1751.
4. Santini F, Pinchera A, Marsili A, et al. Lean body mass is a major determinant of levothyroxine dosage in the treatment of thyroid diseases. J Clin Endocrinol Metab 2005;90(1):124-127.
5. Salvatore D, Bartha T, Harney JW, Larsen PR. Molecular biological and biochemical characterization of the human type 2 selenodeiodinase. Endocrinology 1996;137(8):3308-3315
6. Van der Spek AH, Fliers E, Boelen A. The classic pathways of thyroid hormone metabolism. Mol Cell Endocrinol 2017; 458:29-38.
7. Elfenbein DM, Schaefer S, Shumway C, Chen H, Sippel RS, Schneider DF. Prospective Intervention of a Novel Levothyroxine Dosing Protocol Based on Body Mass Index after Thyroidectomy. J Am Coll Surg 2016;222(1):83-88.
8. Biondi B, Cooper DS. Thyroid hormone therapy for hypothyroidism. Endocrine 2019;66(1):18-26.
9. Fish LH, Schwartz HL, Cavanaugh J, Steffes MW, Bantle JP, Oppenheimer JH. Replacement dose, metabolism, and bioavailability of levothyroxine in the treatment of hypothyroidism. Role of triiodothyronine in pituitary feedback in humans. N Engl J Med 1987;316(13):764-770.
10. Leonard JL, Koerle J. Intracellular pathways of iodothyronine metabolism. Werner, Ingbar's The thyroid. A fundamental and clinical text. Philadelphia: Lippincott Williams, Wilkins; 136–173
11. Ernst FR, Barr P, Elmor R, et al. The Economic Impact of Levothyroxine Dose Adjustments: the CONTROL HE Study. Clin Drug Investig 2017;37(1):71-83.
12. Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA 2004;291(2):228-238.
13. Cunningham JJ, Barzel US. Lean body mass is a predictor of the daily requirement for thyroid hormone in older men and women. J Am Geriatr Soc 1984; 32(3):204-207.
14. Devdhar M, Drooger R, Pehlivanova M, Singh G, Jonklaas J. Levothyroxine replacement doses are affected by gender and weight, but not age. Thyroid 2011;21(8):821-827.
15. Di Donna V, Santoro MG, De Waure C, et al. A new strategy to estimate levothyroxine requirement after total thyroidectomy for benign thyroid disease. Thyroid 2014 Dec 1;24(12):1759–1764
16. Mathiphanit S, Yenseung N, Chatchomchuan W, et al. Profile of Levothyroxine Replacement Therapy in Graves' Disease Patients with Hypothyroidism Post-Radioactive Iodine Ablation: Focus on Different Weight-Based Regimens. J ASEAN Fed Endocr Soc 2022;37(1):62-68.
17. Ratanapornsompong G, Sriphrapradang C. Appropriate dose of levothyroxine replacement therapy for hypothyroid obese patients. J Clin Transl Endocrinol 2021;25:100264.
18. Baehr KM, Lyden E, Treude K, Erickson J, Goldner W. Levothyroxine dose following thyroidectomy is affected by more than just body weight. Laryngoscope 2012;122(4):834-838.
19. Miccoli P, Materazzi G, Rossi L. Levothyroxine Therapy in Thyrodectomized Patients. Front Endocrinol (Lausanne) 2021;11:626268
20. Mistry D, Atkin S, Atkinson H, et al. Predicting thyroxine requirements following total thyroidectomy. Clin Endocrinol (Oxf) 2011;74(3):384-387.
21. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid 2012;22(12):1200-1235.
22. Jonklaas J. Optimal Thyroid Hormone Replacement. Endocr Rev 2022;43(2):366-404.
23. Gordon MB, Gordon MS. Variations in adequate levothyroxine replacement therapy in patients with different causes of hypothyroidism. Endocr Pract 1999;5(5):233-238.

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Diagnostic Radiological Findings in Adult Intussusception: A Retrospective Observational Study

Erişkin İnvaginasyonda Tanısal Radyolojik Bulgular: Retrospektif Gözlemsel Bir Çalışma

Ahmet Akçay[1] | **Banu Karaalioğlu**[2]

[1]Bezmialem Vakif University, Faculty of Medicine, Department of Radiology, İstanbul, Türkiye
[2]Istanbul Medipol University, Faculty of Medicine, Department of Radiology, İstanbul, Türkiye

Sorumlu Yazar | Correspondence Author
Ahmet Akçay
ahmetakcaymd@gmail.com
Address for Correspondence: Bezmialem Vakif University, Faculty of Medicine, Department of Radiology, İstanbul, Türkiye.

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Diagnostic Radiological Findings in Adult Intussusception: A Retrospective Observational Study

ABSTRACT

Objective: This study aimed to characterize computed tomography (CT) imaging features of adult intussusception, identify underlying lead points, and correlate morphological findings (segment length, transverse diameter) with clinical presentation.

Material and Method: Nineteen surgically confirmed adult intussusception cases were retrospectively analyzed. Demographic data, CT findings, intussuscepted segment length, transverse diameter, presence of a lead point, and obstruction status were recorded.

Results: The mean patient age was 57.1 ± 14.1 years. The ileum was the most commonly affected segment (57.9%). A lead point was identified on CT in 94.7% of cases, with lipoma being the most frequent lesion. Malignant lesions were found in 21.1% of patients, consistent with the literature. The transverse diameter was significantly greater in cases with obstruction (*p=0.002*). Although segment length was higher in the obstruction group, the difference was not statistically significant (*p=0.052*).

Conclusion: CT is not only effective in diagnosing adult intussusception but also provides valuable information on its etiology and severity through parameters such as lead point detection and signs of obstruction. CT-derived measurements like transverse diameter and segment length may have predictive value in clinical decision-making. Further large-scale, prospective studies are needed to validate these findings.

Keywords: Adult intussusception, Computed Tomography, Intestinal obstruction.

ÖZET

Amaç: Bu çalışmanın amacı, erişkin intussusepsiyon olgularında BT'nin tanı, etiyoloji ve hastalığın ciddiyetini belirlemedeki rolünü değerlendirmektir.

Gereç ve Yöntem: Çalışmaya cerrahi olarak doğrulanmış erişkin intussusepsiyon tanılı 19 hasta dahil edildi. Hastaların demografik verileri, BT bulguları, intussusepsiyon segmentinin uzunluğu, transvers çapı, lead point varlığı ve obstrüksiyon durumu değerlendirildi.

Bulgular: Hastaların yaş ortalaması 57,1 ± 14,1 yıl idi. En sık tutulan segment ileum (%57,9) olarak belirlendi. Olguların %94,7'sinde BT ile lead point saptandı; en sık görülen lezyon lipom idi. Malign lezyon oranı %21,1 olup, bu oran literatür ile uyumluydu. Obstrüksiyon saptanan olgularda transvers çap anlamlı olarak daha genişti (*p=0,002*). Segment uzunluğu obstrüksiyon grubunda daha fazla olmasına rağmen istatistiksel olarak anlamlı bulunmadı (*p=0,052*).

Sonuç: BT, erişkin intussusepsiyon olgularında yalnızca tanı koymakla kalmayıp, lead point varlığı ve obstrüksiyon gibi parametreler yoluyla hastalığın ciddiyeti hakkında da bilgi sağlamaktadır. Transvers çap ve segment uzunluğu gibi BT temelli ölçümlerin klinik yönetimde öngörücü olabileceği düşünülmektedir. Bu bulguların daha büyük ve prospektif çalışmalarla desteklenmesi gerekmektedir.

Anahtar Sözcükler: Erişkin invaginasyonu, Bilgisayarlı Tomografi, Bağırsak tıkanıklığı.

Introduction

Intussusception refers to the invagination of a proximal intestinal loop, along with its mesentery, into an adjacent distal segment, resulting in the characteristic 'bowel-within-bowel' configuration (1). This anatomical alteration produces the classic radiological appearances known as the 'target sign' and the 'sausage sign' on computed tomography (CT) (2). In adults, intussusception is a rare condition, accounting for approximately 1–5% of all cases of intestinal obstruction. Unlike pediatric cases, where most are idiopathic, adult intussusception is typically associated with an underlying pathology that serves as a lead point for the invagination (2,3). With the increasing use of abdominal CT for evaluating abdominal pain and other medical indications, the incidental detection of intussusception in adults has become more common. Although sometimes transient and asymptomatic, such findings may indicate an underlying serious pathology and should be carefully evaluated (4).

CT is the most sensitive imaging modality for detecting intussusception, with characteristic findings such as the 'target sign' and 'crescent sign' considered pathognomonic. Several studies in the literature have also highlighted CT's high diagnostic accuracy in identifying the lead point responsible for intussusception (4,5). Furthermore, CT plays a crucial role in evaluating potential mass lesions as the underlying cause, determining the presence of bowel obstruction or possible strangulation, and guiding clinical management and surgical planning (1).

This study aims to evaluate the morphological and demographic features of adult intussusception on preoperative CT, with a focus on the detectability of underlying lead point lesions, and to investigate the value of CT measurements in predicting obstruction, supported by radiologic–pathologic correlation.

Material and Method

The study was granted approval by the institutional ethics committee (E-54022451-050.04-194685). Informed consent was obtained from all patients or their legal guardians prior to data inclusion, in accordance with institutional and ethical guidelines. It was structured as a retrospective analysis involving adult individuals (18 years and older) who had a diagnosis of intussusception confirmed through surgical evaluation between 2010 and 2025 and had preoperative abdominal CT imaging available. Relevant patient information was collected from the hospital's electronic medical records and the PACS system. Cases with incomplete data or suboptimal CT image quality were excluded from the study.

Radiological evaluations were jointly conducted by two radiologists with 5 and 9 years of professional experience, both of whom were blinded to clinical and pathological data. A separate analysis of interobserver variability was not carried out. We did not perform a separate interobserver analysis because the cohort was modest; instead, to keep measurements consistent and reduce noise, two radiologists with 5 and 9 years of experience reviewed all scans together under a predefined, standardized protocol, and we will assess reproducibility in a larger multicenter cohort.

Contrast-enhanced abdominal CT scans were acquired during the portal venous phase, following intravenous injection of an iodinated contrast agent. Image acquisition included axial slices covering the region from the diaphragm to the symphysis pubis, with multiplanar reconstructions (MPR) in sagittal and coronal planes. No oral contrast was administered.

CT Evaluation

A bowel-within-bowel configuration demonstrating telescoping of bowel loops, including mesenteric fat and vascular structures, was considered consistent with the target sign. Eccentric localization of mesenteric fat within the intussusceptum, forming a crescent-shaped area of fat attenuation, was defined as the crescent sign (Figure I) (4). The localization of intussusception was determined based on CT images. Focal lesions identified within the bowel wall at the site of intussusception were considered lead points, and their largest dimension was measured along the longest axis. Lesions with fat attenuation originating from the submucosal layer of the bowel wall, distinct from the herniated mesenteric fat within the intussusceptum, were identified as lipomas (Figure II). At the level of intussusception, bowel diameter and the length of the invaginated segment were assessed on CT in three orthogonal planes, and

measurements were taken from the level where they appeared largest, including transverse diameter and invagination length (Figure III). Bowel obstruction was defined as proximal small bowel dilation ≥3 cm or colonic dilatation ≥5 cm, accompanied by air-fluid levels and collapsed distal bowel loops on CT. Radiological findings were evaluated in comparison with surgical notes and pathological reports.

Statistical Analysis

Statistical evaluations were conducted utilizing IBM SPSS Statistics version 25.0 for Windows (IBM Corp., Armonk, NY, USA). To examine distribution characteristics of continuous data, the Shapiro-Wilk test was applied. Variables showing normal distribution were reported as mean ± standard deviation (SD), whereas those lacking normality were described using median values alongside interquartile ranges (IQR). Categorical data were represented in terms of count and percentage.

Group comparisons, such as between individuals with and without bowel obstruction, were analyzed using either the independent samples t-test or the Mann–Whitney U test, selected based on the data distribution characteristics. Categorical variables were compared using the Chi-square test or Fisher's exact test when appropriate. A two-tailed *p-value of <0.05* was considered statistically significant.

Results

Nineteen adult patients who underwent surgery for intussusception were included in the study. The mean age was 57.1 ± 14.1 years (range: 19–77 years). The most common site of intussusception was the ileum, observed in 11 patients (57.9%), followed by the jejunum and colon, each in 4 patients (21.1%). Lipoma was the most identified lesion, present in 6 patients (31.6%). Malignant causes were found in 4 patients, including metastatic malignant melanoma in 2 (10.5%), lymphoma in 1 (5.3%), and adenocarcinoma in 1 (5.3%). Additional lesions included inflammatory fibroid polyps in 2 patients (10.5%), leiomyomas in 2 (10.5%), hemangioma in 1 (5.3%), and heterotopic pancreas in 1 (5.3%). No underlying pathology was identified in one patient (5.3%), and the case was considered idiopathic (Table I).

The target sign was observed in 18 patients (94.7%), while the crescent sign was present in 13 patients (68.4%). In 18 out of 19 cases, a focal lead point was identified on CT, and lesion size measurements were obtained (Table II).

Table I. Patient Demographics, Anatomical Localization, and Pathologic Diagnoses (n = 19)

Characteristic	Value
Number of patients (n)	19
Age (mean ± SD)	57.1 ± 14.1 years
Age range	19–77 years
Sex	
Male	10 (52.6%)
Female	9 (47.4%)
Intussusception Localization	
Ileum	11 (57.9%)
Jejunum	4 (21.1%)
Colon	4 (21.1%)
Pathologic Diagnoses	
Lipoma	6 (31.6%)
Leiomyoma	2 (10.5%)
Hemangioma	1 (5.3%)
Inflammatory fibroid polyp	2 (10.5%)
Heterotopic pancreas	1 (5.3%)
Malignant melanoma metastasis	2 (10.5%)
Colonic adenocarcinoma	1 (5.3%)
Lymphoma	1 (5.3%)
Idiopathic (no lead point found)	4 (21.1%)

SD: standard deviation

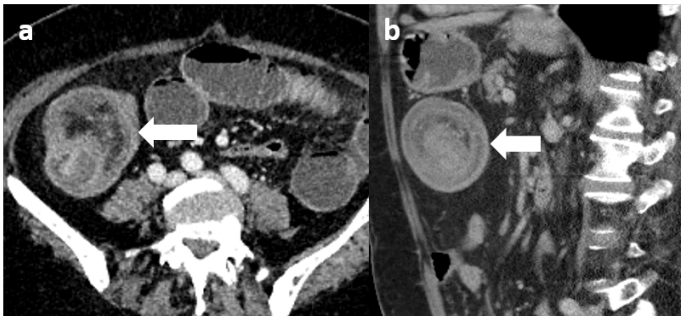

Figure I. Axial contrast-enhanced CT image shows the crescent sign, characterized by herniated mesenteric fat appearing as a crescent-shaped structure between the invaginated bowel loops (a). Sagittal contrast-enhanced CT image reveals a jejunojejunal intussusception with the classic "bowel-within-bowel" appearance, also referred to as the target sign (b).

The single idiopathic case involved an intussusception

located in the distal ileal loops. Although Meckel's diverticulum-like structure was considered the lead point during surgery, no underlying lesion was detected in the postoperative histopathological evaluation. Consistent with this, no distinct focal lesion was observed radiologically in this patient.

Bowel obstruction secondary to intussusception was observed in 8 patients (42.1%), while no signs of obstruction were detected in the remaining 11 patients (57.9%). In a total of 18 cases, the size of the lesion identified as the lead point on CT could be measured. The mean lesion size was 37.8 ± 15.1 mm, with a median of 41 mm (IQR: 20.75 mm). The median lesion size was larger in patients with bowel obstruction [47 mm (IQR: 38–54 mm)] compared to those without obstruction [30 mm (IQR: 25–35 mm)]; however, this difference did not reach statistical significance (*p=0.056*).

Table II. Imaging Findings and Measurements

Finding / Measurement	Number of Patients	% or mean ± SD
Target sign	18	94.7%
Crescent sign	13	68.4%
Mesenteric herniation	16	84.2%
Pathological lead point	18	94.7%
Obstruction	8	42.1%
Segment length (mm)	—	89.5 ± 34.4
Transverse diameter (mm)	—	37.9 ± 8.9

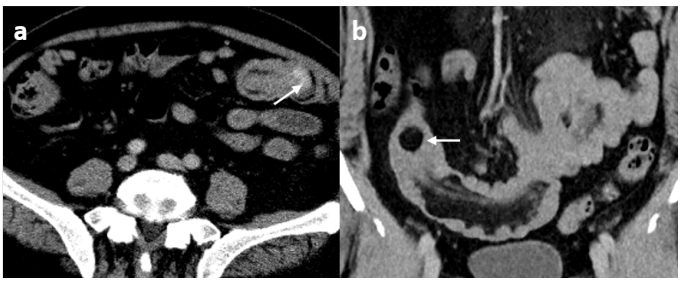

Figure II. Axial contrast-enhanced CT image shows a jejunojejunal intussusception with a hyperdense intraluminal lesion (arrow), consistent with a hemangioma, serving as the leading point (a). Coronal contrast-enhanced CT image demonstrates a colocolic intussusception, with a lipoma identified as the lead point, associated with traction on adjacent mesenteric vessels (b).

According to CT measurements, the mean length of the invaginated segment was 89.5 ± 34.4 mm, and the mean transverse diameter at the level of intussusception was 37.9 ± 8.9 mm. The transverse diameter was significantly greater in the obstruction group (45.4 ± 6.2 mm) compared to the non-obstruction group (32.5 ± 6.4 mm) (*p=0.002*). The mean length of the intussuscepted segment was also greater in patients with obstruction (106.6 ± 29.9 mm) than in those without obstruction (77.0 ± 33.2 mm), although the difference did not reach statistical significance (*p=0.052*).

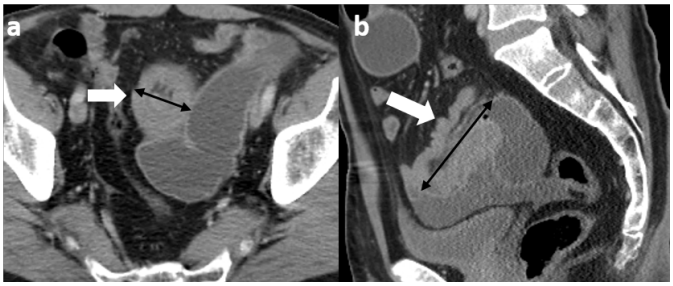

Figure III. Axial contrast-enhanced CT image demonstrates an ileoileal intussusception (white arrow) and the measurement of its transverse diameter (black arrow) (a). Sagittal contrast-enhanced abdominal CT image shows the ileoileal intussusception (white arrow) with measurement of its longitudinal length (black arrow) (b).

Discussion

CT is effective and highly reliable in the diagnosis of intussusception, with the target sign observed in nearly all cases (94.7%), consistent with previous reports in the literature (4-6). The only case in which the target sign was not observed involved a short-segment intussusception caused by a lipoma, a finding consistent with previous reports indicating that subtle or transient cases may lack classic radiological signs (6). In our study, a lead point lesion was identified in 18 of 19 intussusception cases (94.7%), which aligns with the literature reporting a pathological lead point in approximately 70–90% of adult cases (2,4,7). Idiopathic intussusception is considered rare in adults, as also noted by Marinis et al.; similarly, only one case (5.3%) in our series was classified as idiopathic (1). The mean age of patients was 57 years, consistent with previously reported data (4). In line with the literature, the majority of cases in our study were of the intestinal type, with colonic intussusception observed in only 21.1% of patients (4). Malignant tumors were less common than benign

lesions as the underlying cause, in agreement with previous studies. Metastatic malignant melanoma was identified in two cases, while lymphoma and adenocarcinoma were each seen in one case (8,9).

In our study, the transverse diameter at the level of intussusception was significantly greater in patients with bowel obstruction compared to those without. To our knowledge, this specific association has not been previously reported in adult intussusception. The increased transverse diameter may be explained by factors such as luminal accumulation of bowel contents and bowel wall edema secondary to obstruction (10,11). Bowel obstruction is a clinically significant finding in intussusception, as delayed or inadequate intervention may result in severe complications such as strangulation and perforation (11). In a study by Park et al., strangulated intussusception cases showed more prominent mesenteric vascular changes and longer invaginated segment lengths (4). Although our study did not specifically assess strangulation, the length of the intussuscepted segment was greater in obstructed cases than in non-obstructed ones, though this difference was not statistically significant. Early recognition of obstruction and its potential complications—such as mesenteric ischemia—is critical for appropriate clinical management. CT imaging plays a key role in this process. Therefore, the CT-based measurements used in our study, particularly transverse diameter and segment length, may have predictive value in identifying obstruction and ischemia in intussusception cases. Further studies with larger patient populations are warranted to validate these findings.

The study is subject to certain constraints. Since it was carried out retrospectively at a single center, its findings may not be widely generalizable. Furthermore, the limited number of patients included may have decreased the sensitivity of the statistical analysis in identifying less apparent associations. However, adult intussusception is a rare clinical entity, and the inclusion of surgically and histopathologically confirmed cases in our series enhances the reliability of the findings. Despite the limited number of patients, the study provides meaningful radiological and pathological insights that contribute to the growing body of literature on this uncommon condition. Future multicenter prospective studies with larger cohorts are needed to validate and build upon these results.

Adult intussusception is a rare clinical condition, with CT serving as a crucial tool for both diagnosis and treatment planning. Our findings highlight that CT not only confirms the diagnosis but also offers valuable insights into the underlying etiology and severity of the condition, particularly through features such as lead point detection and obstruction assessment. Effective management requires a multidisciplinary approach involving radiology, gastroenterology, and surgery. Early identification of malignancy on imaging is essential for appropriate surgical planning. CT-derived parameters like transverse diameter and segment length may have potential clinical utility. In practice, a larger transverse diameter at the level of intussusception is a practical red flag for obstruction; when considered alongside symptoms and laboratory data, it should prompt faster diagnostic confirmation, closer in-hospital observation, and early surgical input with a lower threshold for timely intervention to avoid ischemia or perforation. Future large-scale, prospective—ideally multicenter—studies are needed to validate these observations, define generalizable thresholds for CT-based measurements, quantify interobserver agreement, and test whether integrating these metrics into triage pathways shortens time-to-surgery and improves patient outcomes.

References

1. Marinis A, Yiallourou A, Samanides L, et al. Intussusception of the bowel in adults: a review. World J Gastroenterol 2009;15(4):407-411.

2. Azar T, Berger DL. Adult intussusception. Ann Surg. 1997;226(2):134-138.

3. Agha FP. Intussusception in adults. AJR Am J Roentgenol 1986;146(3):527-531.

4. Park SB, Ha HK, Kim AY, et al. The diagnostic role of abdominal CT imaging findings in adults intussusception: focused on the vascular compromise. Eur J Radiol 2007;62(3):406-415.

5. Kim YH, Blake MA, Harisinghani MG, et al. Adult intestinal intussusception: CT appearances and identification of a causative lead point. Radiogr Rev Publ Radiol Soc N Am Inc 2006;26(3):733-744.

6. Tresoldi S, Kim YH, Blake MA, et al. Adult intestinal intussusception: can abdominal MDCT distinguish an intussusception caused by a lead point? Abdom Imaging

2008;33(5):582-588.
7. Begos DG, Sandor A, Modlin IM. The diagnosis and management of adult intussusception. Am J Surg 1997;173(2):88-94.
8. Lamki N, Woo CL, Watson AB, Kim HS. Adenomyomatous hamartoma causing ileoileal intussusception in a young child. Clin Imaging 1993;17(3):183-185.
9. Mansberg VJ, Mansberg G, Doust BD. Jejunojejunal intussusception secondary to leiomyoma. Australas Radiol 1996;40(1):72-74.
10. Boudiaf M, Soyer P, Terem C, Pelage JP, Maissiat E, Rymer R. Ct evaluation of small bowel obstruction. Radiogr Rev Publ Radiol Soc N Am Inc 2001;21(3):613-624.
11. Wong L, Sivanesan U, Haider M, Chung AD. Intraluminal causes of mechanical small bowel obstruction: CT findings and diagnostic approach. Eur J Radiol 2025;187:112115.

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Evaluation of Parental Knowledge, Attitudes, and Health Literacy in Common Pediatric Surgical Diseases

Sık Görülen Pediatrik Cerrahi Hastalıklarda Ebeveyn Bilgi, Tutum ve Sağlık Okuryazarlığının Değerlendirilmesi

Nurcan Çoşkun[1] | Tuba Kayır[2]

[1]Hitit University Erol Olçok Training and Research Hospital, Department of Pediatric Surgery, Çorum, Türkiye
[2]Mimar Sinan Family Health Center, Department of Family Medicine, Çorum, Türkiye

Sorumlu Yazar | Correspondence Author
Nurcan Çoşkun
nurcanerguncoskun19@gmail.com
Address for Correspondence: Hitit University Erol Olçok Training and Research Hospital, Department of Pediatric Surgery, 19040, Çorum, Türkiye.

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Evaluation of Parental Knowledge, Attitudes, and Health Literacy in Common Pediatric Surgical Diseases

ABSTRACT

Objective: Pediatric surgical diseases are a significant public health issue due to their morbidity and burden on healthcare systems. This study aimed to assess parents' knowledge, attitudes, and health literacy regarding common surgical diseases and to examine their relationship with sociodemographic factors, as well as to explore the potential impact of these factors on pediatric surgical processes.

Material and Method: In this cross-sectional descriptive study, 121 parents of children aged 0–18 years presenting to family health centers were included. Data were collected through a structured questionnaire including sociodemographics, a 10-item knowledge test, a 10-item attitude scale, and the Health Literacy Scale–Short Form (HLS-SF12). Statistical analyses involved t-tests, ANOVA, and correlation tests.

Results: Of the participants, 71.1% were female and 51.2% were aged 36–45. Knowledge levels were high for appendicitis and circumcision but low for hydrocele and undescended testis. Higher health literacy scores were significantly associated with female gender, higher education, urban residence, civil servant status, and higher income ($p<0.05$). Additionally, 55.4% of the participants stated that they looked for information online, but only 4.1% trusted social media. 57% directly consulted an expert, while 84.3% received a second expert opinion.

Conclusion: Parents' knowledge and health literacy are significantly affected by sociodemographic characteristics. Deficiencies in knowledge about common diseases that can lead to serious complications and timing of treatment can be overcome by strengthening the counseling role of family physicians and disseminating simple, reliable and comprehensible information resources for groups with low health literacy. Structured and systematic education programs, such as school-based initiatives and digital health platforms, could play a pivotal role in achieving these goals.

Keywords: Cross-sectional study, Family physician, Health literacy, Knowledge level, Pediatric surgery.

ÖZET

Amaç: Çocuklarda sık görülen cerrahi hastalıklar, morbidite ve sağlık sistemine yük açısından önemli bir halk sağlığı sorunudur. Bu çalışmada, ebeveynlerin yaygın cerrahi hastalıklara ilişkin bilgi, tutum ve sağlık okuryazarlıklarını değerlendirmek, bunların sosyodemografik faktörlerle ilişkisini incelemek ve bu faktörlerin pediatrik cerrahi süreçleri üzerindeki olası etkilerini araştırmak amaçlanmıştır.

Gereç ve Yöntem: Kesitsel ve tanımlayıcı nitelikteki çalışmaya, aile sağlığı merkezlerine başvuran, 0–18 yaş aralığında çocuğu bulunan 121 ebeveyn dahil edilmiştir. Veriler; sosyodemografik bilgiler, cerrahi hastalıklara yönelik 10 soruluk bilgi testi, 10 maddelik tutum ölçeği ve Sağlık Okuryazarlığı Ölçeği – Kısa Form (HLS-SF12)'dan oluşan anketle toplanmıştır. İstatistiksel analizlerde t-testi, ANOVA ve korelasyon testleri kullanılmıştır.

Bulgular: Katılımcıların %71,1'i kadın, %51,2'si 36–45 yaş aralığındadır. Apandisit ve sünnet hakkında bilgi düzeyi yüksek; hidrosel ve inmemiş testis gibi hastalıklarda bilgi eksiklikleri belirgindir. Yüksek Sağlık okuryazarlığı düzeyi; kadın cinsiyet, yüksek eğitim, memuriyet, şehirde yaşama ve yüksek gelirle anlamlı ilişkilidir ($p<0,05$). Katılımcıların %55,4'ü internetten bilgi aradığını ancak sadece %4,1'inin sosyal medyaya güvendiğini belirtmiştir. %57'si doğrudan uzmana başvururken, %84,3'ü ikinci uzman görüşü almıştır.

Sonuç: Ebeveynlerin bilgi düzeyi ve sağlık okuryazarlığı, sosyodemografik özelliklerden önemli ölçüde etkilenmektedir. Ciddi komplikasyonlara yol açabilecek yaygın hastalıklar ve tedavi zamanlaması konusunda bilgi eksiklikleri, aile hekimlerinin danışmanlık rolünün güçlendirilmesi ve sağlık okuryazarlığı düşük gruplar için basit, güvenilir ve anlaşılır bilgi kaynaklarının yaygınlaştırılmasıyla giderilebilir. Okul temelli girişimler ve dijital sağlık platformları gibi yapılandırılmış ve sistematik eğitim programları bu hedeflere ulaşmada önemli bir rol oynayabilir.

Anahtar Sözcükler: Aile hekimi, Bilgi düzeyi, Çocuk cerrahisi, Kesitsel çalışma, Sağlık okuryazarlığı.

Introduction

Surgical diseases in children constitute a significant public health problem in terms of both morbidity and healthcare system utilization. Surgical diseases such as appendicitis, undescended testicles, inguinal hernias, and circumcision are the most common clinical presentations encountered by pediatric surgeons in their daily practice. Appendicitis is one of the most common causes of acute surgical abdominal pain in childhood, and early diagnosis is of vital importance (1). Undescended testicles are a common condition in male children and, if not treated in time, can increase the risk of infertility and testicular tumors (2). Circumcision is a surgical procedure with both medical and socio-cultural aspects, and the complication rate increases significantly under inappropriate conditions (3).

Timely and appropriate access to healthcare services is largely related to parents' level of knowledge and health literacy (HL). HL refers to an individual's ability to obtain, understand, and apply health information and is defined by the World Health Organization as a fundamental health right (4). Low HL can lead to consequences such as decisions based on misinformation, delayed access, and non-compliance with treatment (5). In Türkiye, the National Health Literacy Survey reported that 64.6% of the population had inadequate or problematic HL, with lower scores observed in rural areas, among older adults, and in those with lower education and income levels (6). These disparities highlight the need for targeted interventions, particularly for parents making healthcare decisions for their children (6). The HL level of parents, who are decision-makers in particular for pediatric patients, can directly affect the entire process from diagnosis to treatment (7).

Parents' HL and knowledge level are decisive factors for timely intervention in pediatric surgical diseases. In this process, family physicians providing primary care play an important role. Family physicians are in a critical position in terms of providing parents with accurate information, early diagnosis, and appropriate referral. The primary objective of this study is to assess parents' knowledge level, attitudes, and HL regarding common surgical diseases in children, to examine their relationship with certain sociodemographic factors, and to explore the potential impact of these factors on pediatric surgical processes.

Material and Method

This study was designed as a descriptive and cross-sectional study. First, approval was obtained from the Hitit University Non-Interventional Research Ethics Committee on May 3, 2025, with decision number 2025-128. The study population consisted of parents who visited family health centers and had children aged 0–18 years. The sample size was calculated using the G*Power 3.1 statistical program. With a significance level of 5% (α=0.05), an effect size of 0.3, and 80% power (1–β=0.80), a minimum of 84 participants were required to conduct the study. However, considering potential losses and analytical validity, the sample size was increased to 121.

The criteria for participation in the study were parents who had children aged 0–18, who agreed to participate in the study voluntarily, and who were competent to complete the questionnaire themselves. Those who did not want to complete the questionnaire, had difficulty communicating, or did not voluntarily participate in the study were excluded. Face-to-face interviews were preferred for administering the questionnaire. Each participant was informed of the purpose of the study, and their consent was obtained. All data were anonymized and used solely for scientific purposes. A four-part questionnaire was used as the data collection tool. This form enabled the systematic collection of data on sociodemographic characteristics, knowledge level, attitudes, and HL within the scope of the study. The Sociodemographic Data Form consists of seven questions covering gender, age, educational status, occupation, income, marital status, and place of residence.

The Knowledge Level Test consists of 10 multiple-choice questions related to common surgical diseases in children (appendicitis, undescended testicles, inguinal hernia, hydrocele, pilonidal sinus, and circumcision). Each correct answer was scored as 1 point, with a total score ranging from 0 to 10.

The knowledge test was developed by the research team based on national pediatric surgery guidelines and previous studies in the literature. Draft questions were reviewed by one pediatric surgeon and one

family medicine specialist to ensure content validity. A pilot test was conducted with 10 parents who were not included in the main study, and minor wording adjustments were made to improve clarity.

Table I. Statistical Findings Regarding the Socio-Demographic Characteristics of the Parents Participating in the Study

Introductory Characteristics	n	%
Age		
18 - 25	3	2.5
26 - 35	27	22.3
36 - 45	62	51.2
46 and above	29	24.0
Gender		
Female	86	71.1
Male	35	28.9
Education Level		
Primary School	29	24.0
Middle School	32	26.4
High School	24	19.8
University	27	22.3
Postgraduate	9	7.4
Occupation		
Not working	51	42.1
Freelancer	11	9.1
Civil servant	23	19.0
Worker	23	19.0
Other	13	10.7
Income Level		
Not working	34	28.1
5000 TL and below	7	5.8
5000 - 10000	17	14.0
10000 - 25000	6	5.0
25000 - 40000	17	14.0
40000 TL and above	40	33.1
Marital Status		
Married	102	84.3
Widowed	19	15.7
Place of Residence		
Village / Town	5	4.1
District	6	5.0
City	110	90.9
Total	121	100

Attitude Survey consists of 10 items on a 3-point Likert scale covering topics such as approach to surgery, traditional methods, trust in physicians, and expectations regarding information provision. (Agree – Undecided – Disagree).

Health Literacy Scale – Short Form (HLS-SF12) is a 12-item, four-point Likert-type measure that assesses individuals' ability to acquire, interpret, and understand health information. Validity and reliability studies have been conducted in Türkiye, and the Cronbach's alpha coefficient is 0.856, indicating a high level of reliability. The scale covers topics such as access to health services, evaluating treatment options, and preventive health behaviors. Responses to each item are scored on a scale from "very difficult (1)" to "very easy (4)." The total score is standardized using the formula (Mean - 1) × 50 / 3 and ranges from 0 to 50. Higher scores represent better HL (8).

Statistical analysis

All analyses were performed using SPSS software (Version 22.0, SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as frequencies (n) and percentages (%), while continuous variables were presented as mean ± standard deviation for normally distributed data or median (min-max) for non-normally distributed data. Normality was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests, supported by graphical evaluations. For comparisons between groups, the appropriate tests were selected based on data distribution: one-way ANOVA with Tukey's post-hoc test for parametric comparisons of multiple groups, Student's t-test for parametric comparisons between two groups, Kruskal-Wallis test with Dunn-Bonferroni post-hoc correction for non-parametric comparisons of multiple groups, and Mann-Whitney U test for non-parametric comparisons between two groups. Descriptive statistics were used to summarize response distributions for knowledge and attitude items. All tests were two-tailed, with statistical significance set at $p<0.05$, and adjustments for multiple comparisons were applied where necessary.

Results

The sociodemographic characteristics of the parents participating in the study are presented in Table 1. When the age distribution of the participants was examined, the highest rate was found to be in the 36-45 age group, with 51.2%. When looking at the gender distribution, the rate of women (71.1%) was higher than that of men (28.9%). In terms of educational

Table II. Distribution and Success Rates of Responses to a Questionnaire On Parents' Level of Knowledge Regarding Common Surgical Diseases In Children

Questions	Options	n	%	Performance	
				Incorrect	Correct
What is the most common symptom of appendicitis?	Headache	6	5.0		
	Abdominal pain	113	93.4	8	113
	Joint swelling	1	0.8	%6.6	%93.4
	Skin rash	1	0.8		
What is the ideal timing for the treatment of undescended testis (cryptorchidism)?	After age 5	31	25.6		
	At age 1	61	50.4	60	61
	Puberty	25	20.7	%49.6	%50.4
	No treatment needed	4	3.3		
In which situation should a doctor be consulted urgently after circumcision?	Mild redness	3	2.5		
	Bleeding or infection	92	76.0	29	92
	Temporary loss of appetite	3	2.5	%24	%76
	All of the above	23	19.0		
What is the appropriate approach in a child diagnosed with inguinal hernia?	Surgical repair is recommended	97	80.2		
	Observation is sufficient	4	3.3	24	97
	Medication is used	12	9.9	%19.8	%80.2
	Physical therapy is applied	8	6.6		
Which statement is correct regarding hydrocele?	It is painless and resolves spontaneously	41	33.9		
	Requires emergency surgery	46	38.0	80	41
	Occurs only in adults	15	12.4	%66.1	%33.9
	None of the above	19	15.7		
Where is the safest place for circumcision to be performed?	At home by elder family members	1	0.8		
	In a Ministry of Health-approved healthcare facility	115	95.0	6	115
	By a traditional circumciser	5	4.1	%5	%95
	Collectively in a schoolyard	0	0		
Can a child who has had appendicitis get it again?	Yes	16	13.2		
	No	89	73.6	32	89
	Annual check-up	15	12.4	%26.4	%73.6
	Antibiotics	1	.8		
Where is pilonidal sinus most commonly seen?	Neck	3	2.5		
	Sacral region (tailbone)	109	90.1	12	109
	Abdomen	2	1.7	%9.9	%90.1
	Armpit	7	5.8		
Which condition in children with inguinal hernia requires emergency surgery?	Mild pain	8	6.6		
	Strangulated hernia	108	89.3	0	121
	Sneezing	2	1.7	0	100
	None of the above	3	2.5		
Which of the following is not recommended in post-circumcision care?	Applying powder	86	71.1		
	Keeping it clean	5	4.1	35	86
	Using prescribed medications	5	4.1	%28.9	%71.1
	Avoiding tight clothing	25	20.7		

status, the most common groups were secondary school (26.4%) and primary school (24%), while the proportion of those with postgraduate education was 7.4%. In terms of occupational distribution, the highest proportions were among those not working (42.1%) and workers/civil servants (each at 19%). When income level was examined, it was seen that 33.1% of participants had an income of 40,000 TL or more. In terms of marital status, the percentage of married individuals (84.3%) was significantly higher

Table III. Distribution of Responses to the Attitude Survey for Parents Regarding Common Surgical Diseases in Children

Questions	Options	n	%
I first consult the family physician when my child has a surgical condition.	Disagree	69	57.0
	Neutral	9	7.4
	Agree	43	35.5
I believe procedures like circumcision should be performed in a hospital setting.	Disagree	7	5.8
	Neutral	1	0.8
	Agree	113	93.4
I search the internet for information about surgical procedures.	Disagree	33	27.3
	Neutral	21	17.4
	Agree	67	55.4
I wait for a referral from the family physician instead of consulting a pediatric surgeon directly.	Disagree	69	57.0
	Neutral	15	12.4
	Agree	37	30.6
I believe traditional methods are safer than surgical treatments.	Disagree	101	83.5
	Neutral	8	6.6
	Agree	12	9.9
The opinion of the family physician is important in my surgical decision-making.	Disagree	49	40.5
	Neutral	25	20.7
	Agree	47	38.8
Cost is a priority for me when making surgical decisions.	Disagree	93	76.9
	Neutral	15	12.4
	Agree	13	10.7
I seek a second opinion when my child needs surgery.	Disagree	11	9.1
	Neutral	8	6.6
	Agree	102	84.3
I trust health information on social media.	Disagree	95	78.5
	Neutral	21	17.4
	Agree	5	4.1
I would like to attend educational seminars about pediatric surgical diseases.	Disagree	21	17.4
	Neutral	36	29.8
	Agree	64	52.9

than that of single individuals. The vast majority of participants (90.9%) lived in cities.

The survey results evaluating parents' knowledge levels regarding common surgical diseases in children are presented in Table 2. Abdominal pain (93.4%) was correctly identified as the most common symptom of appendicitis. 50.4% of participants answered correctly that the ideal time for undescended testicle treatment is 1 year of age. Among the conditions requiring urgent medical consultation after circumcision, bleeding or infection (76%) had the highest correct response rate. The percentage of those who knew that surgical repair was recommended for inguinal hernia treatment was determined to be 80.2%. When examining the responses to the question about hydrocele, 38% of participants gave an incorrect response that hydrocele requires emergency surgery, while 33.9% correctly selected the option 'it is painless and resolves on its own.' 95% of respondents answered correctly that circumcision should be performed in the safest manner at health institutions approved by the Ministry of Health. Parents' responses to other questions can be examined in detail in Table 3.

The survey results evaluating parents' attitudes towards surgical diseases are summarized in Table 3. 93.4% of participants stated that procedures such as circumcision should be performed in a hospital setting. The tendency to search for information about surgical procedures on the internet was accepted by 55.4%. The percentage of those who did not agree with the idea that traditional methods are safer than surgical treatments was determined to be 83.5%. 84.3% of participants stated that they tend to seek a

second opinion when making surgical decisions for their children. The rate of trust in health information on social media remained at only 4.1%. Parents' responses to other questions can be examined in detail in Table 3.

Table IV. Statistical Findings Regarding the Relationship between Socio-demographic Characteristics and the Health Literacy Scale-Short Form

Introductory Characteristics	n	Mean±SD/Medyan (min-max)	*p values*	Post-hoc p values
Age				
18 - 35	30	38.01±5.91	*0.011*[a]	*1-3: 0.007*
36 - 45	62	35.28±6.7		
46 and above	29	32.47±8.25		
Gender				
Female	86	36.34±6.69	*0.010*[b]	-
Male	35	32.7±7.64		
Education Level				
Primary School	29	30.56 (18.06 - 43.06)	*<0.001*[c]	*1-4: <0.001 1-5: <0.001 2-4: <0.001 2-5: 0.001 3-4: 0.030 3-5: 0.030*
Middle School	32	32.64 (25 - 48.61)		
High School	24	34.72 (23.61 - 47.22)		
University	27	41.67 (19.44 - 50)		
Postgraduate	9	43.05 (38.89 - 50)		
Occupation				
Not working	51	33.33 (19.44 - 48.61)	*0.001*[c]	*1-3: 0.007 2-3: 0.001*
Freelancer	11	30.55 (18.06 - 41.67)		
Civil servant	23	40.27 (19.44 - 50)		
Worker	23	34.72 (20.83 - 47.22)		
Other	13	36.11 (25 - 50)		
Income Level				
Not working	34	34.02 (19.44 - 48.61)	0.003[c]	2-6: 0.009
5000 TL and below	7	27.77 (18.06 - 36.11)		
5000 - 10000	17	31.94 (20.83 - 50)		
10000 - 25000	6	34.72 (30.56 - 47.22)		
25000 - 40000	17	33.33 (25 - 50)		
40000 TL and above	40	39.58 (19.44 - 50)		
Marital Status				
Married	102	35.08±7.12	*0.489*[b]	-
Widowed	19	36.33±7.31		
Place of Residence				
Village / Town / District	11	27.77 (19.44 - 48.61)	*0.018*[d]	-
City	110	34.72 (18.06 - 50)		
Total	121			

[a]One way ANOVA test
[b]Student's t-test
[c]Kruskal-Wallis test
[d]Mann Whitney U test

The relationship between sociodemographic characteristics and the short form of the HL Scale is examined in Table 4. Statistically significant differences were found between the short form scores of the HL Scale and the sociodemographic characteristics of age, gender, educational status, occupation, income status, and place of residence (*p=0.011, 0.010, p<0.001, p=0.001, p=0.003, p=0.018*). In addition, box-plots showing the distribution of HL scores across gender and age groups are presented in Figure 1 and Figure 2, respectively. There were no differences in scale scores between marital status groups (*p=0.489*). According to the post-hoc test results, when age groups were compared, the HL scores of the 18-35 age group (38.01±5.91) were found to be significantly higher than those of the 46 and older age group (32.47±8.25) (*p=0.007*). Women's scores (36.34±6.69) were statistically higher than men's (32.7±7.64) (*p=0.010*). HL scores increased significantly with increasing education level; the difference between postgraduate graduates (43.05) and primary school graduates (30.56) was notable. University graduates' HL scores were significantly higher than those of primary school, middle school, and high school graduates (*p<0.001, <0.001, p=0.030*, respectively). The HL scores of postgraduate degree holders were significantly higher than those of primary school, secondary school, and high school graduates (*p<0.001, 0.001, p=0.030,* respectively). When comparing occupational groups, civil servants' HL scores (40.27) were significantly higher than those of unemployed individuals (33.33) and self-employed individuals (30.55) (*p=0.007, p=0.001,* respectively). In terms of income, the HL scores of those with an income of 40,000 TL and above (39.58) were significantly higher than those in the 5,000 TL and below income group (27.77) (*p=0.009*). Additionally, a statistically significant difference was found between the scores of the 5,000–10,000 TL income group (31.94) and the 40,000 TL and above income group (p=0.009). The scores of those with an income level of 40,000 TL and above (39.58) were higher than those with an income below 5,000 TL (27.77) (*p=0.009*). The scores of those living in cities (34.72) were significantly higher than those of residents of villages/towns and districts (27.77) (*p=0.018*).

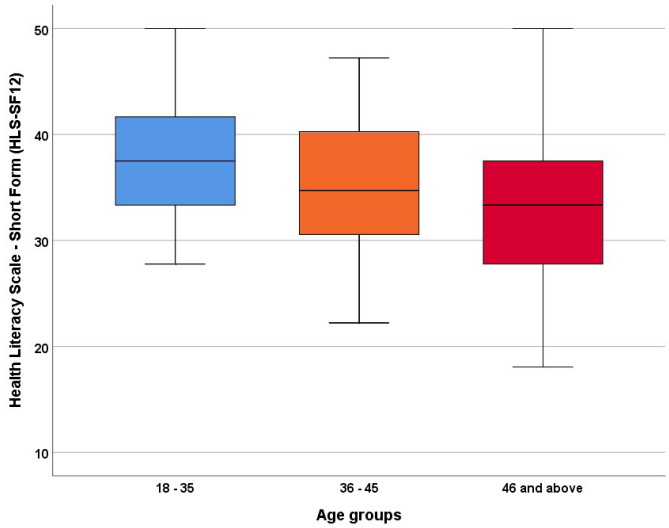

Figure I. Boxplots Showing Comparisons of Health Literacy Scale-Short Form (HLS-SF12) Scores by Age Group

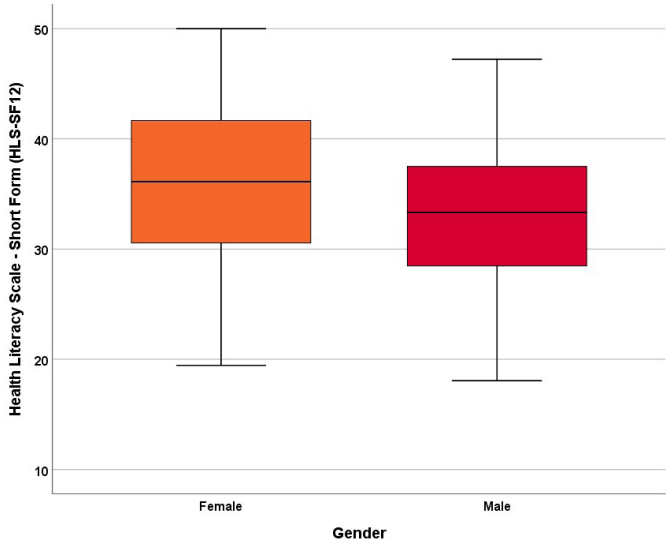

Figure II. Boxplots Showing Comparisons of Health Literacy Scale-Short Form (HLS-SF12) Scores by Gender Group

Discussion

Our study revealed important findings in terms of knowledge gaps, parental attitudes, and demographic factors affecting HL. Our findings show that the level of knowledge is sufficient for some surgical diseases, but there are significant gaps in less known or misconception-prone topics. It was observed that parents' knowledge and HL levels were significantly associated with sociodemographic factors such as age, gender, education, occupation, income, and place of residence. Additionally, it was found that digital sources are frequently used in the search for information, but the level of trust remains low; in the processes of seeking healthcare and making decisions, there is a tendency to seek the opinion of a specialist rather than a family doctor. These general findings indicate that parental behavior toward pediatric surgery is shaped not only by knowledge but also by trust, access, and perceptions of the healthcare system.

Parents' lack of knowledge about pediatric surgical diseases can directly affect not only individual health outcomes but also the burden on the healthcare system. In particular, misperceptions about the urgency of diseases can lead to unnecessary visits to emergency departments, causing congestion in healthcare service delivery and inefficient use of resources. For example, viewing conditions such as hydrocele, which often do not require urgent intervention, as reasons for emergency visits can increase the workload of healthcare workers and cause delays in the management of actual emergency cases. Similarly, parents with misinformation about treatment timing can increase healthcare system costs through unnecessary tests and referrals. Therefore, addressing information gaps will not only improve clinical outcomes but also contribute to the efficient use of healthcare resources.

The data obtained revealed that participants had sufficient knowledge about some pediatric surgical diseases, but there were serious gaps in their knowledge in some critical areas. In particular, high rates of correct answers regarding appendicitis symptoms (93.4%), surgical approach to inguinal hernia (80.2%), and circumcision (95.0%) suggest that awareness of these conditions is high in the community and that frequent media coverage has positively influenced knowledge levels. On the other hand, the lower level of knowledge about less well-known diseases such as undescended testicles and hydrocele indicates that some misconceptions and information gaps persist in society. Only 50.4% of participants correctly knew that the ideal time for treatment of undescended testicles is around 1 year of age. A significant portion of participants believe that this treatment should be postponed to later stages, such as after the age of 5 (25.6%) or during adolescence (20.7%). This misconception paves the way for significant clinical delays that could lead to serious complications in children, such as testicular

atrophy, subfertility, and malignancy (2). Knowledge about hydrocele was limited. Thirty-eight percent believed it requires emergency surgery. In reality, it is usually painless, resolved on its own, and only needs regular monitoring (9). Such misconceptions can cause unnecessary anxiety in families and lead to premature visits to pediatric emergency departments, thereby increasing the workload on the healthcare system. Indeed, a review reported that one in three parents who visited the emergency department had low HL, and that interventions targeting this group could reduce unnecessary visits (10). These findings indicate that health education should not only focus on introducing disease names but also clearly and comprehensively explain details such as the timing of treatment, urgency level, and appropriate referral steps for each disease. It has been demonstrated that written educational materials used for this purpose not only increase parents' knowledge but also enhance their satisfaction and reduce anxiety levels prior to surgical procedures (11). Otal and colleagues have shown that parents informed with simplified educational materials recognize postoperative complications earlier and utilize healthcare services more effectively (12). We believe that family physicians play a critical role in informing parents about these common but often misunderstood surgical conditions, as this is essential for the timely and accurate diagnosis and treatment process.

Yin et al. (2012) reported that parents with low HL trust physician recommendations more (13). In our study, 57% consulted a pediatric surgeon before a family physician. Only 38.8% valued the family physician's opinion, and 84.3% sought a second expert opinion. These findings indicate that parents are seeking trust in the decision-making process. Findings related to the search for digital information are also noteworthy: While 55.4% of participants stated that they conducted internet research on surgical interventions, only 4.1% said they trusted social media information. Parents use digital resources but remain skeptical about their reliability. Indeed, a study evaluating the quality of circumcision videos on YouTube reported that a significant portion of the content was of poor quality, while videos prepared by medical experts were found to be more reliable (14); this finding is consistent with the fact that parents in our study stated that they did not trust the information they found on the internet. To resolve this confusion, we recommend strengthening the advisory role of family physicians, disseminating verified information sources on digital platforms, and effectively using hospital-based information brochures. In addition, the low level of trust in traditional treatment methods (9.9%) is a positive finding in terms of showing that modern medicine and hospital-based services are accepted in society. However, 10.7% of participants stated that cost was a primary factor in their decision to undergo surgery. This percentage suggests that economic concerns may influence decisions to undergo surgical intervention, particularly among socioeconomically disadvantaged groups. In conclusion, it is evident that parents need reliable sources of information in the surgical decision-making process, but they face a dilemma due to information pollution on digital platforms. This situation necessitates not only increasing the advisory role of healthcare professionals but also disseminating accurate and accessible sources of information. Additionally, considering the impact of socioeconomic factors on the decision-making process, it is important to develop financial support mechanisms, particularly for disadvantaged groups. Maintaining public trust in modern medicine and strengthening HL should be supported by multidisciplinary approaches guided by similar studies.

Parental HL encompasses a set of skills and competencies that enable parents to navigate the healthcare system effectively, understand medical instructions, communicate with healthcare providers (HCPs), and make informed choices about their children's health (15). In pediatric surgery, parents' or guardians' HL levels are extremely important in terms of understanding surgical pathologies, the risks and benefits of surgical procedures, and the implementation of instructions during the pre- and post-operative periods (13,16). The findings in our study regarding HL indicate that individuals' capacity to interpret and apply general health information is significantly associated with demographic factors.

The literature reports that gender has little effect on HL (4). In our study, women's HL scores were found to be higher than men's (p=0.010). This finding can be explained by reasons such as women being more closely involved in children's health and seeking health services more frequently. A study investigating HL among parents of children with Hirschsprung's disease reported a significant increase in HL among those over 40 years of age (17). Another study reported a decrease with aging (4). In contrast to the literature, our study found that HL was highest among those aged 18–35 and significantly lower among those aged 46 and older (p=0.011). This may be related to differences in the use of health information tools (e.g., digital media). The effect of educational level on HL was clearly demonstrated in our study. HL scores were significantly higher among individuals with university and postgraduate education compared to primary, middle school, and high school graduates (*p<0.001*). This result is a finding commonly reported in the literature and indicates that health education policies should focus specifically on groups with low educational levels (4,15,17). In the study conducted by Kampouroglou et al., the HL rate was reported to be high among healthcare workers (18). In our study, when examined by occupational group, civil servants had higher HL scores than other occupational groups (*p=0.001*). This result may be due to the presence of healthcare professionals in this group and the fact that most of them are university graduates.

A significant relationship was also found between income level and HL (*p=0.003*). Participants who reported an income of 40,000 TL or more had higher literacy scores. This finding is consistent with the literature suggesting that economic resources facilitate both access to health services and access to health information (4,16,18). When evaluated by place of residence, individuals living in provincial centers had higher HL scores than those living in rural areas (*p=0.018*). The ease of access to healthcare services and the diversity of information sources in urban areas may be among the main reasons for this difference.

There are very few studies in the international literature examining the HL of parents of pediatric surgery patients. However, no such studies have been found in Türkiye. This study is unique in that it is the first study in our country to evaluate the HL of parents in the field of pediatric surgery, and it makes a pioneering contribution to this field. Our study revealed important findings in terms of knowledge gaps, parental attitudes, and demographic factors affecting HL. The data obtained are consistent with the limited number of studies related to HL in the field of pediatric surgery. Previous studies emphasizing that individuals with low HL can benefit from appropriate interventions and that literacy-sensitive approaches should provide understandable and accessible information for all patients support our findings (19). Indeed, it has been observed that parents with high HL have higher levels of knowledge. This suggests that pediatric surgeons adapting their communication language by removing technical terms and tailoring it to parents' needs could enhance patient understanding, participation, and care quality. In addition, although Keim Malpass et al. (2015) conducted a systematic review of parental HL among children with special health care needs, their study emphasized the overall scarcity and heterogeneity of measurement tools and outcomes (20). Lawrence (2021) examined the direct link between parental HL and medication errors in children, demonstrating a specific outcome-related methodological approach (21). Reddy et al. in a pediatric intensive care unit setting, applied a mixed-methods design—combining quantitative screening via the Newest Vital Sign tool with qualitative insights from healthcare providers—to assess caregiver HL and implementation challenges (22). These diverse methodological approaches—ranging from systematic review, outcome-focused analysis, to mixed-methods in critical care—highlight the novelty and methodological rigor of our own study, which integrates a disease-specific knowledge test with sociodemographic analysis in a Turkish pediatric surgery context.

For strategies aimed at improving HL to be effective, concrete, accessible, and sustainable interventions must be planned. In this context, it is important to strengthen the advisory role of family doctors and to implement structured education models to improve parents' HL. School-based parent

education programs can provide both children and parents with systematic access to health information; these programs can be structured in collaboration with family physicians and pediatric surgeons to cover topics such as early signs of surgical diseases, treatment processes, and emergency management. In addition, mobile health applications with reliable content and community-based workshops managed by health professionals can enable parents to access the information they need without time and space constraints. These applications, which include short videos about diseases, interactive knowledge tests, and referral guides, will both increase the level of knowledge and reduce access to misinformation.

This study is unique in that it is the first research in Türkiye to jointly assess parents' knowledge level, attitudes, and HL regarding pediatric surgical diseases. The study obtained a comprehensive data set using both an objective knowledge test and a HL scale. The questions were prepared based on the most common diseases encountered in clinical practice, ensuring that the findings can be directly reflected in field applications. In addition, the sample structure, which covers different sociodemographic groups, increases the generalizability of the results. The main limitation of our study is that the measurement tools used to assess HL show methodological differences. This makes it difficult to directly compare findings in the literature and generalize the results. In particular, the lack of standardization in terms of content and evaluation of knowledge level questions limits comparative interpretations. The knowledge level questionnaire used in this study was originally developed, and direct comparison with the existing literature is not methodologically appropriate. However, this does not diminish the study's contribution to the field; on the contrary, it provides important data specific to the local health system and parental attitudes. In addition, the fact that the data was collected using a self-reporting method may carry the risk of social desirability bias; in particular, there is a possibility that parents may consciously or unconsciously tend to overstate their level of knowledge. To mitigate this effect, the survey questions were formulated as objective items with clearly defined correct/incorrect answers and were administered anonymously. Additionally, the study was conducted only in family health centers in specific regions. Research using broader and more diverse samples representing different geographical regions would strengthen the generalizability of the findings.

Conclusion

The findings emphasize the necessity of targeted interventions (e.g., simplified educational materials, family physician-pediatric surgeon collaboration, verified content on digital platforms), particularly in groups with low HL and socioeconomic disadvantages. Additionally, it is recommended to expand community-based programs that increase HL to facilitate parents' access to reliable information and ensure their active participation in surgical decision-making processes. These steps will contribute to early diagnosis, appropriate referral, and treatment compliance in pediatric surgery, thereby improving public health outcomes and ensure their active participation in surgical decision-making processes. Structured, systematic education programs, such as school-based initiatives and digital health platforms, could play a key role in achieving these goals.

The integration of HL assessment systems in outpatient settings can enable the early identification of parents' knowledge and understanding levels and the development of appropriate information strategies. Short, standardized HL screening forms integrated into the patient admission process can help to quickly identify risk groups. Thus, parents with low HL can be provided with educational materials about surgical diseases that are more understandable, visually supported, and based on step-by-step explanations. This approach will both improve the quality of clinical communication and strengthen treatment compliance and patient safety.

References

1. Rentea RM, St Peter SD. Pediatric appendicitis. Surg Clin North Am 2017;97:93–112.
2. Nguyen V, Ngo L, Jaqua EE. Cryptorchidism (Undescended Testicle). Am Fam Physician 2023;108(4):378-385.
3. Shabanzadeh DM, Clausen S, Maigaard K, Fode M. Complications of Male Circumcision - A Systematic Review, Meta-Analysis,

and Meta-Regression. Urology 2021;152:25-34.
4. Sørensen K, Pelikan JM, Röthlin F, et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health 2015;25(6):1053-1058.
5. Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low health literacy and health outcomes: an updated systematic review. Ann Intern Med 2011;155(2):97-107.
6. Abacigil Ergin F, Harlak H, Okyay P. Health literacy and related factors among university students. Asia Pac J Public Health 2019;31(3):259–267
7. Pawellek M, Kopf FM, Egger N, Dresch C, Matterne U, Brandstetter S. Pathways linking parental health literacy with health behaviours directed at the child: a scoping review. Health Promot Int 2022;37(2):daab154.
8. Yılmaz SK, Eskici G. Validity and Reliability Study of the Turkish Form of the Health Literacy Scale Short Form and Digital Healthy Diet Literacy Scale. Izmir Katip Celebi Univ Fac Health Sci J 2021;6(3):19-25.
9. Patoulias I, Koutsogiannis E, Panopoulos I, Michou P, Feidantsis T, Patoulias D. Hydrocele in Pediatric Population. Acta Medica (Hradec Kralove) 2020;63(2):57-62.
10. Morrison AK, Myrvik MP, Brousseau DC, Hoffmann RG, Stanley RM. The relationship between parent health literacy and pediatric emergency department utilization: a systematic review. Acad Pediatr 2013;13(5):421-429.
11. Landier M, Villemagne T, Le Touze A, et al. The position of a written document in preoperative information for pediatric surgery: A randomized controlled trial on parental anxiety, knowledge, and satisfaction. J Pediatr Surg 2018;53(3):375-380.
12. Otal D, Wizowski L, Pemberton J, Nagel K, Fitzgerald P, Walton JM. Parent health literacy and satisfaction with plain language education materials in a pediatric surgery outpatient clinic: a pilot study. J Pediatr Surg 2012;47(5):964-969.
13. Yin SH, Dreyer BP, Vivar KL, MacFarland, Schaick L, Mendelsohn AL. Perceived Barriers to Care and Attitudes Towards Shared Decision-making Among Low Socioeconomic Status Parents: Role of Health Literacy. Acad Pediatr 2012;12(2):117–124.
14. Çoşkun N, Demir E. Analysis of YouTube Videos on Circumcision: Assessment of Reliability and Quality for Patients and Parents. Eur J Ther 2024;30(5):626–637.
15. Morrison AK, Glick A, Yin HS. Health Literacy: Implications for Child Health. Pediatr Rev 2019;40(6):263-277.
16. Kampouroglou G, Velonaki VS, Pavlopoulou ID, Fildissis G, Tsoumakas K. Parental health literacy in the pediatric surgical setting. Chirurgia (Bucur) 2019;114:326–330.
17. Olsbø S, Kiserud SG, Hermansen Å, Hamilton Larsen M, Bjørnland K. Health literacy in parents of children with Hirschsprung disease: a novel study. Pediatr Surg Int 2024;41(1):21.
18. Kampouroglou G, Velonaki VS, Pavlopoulou ID, et al. Health literacy of parents/caregivers of paediatric surgical patients: A study on 1000 individuals. Afr J Paediatr Surg 2021;18(2):85-89.
19. Jaensson M, Josefin W, Dahlberg K. Health literacy friendly organizations - A scoping review about promoting health literacy in a surgical setting. Patient Educ Couns 2024;125:108291.
20. Keim Malpass J, Letzkus LC, Kennedy C. Parent/caregiver HL among children with special health care needs: a systematic review of the literature. BMC Pediatr 2015;15:92.
21. Lawrence PR. The relationship of parental HL to medication errors. J Pediatr Health Care 2021;35(2):156-164
22. Reddy AR, Doshi AK, Mak A, et al. Assessing the HL of caregivers in the pediatric intensive care unit: a mixed methods study. Front Pediatr 2023;11:1308673.

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C-reactive Protein as an Early Marker for Postoperative Pancreatic Fistula After Pancreaticoduodenectomy

Pankreatikoduodenektomi Sonrası Gelişen Postoperatif Pankreatik Fistül İçin Erken Bir Belirteç Olarak C-Reaktif Protein

Ahmet Cihangir Emral[1] | **Mustafa Kerem**[2]

[1]Atılım University, Faculty of Medicine, Medicana International Ankara Hospital, Department of General Surgery, Ankara, Türkiye
[2]Gazi University, Faculty of Medicine, Gazi University Training and Research Hospital, Department of General Surgery, Ankara, Türkiye

Sorumlu Yazar | Correspondence Author
Ahmet Cihangir Emral
cihangiremral@hotmail.com
Address for Correspondence: Department of General Surgery, Atılım University Faculty of Medicine, Ankara, Türkiye.

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C-reactive Protein as an Early Marker for Postoperative Pancreatic Fistula After Pancreaticoduodenectomy

ABSTRACT

Objective: Clinically relevant postoperative pancreatic fistula (CR-POPF) remains one of the most serious complications following pancreaticoduodenectomy (PD), leading to increased morbidity and secondary adverse events. Early identification of CR-POPF risk is essential for timely intervention and optimal drain management. This study aimed to evaluate the predictive value of serum C-reactive protein (CRP) levels on postoperative day 3 (POD 3) for the development of CR-POPF.

Material and Method: We retrospectively analyzed 112 patients who underwent PD between March 2020 and February 2025. Patients with distal or total pancreatectomy, neoadjuvant therapy, poorly controlled diabetes, immunosuppression, or anastomotic leaks unrelated to the pancreas were excluded. Serum CRP levels, drain amylase concentration, and drainage volume were recorded on POD 3. CR-POPF was defined according to International Study Group on Pancreatic Surgery (ISGPS) criteria. Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic performance of CRP. Multivariable logistic regression was used to identify independent risk factors for CR-POPF.

Results: CR-POPF occurred in 17 patients (15.2%). These patients had significantly softer pancreatic texture and smaller duct diameters ($p<0.01$). ROC analysis revealed that a POD 3 CRP level >161 mg/L predicted CR-POPF with an area under the curve (AUC) of 0.77, sensitivity of 82.4%, and specificity of 66.3%. Logistic regression identified small duct diameter and soft pancreatic texture as independent predictors of CR-POPF.

Conclusion: Elevated POD 3 serum CRP levels are significantly associated with CR-POPF development after PD. Incorporating CRP into routine postoperative assessment may enhance early risk stratification, support clinical decision-making, and guide individualized drain management strategies.

Keywords: C-Reactive Protein, Drain management, Postoperative Pancreatic Fistula, Pancreaticoduodenectomy.

ÖZET

Amaç: Pankreatikoduodenektomi (PD) sonrası gelişen klinik olarak anlamlı postoperatif pankreatik fistül (CR-POPF), cerrahi sonrası morbiditenin en önemli nedenlerinden biri olup, sekonder komplikasyonlara da zemin hazırlamaktadır. CR-POPF'nin erken dönemde tanınması, zamanında müdahale ve uygun dren yönetimi açısından kritik öneme sahiptir. Bu çalışmanın amacı, postoperatif 3. gün (POD 3) serum C-reaktif protein (CRP) düzeylerinin CR-POPF gelişimini öngörmedeki değerini değerlendirmektir.

Gereç ve Yöntem: Mart 2020 ile Şubat 2025 arasında merkezimizde PD uygulanan 112 hasta retrospektif olarak analiz edildi. Total veya distal pankreatektomi yapılanlar, neoadjuvan tedavi alanlar, kontrolsüz diyabeti olanlar, immünsüprese hastalar ve pankreas dışı anastomoz kaçağı gelişenler çalışma dışı bırakıldı. Postoperatif 3. gün serum CRP düzeyleri, dren amilaz konsantrasyonu ve drenaj hacmi kaydedildi. CR-POPF, Uluslararası Pankreas Cerrahisi Çalışma Grubu (ISGPS) kriterlerine göre tanımlandı. ROC eğrisi analizi ile CRP düzeylerinin tanısal performansı değerlendirildi. Ayrıca, çok değişkenli lojistik regresyon analizi ile CR-POPF için bağımsız risk faktörleri belirlendi.

Bulgular: CR-POPF, 17 hastada (%15,2) gelişti. Bu hastalarda pankreas duktus çapı anlamlı şekilde daha dar ve doku yapısı daha yumuşaktı ($p<0,01$). ROC analizinde, POD 3 CRP düzeyi >161 mg/L olan hastalarda CR-POPF gelişimini öngörmede AUC 0,77, sensitivite %82,4 ve spesifisite %66,3 olarak bulundu. Lojistik regresyon analizinde, dar pankreatik duktus çapı ve yumuşak pankreas dokusu CR-POPF için bağımsız risk faktörleri olarak saptandı.

Sonuç: Pankreatikoduodenektomi sonrası 3. gün serum CRP düzeylerinin yüksek olması, CR-POPF gelişimini öngörmede anlamlı bir belirteçtir. CRP düzeylerinin rutin postoperatif değerlendirmeye dahil edilmesi, erken risk sınıflamasını kolaylaştırarak hasta yönetimi ve dren çekilme zamanlamasında klinik karar sürecine katkı sağlayabilir.

Anahtar Sözcükler: C-Reaktif Protein, Dren yönetimi, Postoperatif Pankreatik Fistül, Pankreatikoduodenektomi.

Introduction

Advancements in pancreatic surgery and perioperative management have significantly reduced postoperative morbidity and mortality. However, clinically relevant postoperative pancreatic fistula (CR-POPF) remains a common and serious complication that may also predispose patients to other postoperative adverse events (1,2). Consequently, numerous methods have been investigated to predict POPF in advance, and various risk factors have been identified (3–6).

Drain management plays a critical role in pancreatic surgery, both in preventing postoperative complications and enhancing patient recovery. Accurate prediction of CR-POPF allows for better decision-making regarding the duration of drain placement. Early drain removal in low-risk patients and prolonged drainage in high-risk cases are key strategies that directly affect clinical outcomes. Prolonged drainage beyond necessity has been associated with increased risk of complications. In clinical practice, drain removal is generally performed based on the surgeon's assessment, once the risk of POPF is deemed minimal. Therefore, early prediction of POPF is crucial for optimizing the timing of drain removal, which can accelerate recovery and facilitate earlier hospital discharge (7,8).

Complications associated with POPF include intra-abdominal abscess, delayed gastric emptying, hemorrhage, sepsis, and mortality. Early diagnosis of POPF enables timely interventions such as antibiotic therapy or initiation of parenteral nutrition, before clinical deterioration occurs. Furthermore, in patients who do not develop POPF, early transition to enteral feeding may contribute to improved recovery (3,9).

C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver. It begins to rise approximately six hours after the onset of inflammation, peaks around 48 hours, and—due to its relatively constant plasma half-life of approximately 19 hours—typically begins to decline by the third postoperative day in the absence of ongoing inflammatory stimuli (10,11). In recent years, CRP has been studied extensively for its predictive value in detecting anastomotic leakage following colorectal surgery and infectious complications after major abdominal operations (12,13). These findings have led to increasing interest in the potential role of CRP as a predictive marker for the development of CR-POPF after pancreatic resections (14–16).

The aim of this study was to evaluate the predictive value of serum C-reactive protein (CRP) levels on postoperative day 3 (POD 3) for the development of CR-POPF in patients undergoing pancreaticoduodenectomy (PD).

Material and Method

Patients who underwent pancreaticoduodenectomy (PD) at our institution between March 2020 and February 2025 were retrospectively analyzed using prospectively collected clinical data. Patients aged 18 to 75 years who underwent PD were included in the study. Approval of the study was obtained from the Ethics Committee of Medicana International Ankara Hospital (Decision no: 2023/43, Date: 14.12.2023), and the study was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective design of the study.

Exclusion criteria were as follows: patients who underwent total or distal pancreatectomy, those with unresectable tumors, immunosuppressed individuals, patients with a history of chronic steroid use or rheumatologic disease, those who received neoadjuvant therapy, patients with poorly controlled diabetes mellitus (HbA1c >10), and those who developed biliary or intestinal anastomotic leaks. CR-POPF was defined according to the criteria established by the International Study Group on Pancreatic Surgery (ISGPS) (17). All surgical procedures were performed by a single hepatobiliary surgeon (M.K.) with over 20 years of experience. A 10-mm flat silicone drain was routinely placed posterior to the pancreatojejunostomy. POD 1 was defined as the first 24-hour period following completion of surgery. Drain amylase levels were measured on postoperative days (POD) 1 and 3, and thereafter as clinically indicated. On POD 3, serum CRP levels (mg/L), drain amylase levels (U/L), drainage volume (mL), and drain fluid appearance (e.g., serous, pancreatic leak, biliary leak, or intestinal leak) were routinely assessed. The reference range for serum CRP levels in our institution is 0–5 mg/L. Octreotide was not used in either the preoperative or postoperative period. Preoperative

biliary drainage was not routinely performed.

Drain removal on POD 3 was considered for patients whose drain amylase concentrations and drainage volumes were below institutional threshold values, whose drain output was serous, who had stable vital signs, and who tolerated oral intake (18). In patients deemed to be at high risk for CR-POPF on POD 3, reassessment was performed on POD 5, and drains were removed if appropriate. Patients clinically suspected of having CR-POPF were further evaluated with close vital sign monitoring and radiological imaging (abdominal ultrasonography or computed tomography). However, the final decision regarding drain removal was made by the operating surgeon based on an overall clinical assessment, which included intraoperative findings, postoperative course, and patient-specific factors. As such, some degree of subjectivity may have influenced the timing of drain removal, especially in borderline cases with inconclusive clinical parameters.

In cases of sudden reduction or cessation of drainage, 10 mL of sterile saline was used to irrigate the drain in order to exclude mechanical obstruction. All patients received intravenous (or oral, if tolerated) antibiotic therapy consisting of ceftriaxone (2 × 1000 mg/day) and metronidazole (3 × 500 mg/day) for five days postoperatively.

Demographic data and postoperative complications—including CR-POPF, hemorrhage, intra-abdominal infection or abscess, and delayed gastric emptying (DGE) were recorded. Postoperative complications were classified according to ISGPS criteria (19–21).

Statistical Analysis

Statistical analysis was performed using SPSS version 27 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed by Skewness and Kurtosis tests. Normally distributed data are presented as mean ± standard deviation (SD), while non-normally distributed data are expressed as median (min-max). Categorical variables are reported as counts and percentages. Group comparisons were performed using the independent-samples t-test, the Mann–Whitney U test, or the chi-square test, as appropriate.

For ROC analysis, the development of CR-POPF was defined as the primary endpoint. Areas under the receiver operating characteristic (ROC) curve were calculated to evaluate CRP levels as predictors of POPF. ROC analysis was conducted based on patients' CRP values on the POD 3. The results of the ROC analysis, including sensitivity and 1-specificity values, were examined, and CRP values with the highest sensitivity and specificity were selected as cut-off points. Finally, the Area Under the Curve (AUC) and p-values were compared.

Multivariable logistic regression analysis was conducted to identify factors associated with the development of pancreatic fistula. The dependent variable was the presence of pancreatic fistula (yes/no), and the independent variables included age, gender, BMI, pancreatic duct diameter (mm), pancreatic texture (soft/hard), vascular repair, and pathology(benign/malign). The significance of each variable in the model was assessed using the Wald test, with a p-value < 0.05 considered statistically significant.

Results

A total of 112 patients who met the inclusion criteria were enrolled in the study, comprising 70 males and 42 females. Postoperative complications occurred in 24 patients (21.4%). The most frequent complication was clinically relevant postoperative pancreatic fistula (CR-POPF), observed in 17 patients (15.2%), followed by intra-abdominal infection in 9 patients (8.0%), postoperative bleeding in 8 patients (7.1%), and delayed gastric emptying in 6 patients (5.4%). Notably, some patients experienced more than one type of complication. Early postoperative mortality occurred in two patients due to Grade C postoperative pancreatic fistula.

Patients who developed CR-POPF had significantly smaller pancreatic duct diameters and softer pancreatic texture ($p<0.01$ for both). No significant differences were found between the groups regarding age, body mass index (BMI), gender distribution, vascular reconstruction frequency, or pathological diagnosis ($p>0.05$ for all). A detailed comparison of clinical and demographic characteristics between patients with and without CR-POPF is shown in Table I.

Multivariate logistic regression analysis identifying independent predictors of clinically relevant

postoperative pancreatic fistula (CR-POPF) is presented in Table II. Among the variables included in the model, CRP level on postoperative day 3, pancreatic duct diameter, and pancreatic texture were found to be statistically significant independent predictors. Specifically, each 1 mg/L increase in CRP level on POD 3 was associated with a 2% increase in the odds of developing CR-POPF (OR=1.02; 95% CI, 1.01–1.03; *p=0.002*). Additionally, a 1 mm increase in pancreatic duct diameter was associated with a 64% reduction in the odds of CR-POPF (OR = 0.36; 95% CI, 0.19–0.71; *p=0.003*). The presence of hard pancreatic texture also significantly decreased the risk compared to soft texture (OR = 0.25; 95% CI, 0.06–0.92; *p=0.04*). Other variables assessed in the model—including age, gender, BMI, vascular reconstruction, and pathology type—were not significantly associated with the occurrence of CR-POPF (p>0.05 for all).

Table I. Comparison of Clinical and Demographic Variables Between Patients with and Without CR-POPF

Variable	CR-POPF (n = 17)	Non-POPF (n = 95)	*p-value*
Age (years)	66.4±9.9	62.7±12.4	*0.3*
Gender, n (%) Female Male	 5 (29.4%) 12 (70.6%)	 37 (38.9%) 58 (61.1%)	*0.4*
Body Mass Index (BMI, (kg/m^2))	26.9±4.4	27.4±3.9	*0.6*
Pancreatic texture, n (%) Soft Hard	 11(64.7%) 6 (35.3%)	 18 (18.9%) 77 (81.1%)	*<0.01*
Pancreatic duct diameter (mm)	3.4±1.1	4.6±1.7	*<0.01*
Vascular Reconstruction, n (%)	3 (17.6%)	21 (22.1%)	*0.7*
Pathology, n (%) Benign Malign	 2 (11.8%) 15 (88.2%)	 12 (12.6%) 83 (87.4%)	*0.9*

*Values are presented as mean ± standard deviation or number (percentage), as appropriate.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of C-reactive protein (CRP) levels on postoperative day 3 (POD 3 CRP) for clinically relevant postoperative pancreatic fistula (CR-POPF). The analysis demonstrated good diagnostic accuracy, with an area under the curve (AUC) of 0.777 (95% CI: 0.680–0.874; *p<0.001*). A CRP cut-off value of 161 mg/L yielded a sensitivity of 82.4% and a specificity of 66.3% in identifying patients at risk for CR-POPF. The ROC curve for POD 3 CRP levels is illustrated in Figure I.

Table II. Multivariate Logistic Regression Analysis for Predictors of CR-POPF

Variable	B (SE)	Wald	p-value	OR (Exp(B)) [95% CI]
Age	0.04 (0.03)	1.81	*0.18*	1.05 [0.98–1.11]
Gender	0.86 (0.74)	1.36	*0.24*	2.36 [0.56–10.06]
BMI	0.00 (0.09)	0.00	*0.99*	1 [0.84–1.19]
Pancreatic Duct Diameter	–1.01 (0.34)	8.93	*0.003*	0.36 [0.19–0.71]
Pancreatic Texture	-1.38 (0.66)	4.35	*0.04*	0.25 [0.06–0.92]
Vascular Reconstruction	0.50 (0.90)	0.31	*0.58*	1.64 [0.28–9.52]
Pathology	1.42 (0.97)	1.37	*0.24*	4.15 [0.38–45.16]
CRP (POD 3, mg/L)	0.02 (0.01)	9.56	*0.002*	1.02 [1.01–1.03]

*OR = odds ratio; CI = confidence interval; SE = standard error

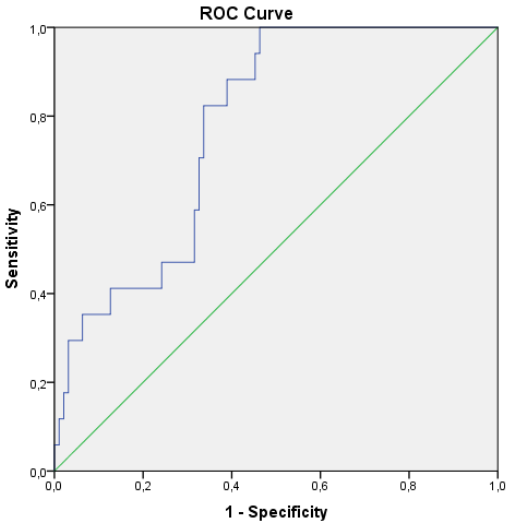

Figure I. Receiver operating characteristic (ROC) curve of postoperative day 3 CRP levels for predicting CR-POPF. The area under the curve (AUC) was 0.777 (95% CI: 0.680–0.874), indicating good diagnostic accuracy

Discussion

In pancreatic surgery, the most significant complication is the development of CR-POPF. This condition not only increases morbidity due to primary effects such as peritonitis, but also predisposes patients to secondary complications, including hemorrhage and intra-abdominal infections (22). To date, there is no perfect test that can predict CR-POPF with 100% accuracy. We believe that the

most critical factor in this context is the experience of the hepatopancreatobiliary (HPB) surgeon.

An experienced pancreatic surgeon evaluates the patient holistically taking into account preoperative factors such as malnutrition, receipt of neoadjuvant therapy, or comorbidities; intraoperative findings including pancreatic texture (soft vs. hard) and the diameter of the pancreatic duct; as well as postoperative indicators such as vital signs, laboratory results, drain amylase concentration, drainage volume, and the appearance of the drain fluid. Such a comprehensive and integrative approach is essential for optimal management and early identification of CR-POPF risk.

Bassi et al. (8) identified soft pancreatic texture, delayed drain removal, median albumin and serum amylase levels on postoperative day (POD) 1, and preoperative weight loss greater than 10% as risk factors for CR-POPF. In contrast, Kawai et al. (7) reported that intraoperative bleeding, longer operative time, and early drain removal were significant risk factors, suggesting that neither preoperative factors nor pancreatic tissue characteristics reliably predicted POPF risk. According to this study, a small pancreatic duct diameter and soft pancreatic texture were also identified as significant risk factors for CR-POPF in our clinic. Therefore, we believe that pancreatic surgeons should consider institution-specific risk profiles when managing their patients postoperatively.

Guilbaud et al. (14) reported that a CRP level >100 mg/L on POD 1 was predictive of CR-POPF with an AUC of 0.70. Welsch et al. (22) showed that a POD 4 CRP level >140 mg/L predicted inflammatory postoperative complications with an AUC of 0.86. Hashimoto et al. (4) demonstrated that a CRP level <150 mg/L on POD 3, when combined with drain amylase values, improved the prediction of POPF. Mintziras et al. (23) identified a CRP level >203 mg/L on POD 3 as an independent risk factor for CR-POPF. In this study, a CRP level >161 mg/L on POD 3 was found to be a significant risk factor for CR-POPF, with an AUC of 0.77. Although the cutoff values vary slightly across studies, these thresholds may assist in the early identification of patients at higher risk for CR-POPF.

However, when applying such cutoffs in clinical practice, the potential trade-off between missed diagnoses and false positives must be carefully considered. Although the proposed CRP cut-off value (>161 mg/L on POD 3) demonstrated good predictive performance, it is essential to reflect on the clinical implications of false-positive and false-negative results. For instance, patients with elevated CRP levels who do not develop CR-POPF may be subjected to unnecessarily prolonged drain placement. This, in turn, may increase the risk of intra-abdominal infections due to retrograde contamination or irritation from the drain itself. Additionally, false-positive interpretations could lead to unnecessary imaging studies, delays in initiating oral intake, and prolonged hospital stay (8,24). Conversely, false-negative cases—patients with CRP levels below the cut-off who still develop clinically relevant fistulas—also warrant caution. These cases highlight the limitations of relying solely on a single laboratory parameter and underscore the importance of comprehensive clinical evaluation. Therefore, we believe that HPB surgeons should not base postoperative decisions solely on CRP values but rather integrate them with clinical judgment, intraoperative findings, and institutional experience for individualized drain management.

HPB surgeons must evaluate all relevant risk factors when assessing CR-POPF risk. Among these, the most used conventional method is measuring the drain amylase concentration. However, in certain clinical scenarios—such as patients with ascites, chylous drainage due to extensive lymphadenectomy, those who have undergone vascular procedures, or in cases where the abdomen has been irrigated with saline—the drain amylase concentration may be misleadingly low. Similarly, obstructed drains may yield falsely low drainage volumes, or the fluid collection may not be adequately captured if it forms away from the drain site. Therefore, the use of an objective laboratory parameter like CRP may provide additional guidance to HPB surgeons. From this perspective, this study showed that CRP levels on POD 3, an increasingly recognized inflammatory marker, were significantly associated with the development of POPF and could support HPB surgeons in early risk assessment and postoperative decision-making. In patients in whom drain amylase levels fail to predict CR-POPF,

elevated CRP levels exceeding the defined cutoff may warrant further evaluation with non-invasive and cost-effective imaging modalities such as ultrasonography, potentially revealing clinically silent CR-POPF that would otherwise remain undetected. Recent studies have underscored the advantages of early drain removal in low-risk patients undergoing pancreatic surgery (24,25). Early identification of CR-POPF allows timely intervention before the complication progresses to more severe outcomes. Therefore, accurate recognition of low-risk patients is critical for safe early drain removal, and we believe that serum CRP levels constitute a valuable element of this risk stratification process and should not be overlooked.

One of the main limitations of this study, in addition to its retrospective design, is the relatively low number of patients with CR-POPF. Moreover, serum CRP levels may also be elevated due to non-pancreas-specific infectious or inflammatory conditions, such as respiratory tract infections or urinary tract infections. Therefore, such confounding factors should be taken into account when interpreting CRP values in the postoperative setting.

Conclusion

In patients undergoing PD, POD 3 serum CRP levels represent a strong early indicator of CR-POPF risk and should be adopted as a routine part of postoperative decision-making for patient and drain management.

References

1. Serene TEL, G SV, Padmakumar JS et al. Predictive value of post-operative drain amylase levels for post-operative pancreatic fistula. Ann Hepatobiliary Pancreat Surg 2018;22(4):397-404.
2. Büchler MW, Friess H, Wagner M, et al. Pancreatic fistula after pancreatic head resection. Br J Surg 2000;87: 883-889.
3. Liu Y, Li Y, Wang L, et al. Predictive value of drain pancreatic amylase concentration for postoperative pancreatic fistula on postoperative day 1 after pancreatic resection: An updated meta-analysis. Medicine (Baltimore) 2018;97(38):e12487.
4. Hashimoto D, Satoi S, Yamamoto T, et al. Validation of the triple-checked criteria for drain management after pancreatectomy. J Hepatobiliary Pancreat Sci 2022;29(2):271-281.
5. Koek S, Wiegele S, Ballal M. Drain fluid amylase and lipase as a predictive factor of postoperative pancreatic fistula. ANZ J Surg. 2022;92(3):414-418.
6. Callery MP, Pratt WB, Kent TS, et al. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg 2013;216(1):1-14.
7. Kawai M, Tani M, Terasawa H et al. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. Ann Surg 2006;244(1):1-7.
8. Bassi C, Molinari E, Malleo G, et al. Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. Ann Surg 2010;252(2):207-214.
9. Yang J, Huang Q, Wang C. Postoperative drain amylase predicts pancreatic fistula in pancreatic surgery: A systematic review and meta-analysis. Int J Surg 2015;22:38-45.
10. Rajab IM, Hart PC, Potempa LA. How C-Reactive Protein Structural Isoforms With Distinctive Bioactivities Affect Disease Progression. Front Immunol 2020;11:2126.
11. Sproston NR, Ashworth JJ. Role of C-Reactive Protein at Sites of Inflammation and Infection. Front Immunol 2018;9:754.
12. Singh PP, Zeng IS, Srinivasa S, et al. Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. Br J Surg 2014;101(4):339-346.
13. Ortega-Deballon P, Facy O, Rat P. C-reactive protein to rule out infections after major abdominal surgery. Int J Colorectal Dis 2016;31(3):779-780.
14. Guilbaud T, Birnbaum DJ, Lemoine C, et al. C-Reactive Protein on Postoperative Day 1 Is a Reliable Predictor of Pancreas-Specific Complications After Pancreaticoduodenectomy. J Gastrointest Surg 2018;22(5):818-830.
15. Ma J, Jiang P, Ji B, et al. Post-operative procalcitonin and C-reactive protein predict pancreatic fistula after laparoscopic pancreatoduodenectomy. BMC Surg 2021;21(1):171.
16. Chen G, Yi H, Zhang J. Diagnostic value of C-reactive protein and procalcitonin for postoperative pancreatic fistula following pancreatoduodenectomy: a systematic review and meta-analysis. Gland Surg 2021;10(12):3252-3263.
17. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery 2017;161(3):584-591.
18. Emral AC, Çetinkaya G, Dikmen K, Kerem M. The Predictive Effect of "Real Amylase Value": A More Accurate Predictor for Postoperative Pancreatic Fistula. ANZ J Surg. 2025;doi.org/10.1111/ans.70276
19. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the

International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007;142(5):761-768.
20. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery 2007;142(1):20-25.
21. Nebbia M, Capretti G, Nappo G, Zerbi A. Updates in the management of postoperative pancreatic fistula. Int J Surg 2024;110(10):6135-6144.
22. Welsch T, Frommhold K, Hinz U, et al. Persisting elevation of C-reactive protein after pancreatic resections can indicate developing inflammatory complications. Surgery 2008;143(1):20-28.
23. Mintziras I, Maurer E, Kanngiesser V, Bartsch DK. C-reactive protein and drain amylase accurately predict clinically relevant pancreatic fistula after partial pancreaticoduodenectomy. Int J Surg 2020;76:53-58.
24. Wu AGR, Mohan R, Fong KY, et al. Early vs late drain removal after pancreatic resection-a systematic review and meta-analysis. Langenbecks Arch Surg 2023;408(1):317.
25. Zhu S, Yin M, Xu W, et al. Early Drain Removal Versus Routine Drain Removal After Pancreaticoduodenectomy and/or Distal Pancreatectomy: A Meta-Analysis and Systematic Review. Dig Dis Sci 2024;69(9):3450-3465.

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Validity and Reliability of the Turkish Version of the Glucose Monitoring Satisfaction Survey

Glukoz İzleme Memnuniyet Anketi'nin Türkçe Versiyonunun Geçerlilik ve Güvenilirlik Çalışması

Tuğba Bilgehan[1] | İsmail Toygar[2]

[1]Ankara Yıldırım Beyazıt University, Faculty of Health Sciences, Department of Internal Medicine Nursing, Ankara, Türkiye
[2]Muğla Sıtkı Koçman University, Fethiye Faculty of Health Sciences, Muğla, Türkiye

Sorumlu Yazar | Correspondence Author
Tuğba Bilgehan
tgb.bilgehan@gmail.com
Address for Correspondence: Ankara Yıldırım Beyazıt University, Faculty of Health Sciences, B Block, 2nd Floor, Esenboğa, Ankara, Türkiye

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Validity and Reliability of the Turkish Version of the Glucose Monitoring Satisfaction Survey

ABSTRACT

Objective: The Glucose Monitoring Satisfaction Survey (GMSS) is crucial for assessing diabetes management, but its psychometric properties in Turkish patients remain unexplored. This study aimed to evaluate the validity and reliability of the Turkish version of the GMSS.

Material and Method: This methodological, descriptive, and correlational study was conducted with 220 patients with type 1 diabetes between October 2023 and February 2024. Data were collected online using a sociodemographic questionnaire, the GMSS, and the WHO-5 Well-Being Index. Statistical analyses were performed with IBM SPSS v27 and IBM SPSS Amos v24. Reliability was evaluated with Cronbach's alpha coefficients for the overall scale and each subscale, Spearman-Brown Split-Half analysis, item–total correlations, and "Cronbach's alpha if item deleted." Validity was examined through language validity, expert-based content validity, and construct validity using Confirmatory Factor Analysis (CFA). Assumptions for CFA were checked, and the maximum likelihood method was applied. Parallel form reliability was also assessed with WHO-5.

Results: Item-level content validity indexes ranged between 0.80 and 1.00, while the scale-level index was 0.960. Cronbach's alpha was 0.897 for the overall scale and ranged between 0.85 and 0.90 across the four subscales. Item–total correlations varied from 0.347 to 0.719, and "alpha if item deleted" values remained above 0.85. The Spearman-Brown Split-Half coefficient was 0.885. CFA supported the four-factor model with acceptable fit indices. Parallel form reliability showed significant positive correlations between the GMSS and WHO-5 ($p<0.001$).

Conclusion: The Turkish version of the GMSS demonstrated strong validity and reliability for assessing satisfaction with glucose monitoring in type 1 diabetes patients. However, the predominance of female participants (72.7%) may limit the generalizability of the findings and should be considered in future research.

Keywords: Blood glucose monitoring, Patient satisfaction, Reliability, Type 1 Diabetes, Validity.

ÖZET

Amaç: Glukoz İzleme Memnuniyet Anketi, diyabet yönetimini değerlendirmek için önemli bir araçtır, ancak Türk hastalardaki geçerliliği ve güvenilirliği henüz araştırılmamıştır. Bu çalışma, Glukoz İzleme Memnuniyet Anketi'nin Türkçe versiyonunun geçerliliğini ve güvenilirliğini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Bu metodolojik, tanımlayıcı ve korelasyonel çalışma, Ekim 2023 ile Şubat 2024 arasında, Tip 1 Diyabet tanısı almış 220 hasta ile gerçekleştirilmiştir. Çalışma verileri, Anket Formu, Glukoz İzleme Memnuniyet Anketi ve DSÖ-5 İyi Oluş İndeksi kullanılarak çevrimiçi anket tekniği ile toplanmıştır. İstatistiksel analizler IBM SPSS v27 ve IBM SPSS Amos v24 kullanılarak yapılmıştır. Güvenirlik analizlerinde ölçeğin tümü ve dört alt boyutu için Cronbach alfa katsayıları, madde-toplam korelasyonları, "madde silindiğinde Cronbach alfa" değerleri ve Spearman-Brown Split-Half analizi incelenmiştir. Yapı geçerliliği, Doğrulayıcı Faktör Analizi (DFA) ile test edilmiş, varsayımlar kontrol edilmiştir ve maksimum olabilirlik yöntemi kullanılmıştır. Ayrıca, DSÖ-5 İyi Oluş İndeksi ile paralel form güvenirliği değerlendirilmiştir.

Bulgular: Madde düzeyindeki içerik geçerliliği indeksleri 0.80 ile 1 arasında değişirken, ölçek düzeyindeki içerik geçerliliği indeksi 0.960 bulunmuştur. Ölçeğin Cronbach alfa katsayısı 0,897, alt boyutlar için ise 0,85 ile 0,90 arasında hesaplanmıştır. Madde-ölçek korelasyonları 0,347 ile 0,719 arasında değişmiştir ve "madde silindiğinde alfa" değerleri 0,85'in üzerinde kalmıştır. Spearman-Brown Split-Half analizinde ölçeğin iki yarısı arasında yüksek düzeyde pozitif yönlü bir korelasyon (0,885) bulunmuştur. DFA, dört faktörlü yapıyı doğrulamış ve uyum indeksleri kabul edilebilir düzeyde bulunmuştur. DSÖ-5 İndeksi ile hem ölçek hem de tüm alt boyutları arasında istatistiksel olarak anlamlı pozitif korelasyonlar gözlemlenmiştir ($p<0,001$).

Sonuç: Bu çalışma, Glukoz İzleme Memnuniyet Anketi'nin, Türk toplumunda Tip 1 Diyabet hastalarında glukoz izleme memnuniyetini ölçmek için geçerli ve güvenilir bir araç olduğunu göstermektedir. Ancak, katılımcıların çoğunluğunu kadınların (%72,7) oluşturması, sonuçların genellenebilirliğini sınırlayabilir. Bu durum, gelecekteki araştırmalarda dikkate alınmalıdır.

Anahtar Sözcükler: Geçerlilik, Güvenilirlik, Kan glukoz izleme, Memnuniyet, Tip 1 diyabet.

Introduction

Diabetes stands among the four non-communicable diseases (NCDs) highlighted by the World Health Organization (1). Type 1 diabetes (T1D) makes up about 5–10% of the global diabetes prevalence (2). The condition is characterized by autoimmune degeneration of β-cells in the pancreatic islets, resulting in severe insulin depletion (3). Monitoring glycemic status is widely acknowledged as fundamental in diabetes management; accordingly, glucose monitoring is deemed the key to achieving optimal glycemic targets (4).

The American Diabetes Association (ADA) recommends that individuals on intensive insulin therapy, which includes multiple dose insulin (MDI) or continuous subcutaneous insulin infusion (CSII), self-monitor blood glucose (SMBG) before meals and snacks, intermittently after meals, at bedtime, before physical activity, when hypoglycemia is suspected, after treatment for hypoglycemia, and before performing critical activities such as driving. For some people, this requires testing six to 10 times a day (or more) (5). Similar recommendations have been made by other organizations as well (6,7).

For individuals diagnosed with T1D, regular glucose testing is imperative for the safe and efficient management of blood glucose levels (3). These individuals commonly utilize either SMBG through fingersticks and a glucose meter or opt for continuous glucose monitoring (CGM) methods to monitor their glucose levels (8, 9, 10). CGM is a minimally invasive method for tracking blood glucose levels. CGM records glucose levels constantly, in contrast to SMBG, which offers intermittent measurements of glucose levels. There exist three categories of continuous glucose monitoring systems: professional CGM (P-CGM), real-time CGM (RT-CGM), and intermittent scanned CGM (isCGM). Each system possesses distinct qualities (9-11).

Self-monitoring of blood glucose and CGM each present notable drawbacks that affect their usability and effectiveness. SMBG requires frequent finger pricks, which many patients find painful and inconvenient, leading to poor adherence (12,13). While less invasive, CGM can still cause discomfort due to sensor insertion and the need for regular calibration (14,15). Recent technological advances in CGM have been met with concerns regarding their impact on user satisfaction and the occurrence of adverse events when compared with the more established SMBG method. Intermittently scanned isCGM has been shown to enhance satisfaction rates while concurrently exhibiting adverse effects (12). A significant impediment to the widespread adoption of these technologies is their financial burden; CGM devices, in particular, are deemed excessively costly for a substantial proportion of the population, thereby impeding accessibility and adherence (16). Additionally, technical and interference issues can affect the accuracy of both methods. SMBG readings may be influenced by substances such as ascorbic acid, while CGM, despite its continuous monitoring capabilities, can suffer from technical limitations that occasionally necessitate SMBG confirmation (15,17).

Adherence to glucose monitoring systems remains a critical challenge in the management of diabetes. Research findings indicate that adherence rates for SMBG are below 50%, with time constraints, forgetfulness, and self-consciousness being identified as key barriers (13,18). Several factors influence adherence levels: higher education, ownership of a glucose meter, and specific treatment regimens, such as oral hypoglycemic drugs, correlate with better adherence (18,19). For CGM, patients' readiness for behavior change has been identified as a significant determinant of adherence (20). Intervention strategies conceived with the intention of enhancing adherence have demonstrated efficacy. Educational and motivational approaches, including cognitive behavioral therapy and motivational interviewing, have been shown to be effective in improving adherence to SMBG. Similarly, lifestyle and behavioral counseling have been found to enhance adherence to CGM and improve glycemic outcomes (20). Addressing these multifaceted barriers through tailored interventions is imperative to optimize the effectiveness of both SMBG and CGM systems in diabetes care (14).

Patient satisfaction with blood glucose monitoring systems is critical in adherence to diabetes management protocols. Research has demonstrated that elevated satisfaction with blood glucose monitoring systems is associated with superior adherence to medication and self-monitoring routines among patients with

diabetes (21-23). Conversely, individuals utilizing CGM may encounter various forms of dissatisfaction, including sensitivities to the device, such as local skin reactions, concerns about body image, feelings of being different from others, discomfort, and unpredictable errors (7,24,25). Consequently, it is imperative to closely monitor patients' satisfaction with the blood glucose monitoring system.

The Glucose Monitoring Satisfaction Survey (GMSS) was developed by Polonsky et al. (2015) (26). The Chinese version of the survey was constructed by Lu et al. (2020) (27). Studies evaluating the GMSS in individuals with diabetes are available in the literature (28-31). However, no Turkish validity and reliability study has yet been conducted. To date, there is no instrument for measuring glucose monitoring satisfaction among Turkish patients with type 1 diabetes. Therefore, this study aimed to investigate the validity and reliability of the Glucose Monitoring Satisfaction Survey within Turkish society.

Material and Method

Study Design and Settings

The study investigated the validity and reliability of the Glucose Monitoring Satisfaction Survey for Turkish society. The study was conducted using snowball sampling between October 2023 and February 2024. The survey link was disseminated to patients using social media platforms, including WhatsApp and Instagram. To conduct the study, permission was obtained from the Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (Research code: 2023-362, Approval number: 362-08). Participants provided their informed consent online after reviewing the study's aim, content, and data privacy principles. The research adhered to the principles of the Helsinki Declaration. Additionally, written permission was obtained from the original scale developer via email.

Sample

A power analysis was conducted to ascertain the minimal sample size necessary for the investigation, utilizing the anticipated Cronbach's alpha. The expected Cronbach's alpha was 0.80, and the analysis was conducted under the following conditions: 95% confidence interval, type 1 error 0.05, 15-item scale, and an expected dropout rate of 10%. Under the above conditions, the minimum required sample size was found to be 153. The recommendations of Bonett were followed for the calculation of the sample size (32, 33). The study was terminated after recruiting 220 participants.

Inclusion and Exclusion Criteria

The study population comprised individuals aged 18 years or older who had been diagnosed with type 1 diabetes mellitus for a minimum of one year before the study's commencement to assess their satisfaction with the glucose monitoring system after a sustained period of use. The study participants were required to be able to communicate in Turkish, to have owned and consistently utilized a primary blood glucose meter for a minimum period of three months (at least once a week), and to have been willing to participate in the study. Patients were expected to utilize the glucose meter at least once per week to evaluate their satisfaction with the device. All of these conditions were confirmed through questions presented to the participants at the beginning of the online survey, where their consent was obtained.

Data Collection

The Questionnaire Form, the Glucose Monitoring Satisfaction Survey (GMSS), and the WHO-5 Well-Being Index were used for data collection. Data were gathered using an online survey. The research adhered to the standards for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

Questionnaire Form

The researchers created this form based on relevant literature. It comprises 11 items that investigate the sociodemographic and disease-related characteristics of the patients. The sociodemographic characteristics encompassed age, gender, marital status, education level, and working status. The disease-related characteristics included comorbidities, disease duration, glucose monitoring system, HbA1c level, satisfaction with the glucose monitoring system, and opinions on the usability of the glucose monitoring system (26, 27, 30).

Glucose Monitoring Satisfaction Survey (GMSS)

Polonsky et al. developed the scale. The scale comprises 15 items and 4 factors: Openness, Emotional Burden, Behavioral Burden, and Trust. Items are answered on a 5-point Likert scale ranging from strongly disagree to strongly agree. For 11 items, reverse responses were used to calculate the total score. The scale ranged in total score from 15 to 75. Higher scores indicate higher levels of Glucose Monitoring System Satisfaction. The scale has a Cronbach's alpha value of 0.86 (26).

WHO-5 Well-being Index

The scale is a short measure of well-being, consisting of five items. The total score ranges from 0 to 100, with each item scored between 0 (never) and 5 (always). To calculate the total score, multiply the sum of the five items by four. The scale was used in a parallel form in the current study. Cronbach's alpha value of the Turkish version was 0.83 (34).

Validity of the Turkish Version of GMSS

Language Validity

Forward and backward translations were utilized. Two independent experts, both native Turkish speakers with proficiency in English, conducted the translation process. These experts were affiliated with academic institutions in the field of health sciences. One translator was informed about the study objectives, while the other was instructed to translate naturally without bias (37). The back-translation was performed by two native English speakers proficient in Turkish but not involved in the initial translation. No semantic differences were found.

Content Validity

The content validity was assessed using the Davis method. Ten experts scored each item on a 4-point scale. The item-level content validity indexes (I-CVI) and scale-level CVI (S-CVI) were calculated. Following Lawshe's criteria, CVR ≥0.50 was considered acceptable (40, 41).

Construct Validity

Confirmatory factor analysis (CFA) was performed to test the original four-factor structure. Before CFA, assumptions such as multivariate normality, sample adequacy, and absence of multicollinearity were checked. The maximum likelihood estimation method was preferred, as the data met normality assumptions. Model fit indices ($\chi 2$, SRMR, GFI, AGFI, CFI, RMSEA) were used to evaluate the model (42, 43). Additionally, convergent validity was examined using composite reliability (CR) and average variance extracted (AVE).

Reliability of the Turkish Version of GMSS

Cronbach's Alpha

Cronbach's alpha coefficients were calculated for the overall scale and each subscale. Item–total correlations and "Cronbach's alpha if item deleted" were also reported to evaluate the contribution of each item.

Spearman-Brown Split-Half Analysis

The correlation between the two halves of the scale was calculated, and the Spearman-Brown coefficient was reported.

Parallel Form Reliability

Parallel form reliability was assessed by correlating the GMSS scores with the WHO-5 Well-being Index.

Stability

A test–retest design was not applied due to the online survey method and limited accessibility to the same participants. Instead, parallel form reliability with WHO-5 was used as the primary stability indicator.

Statistical Analysis

Descriptive statistics (frequency, %, mean ± SD) were presented. Reliability analyses included Cronbach's alpha (overall and subscales), item–total correlations, and alpha if item deleted. Construct validity was examined with CFA in Amos v24. Content validity indexes were calculated based on expert ratings. Convergent validity was evaluated with CR and AVE. Correlations with the WHO-5 were used for parallel form reliability. IBM SPSS v27 and Amos v24 were used for analyses, with significance set at $p<0.05$.

Results

Most of the patients were female (72.7%) and single (59.1%). The mean age of the participants was 34.90±12.55 years, while the mean duration of the disease was 11.55±12.18 years. Other sociodemographic and disease-related characteristics of the participants are presented in Table I. The predominance of female participants should be considered when interpreting the generalizability of the findings.

Table I. Sociodemographic and Disease-related Characteristics of the Participants (n=220)

		n	%
Gender	Female	160	72.7
	Male	60	27.3
Marital Status	Married	90	40.9
	Single	130	59.1
Education Level	Primary School	29	13.2
	High School	96	43.6
	Bachelor's Degree	83	37.7
	Master's Degree or higher	12	5.5
Working Status	Full-time employee	64	29.1
	Half-time employee	8	3.6
	Not working (including students and retirees)	148	67.3
Comorbidity	Yes	53	24.1
	No	167	75.9
Glucose monitoring system	Glucometer with pen strip	114	51.8
	Continuous Glucose Monitoring Device	105	47.7
	Genteel	1	0.5
Are you satisfied with your current glucose monitoring system?	Very satisficed	52	23.6
	Satisfied	96	43.6
	Neutral	39	17.7
	Dissatisfied	22	10.0
	Completely dissatisfied	11	5.0
Usability of the current glucose monitoring system	Easy to use	176	80.0
	Not easy to use	28	12.7
	Undecided	16	7.3
		Mean±SD	
Age (years)		34.90±12.55	
Disease duration (years)		11.55±12.18	
A1c (%)		7.54±1.42	

Validity of the Turkish Version of GMSS

The content validity index was computed at both the item and scale levels. The item-level content validity indexes varied from 0.80 to 1.00, and the scale-level content validity index was 0.960 (Table II). According to the experts, the scale's CVR ranged from 0.60 to 1.00, and the average score of the CVR was 0.946.

Table II. Item-level (I-CVI) and Scale-level (S-CVI) content validity index of the Turkish Version of GMSS

Item No	I-CVI
1	0.90
2	0.90
3	1.00
4	1.00
5	1.00
6	1.00
7	1.00
8	0.90
9	0.80
10	0.90
11	1.00
12	1.00
13	1.00
14	1.00
15	1.00
S-CVI (Scale total)	**0.96**

I-CVI = Item Content Validity Index; S-CVI = Scale Content Validity Index. Values ≥0.80 indicate acceptable content validity.

Confirmatory factor analysis was used to determine construct validity. The original four-factor structure of the scale was tested in the model. Model fit indices indicated acceptable values (χ^2/df=1.528; GFI=0.933; AGFI=0.902; CFI=0.965; RMSEA=0.049; SRMR=0.083) (Table III). The convergent analysis yielded CR values ranging from 0.74 to 0.78 and AVE values ranging from 0.44 to 0.50. Although some AVE values were slightly below the 0.50 threshold, convergent validity was supported since CR values exceeded AVE. The factor loadings of the items ranged from 0.39 to 0.80, according to CFA (Figure I).

Table III. Confirmatory factor analysis (CFA) model fit indices of the Turkish Version of GMSS

Fit Index	Current Study	Acceptable Fit Levels
χ^2/df (CMIN/df)	1.528	1 ≤ χ^2/df ≤ 3 (good); ≤ 5 (acceptable)
SRMR	0.083	≤ 0.08 (good); ≤ 0.10 (acceptable)
GFI	0.933	≥ 0.90
AGFI	0.902	≥ 0.90
CFI	0.965	≥ 0.95
RMSEA	0.049	≤ 0.05 (good); ≤ 0.08 (acceptable)

CMIN/df = Chi-square/df ratio; SRMR = Standardized Root Mean Square Residuals; GFI = Goodness of Fit Index; AGFI = Adjusted Goodness of Fit Index; CFI = Comparative Fit Index; RMSEA = Root Mean Square Error of Approximation.

The Cronbach's alpha coefficient for the overall scale was 0.897. Cronbach's alpha values for the subscales were 0.753 (Openness), 0.756 (Emotional Burden), 0.776 (Behavioral Burden), and 0.742 (Trust).

Table IV. Item–total correlations and Cronbach's alpha values if item deleted for the Turkish Version of GMSS (n=220)

Item No	Subscale	Item–Total Correlation	Cronbach's Alpha if Item Deleted
1	Openness	0.538	0.887
8	Openness	0.605	0.884
10	Openness	0.347	0.893
14	Openness	0.559	0.886
2	Emotional Burden	0.347	0.895
5	Emotional Burden	0.719	0.879
9	Emotional Burden	0.641	0.882
13	Emotional Burden	0.708	0.879
3	Behavioral Burden	0.603	0.884
6	Behavioral Burden	0.638	0.882
11	Behavioral Burden	0.566	0.885
15	Behavioral Burden	0.572	0.885
4	Trust	0.494	0.888
7	Trust	0.507	0.888
12	Trust	0.595	0.884

Item–total correlations >0.30 indicate acceptable item discrimination. All "Cronbach's alpha if item deleted" values remained above 0.87, showing that no item deletion improved reliability.

The correlations between items and the scale varied from 0.347 to 0.719. For each subscale, item–total correlations ranged from 0.32 to 0.70, and "Cronbach's alpha if item deleted" values remained above 0.70, indicating that no item removal improved reliability (Table IV).

Table V. Split-half reliability analysis of the Turkish Version of GMSS (n=220)

Test	Value
Cronbach's Alpha (first half, 8 items)	0.810
Cronbach's Alpha (second half, 7 items)	0.806
Correlation between forms	0.793
Spearman-Brown coefficient	0.885
Guttman Split-Half coefficient	0.883

Spearman-Brown and Guttman coefficients above 0.80 indicate a high level of internal consistency for the two halves of the scale.

In the Spearman-Brown split-half analysis, the two halves of the scale showed a strong positive correlation (*r=0.793*) and a high degree of internal consistency (Spearman-Brown coefficient=0.885; Guttman coefficient=0.883) (Table V).

Table VI. Parallel Form Reliability between GMSS and WHO-5 Well-being Index (n=220)

		Openness	Emotional Burden	Behavioral Burden	Trust	GMSS Total	WHO 5 Well-being Index
Openness	r	1	0.537**	0.565**	0.408**	0.770**	0.345**
	p		<0.001	<0.001	<0.001	<0.001	<0.001
Emotional Burden	r	0.537**	1	0.674**	0.616**	0.878**	0.251**
	p	<0.001		<0.001	<0.001	<0.001	<0.001
Behavioral Burden	r	0.565**	0.674**	1	0.484**	0.858**	0.169*
	p	<0.001	<0.001		<0.001	<0.001	0.012
Trust	r	0.408**	0.616**	0.484**	1	0.740**	0.134*
	p	<0.001	<0.001	<0.001		<0.001	0.047
GMSS Total	r	0.770**	0.878**	0.858**	0.740**	1	0.277**
	p	<0.001	<0.001	<0.001	<0.001		<0.001
WHO 5 Well-being Index	r	0.345**	0.251**	0.169*	0.134*	0.277**	1
	p	<0.001	<0.001	0.012	0.047	<0.001	

** Correlation is significant at the 0.01 level. * Correlation is significant at the 0.05 level.
GMSS: Glucose Monitoring Satisfaction Survey

Parallel form reliability demonstrated statistically significant positive correlations between the WHO-5 Well-being Index and both the overall GMSS score and all four subdimensions (*r=0.42–0.56, p<0.001*) (Table VI).

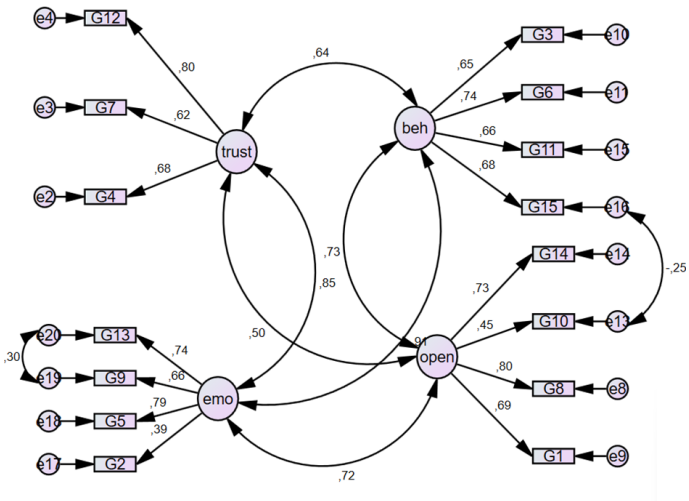

Figure I. Confirmatory Factor Analysis Model with Standardized Estimates

Discussion

Patient satisfaction with blood glucose monitoring devices is essential for maintaining healthy blood glucose levels. Turkish society needs a valid and reliable scale to measure patient satisfaction with the glucose monitoring device. GMSS is a valid and reliable instrument used in the following languages: English, Danish, Dutch, German/Austrian, German/German, Indonesian, Norwegian, Swedish, and Chinese (27, 49). This study assessed the validity and reliability of the Turkish version of the Glucose Monitoring Satisfaction Survey.

In the field of scale development or adaptation, it is widely recognized that when the Item Content Validity Index (I-CVI) and Scale Content Validity Index (S-CVI) values exceed 0.80, expert opinions converge, indicating substantial agreement on the relevance and appropriateness of scale items (50, 51). The findings of the present study indicate that the GMSS possesses favorable I-CVI and S-CVI scores, signifying expert consensus on the items' suitability for Turkish culture and their acceptable representation of the target domain (I-CVI: 0.80–1.00; S-CVI: 0.96). The results indicate that the GMSS possesses item content validity, enhancing confidence in its efficacy for evaluating satisfaction with blood glucose monitoring devices in individuals with T1D. Consistent with the present study, Lu et al. indicated that the CVI for the Chinese version of the scale was 0.910 (27). In the present study, the CVR of the scale was found to range from 0.60 to 1.0. By Lawshe's criteria, the CVR of each item was deemed to be at an acceptable level (41). Consequently, no item was removed from the scale during this study phase.

The fit indices of the confirmatory factor analysis in the literature indicate that the values of χ2/DF, GFI, AGFI, CFI, and RMSEA should meet acceptable standards (52-55). In the confirmatory factor analysis (CFA) of the Turkish version of the scale, the χ2/df ratio, SRMR, GFI, AGFI, CFI, and RMSEA values, which assess the model's fit to the data, were deemed satisfactory. This study indicates that a χ2/df ratio < 3, GFI and AGFI values ≥0.90, CFI values ≥0.95, and SR and RMSEA values ≥0.10 and <0.05 signify a perfect or adequate model fit (56). The Confirmatory Factor Analysis (CFA) demonstrated that all factor loadings above 0.39 signify acceptable loadings. Moreover, the model's fit was deemed adequate according to various model fit indices in Confirmatory Factor Analysis (CFA) (51,53,54,56). The CFA results revealed that all items exhibited factor loadings exceeding 0.30. Factor loadings were reported to be between 0.612 and 0.913 in the Chinese version of the scale (27). Thus, the model fit for the Turkish version of the GSMM was deemed highly robust, maintaining its original four-factor structure.

In the present study, the CR value was higher than 0.70, and the CR value was higher than the AVE value, which ranged from 0.44 to 0.50. While the threshold of 0.50 is a standard benchmark, it is acknowledged that some researchers may be willing to accept lower AVE values, provided that other validity and reliability indicators are deemed to be strong. To illustrate this point, consider a scenario with high composite reliability (above 0.70). In such a case, it is posited that the lower AVE could be compensated for, thereby suggesting that the construct is still reliable and valid overall (57). In the present study, the other reliability and validity parameters were found to be at an acceptable level. While the AVE was slightly lower than 0.50 for some domains, the results indicate a robust and reliable model. For this reason, researchers preferred to keep the tool's original factor structure.

Internal consistency dependability was evaluated utilizing Cronbach's alpha coefficient values and the split-half approach, as advocated in the literature (54, 55, 58). This study reveals that Cronbach's alpha values above 0.70 for both halves, demonstrating robust and substantial correlations between them, with Spearman-Brown and Guttman split-half coefficients surpassing 0.80 (53-55). The present investigation produced Cronbach's alpha values over 0.70 for both halves, alongside Spearman-Brown and Guttman split-half coefficients surpassing 0.80, signifying a substantial degree of dependability. The results demonstrate a robust correlation among the components, reflecting the underlying structure. The Cronbach's alpha values for the Chinese version were 0.87, 0.82, 0.83, 0.81, and 0.83 for the GMSS-T1DM total and its openness, emotional load, behavioral burden, and trust subscales, respectively.

Cronbach's alpha coefficient indicates a scale's internal consistency, demonstrating the degree to which items are interconnected and assess the same underlying concept. Alpha scores ranging from 0.60 to 0.80 signify internal consistency, and values between 0.80 and 1.00 denote high internal consistency (50, 52, 54). The Cronbach's alpha coefficient for the entire scale in this study was 0.897, signifying strong internal consistency. The alpha values for the openness, emotional burden, behavioral burden, and trust subscales were 0.753, 0.756, 0.776, and 0.742, respectively. The original version had a Cronbach alpha of 0.86 (26). These values indicate acceptable internal consistency within each subscale. The findings suggest that the items effectively measure the intended constructs, exhibit significant correlations with their respective subscale, and demonstrate reliability for the overall scale and its subscales.

Item-scale correlation evaluates the association between individual item scores and the overall score of the assessment instrument (50,52,53,54). A higher correlation suggests that the item aligns well with the measured theoretical framework, with a recommended threshold of >0.30 (51,52,58). In our study, item-scale correlations ranged from 0.347 to 0.719.

Another method is parallel form's reliability, which investigates the tool's stability (58). The current study found positive and statistically significant relationships between the WHO 5 Well-being Index and GSMM. This outcome indicates that the findings of the two scales were congruent. The scale's original version also shows a statistically significant positive relationship with WHO-5 (26). Statistically significant relationships existed between the Chinese version of the scale and the WHO-5 (27).

According to the aforementioned analysis, the scale was a valid and reliable tool for measuring satisfaction with the glucose monitoring system in Turkish society. The sample size was considered adequate to test the hypothesis according to the estimated Cronbach's alpha in the power analysis and the achieved Cronbach's alpha. However, we also recommend further validity and reliability analysis in different samples in Turkey to show the repeatability of the measurement tool and to avoid sample bias. The study was conducted with patients with T1D, and there is a need for another valid and reliable survey for patients with Type 2 Diabetes.

This study's validity and reliability assessments revealed that the GMSS (Glucose Monitoring Satisfaction Survey) is a valid and reliable instrument for evaluating the satisfaction of individuals with T1D concerning their glucose monitoring devices throughout Turkish society. The scale objectively assesses individuals with T1D on their satisfaction with blood glucose monitoring equipment. Moreover, the GMSS enables healthcare practitioners and researchers to comprehend this particular group's preferences and requirements, promoting customized therapies and enhancements in diabetes management. The GMSS can be an essential instrument for cross-cultural comparative studies, allowing researchers to evaluate the satisfaction levels of persons with T1D across various cultural contexts.

This study has several limitations. First, the snowball sampling technique and online survey methodology may affect generalizability. Second, the sample was predominantly female (72.7%), which may introduce gender-related bias and limit the generalizability of the results to the broader T1D population. Third, test–retest reliability was not assessed due to the online design and difficulty in re-contacting participants. Although convergent validity was examined (CR and AVE), discriminant validity was not tested, and future research should address this gap. Finally, this study included only patients with T1D; therefore, there is a need to develop or adapt similar instruments for individuals with type 2 diabetes.

References

1. Organization WH. Global action plan for the prevention and control of noncommunicable diseases 2013-2020: World Health Organization; 2013.

2. Mobasseri M, Shirmohammadi M, Amiri T, Vahed N, Hosseini Fard H, Ghojazadeh M. Prevalence and incidence of type 1 diabetes in the world: a systematic review and meta-analysis. Health Promot Perspect 2020;10(2):98-115.

3. American Diabetes Association (ADA). Care in diabetes 2019. Diabetes care 2019;42(1):13-28.

4. American Diabetes Association (ADA) 6. Glycemic targets:

standards of medical care in diabetes—2019. Diabetes Care. 2019 42(Supplement 1):61-70.
5. Association AD. 7. Approaches to glycemic treatment. Diabetes care 2015;38(S1):41-48.
6. Bailey TS, Grunberger G, Bode BW, et al. American Association of Clinical Endocrinologists and American College of Endocrinology 2016 Outpatient Glucose Monitoring Consensus Statement. Endocr Pract 2016;22(2):231-261.
7. Health NIf, Excellence C. Type 1 diabetes in adults: diagnosis and management: NICE; 2015.
8. Czupryniak L, Barkai L, Bolgarska S et al. Self-monitoring of blood glucose in diabetes: from evidence to clinical reality in Central and Eastern Europe--recommendations from the international Central-Eastern European expert group. Diabetes Technol Ther 2014;16(7):460-475.
9. Visser MM, Charleer S, Fieuws S, et al. Comparing real-time and intermittently scanned continuous glucose monitoring in adults with type 1 diabetes (ALERTT1): a 6-month, prospective, multicentre, randomised controlled trial. Lancet 2021;397(10291):2275-2283.
10. Franceschi R, Micheli F, Mozzillo E, et al. Intermittently Scanned and Continuous Glucose Monitor Systems: A Systematic Review on Psychological Outcomes in Pediatric Patients. Front Pediatr 2021;9:660173.
11. Teo E, Hassan N, Tam W, Koh S. Effectiveness of continuous glucose monitoring in maintaining glycaemic control among people with type 1 diabetes mellitus: a systematic review of randomised controlled trials and meta-analysis. Diabetologia 2022;65(4):604-619.
12. Seidu S, Kunutsor SK, Ajjan RA, Choudhary P. Efficacy and Safety of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring in Patients with Type 2 Diabetes: A Systematic Review and Meta-analysis of Interventional Evidence. Diabetes Care 2024;47(1):169-179.
13. Mostrom P, Ahlen E, Imberg H, Hansson PO, Lind M. Adherence of self-monitoring of blood glucose in persons with type 1 diabetes in Sweden. Bmj Open Diab Res Ca 2017;5(1):e000342.
14. Taylor PJ, Thompson CH, Brinkworth GD. Effectiveness and acceptability of continuous glucose monitoring for type 2 diabetes management: A narrative review. J Diabetes Investig 2018;9(4):713-725.
15. Girardin CM, Huot C, Gonthier M, Delvin E. Continuous glucose monitoring: a review of biochemical perspectives and clinical use in type 1 diabetes. Clin Biochem 2009;42(3):136-142.
16. Harrison S, McKane J, Clement A, et al. Continuous Monitoring of Glucose for Type 1 Diabetes: A Health Technology Assessment. Ontario health technology assessment series 2018;18 2:1-160.
17. Hauss O, Hinzmann R, Huffman B. Drug Interference in Self-Monitoring of Blood Glucose and the Impact on Patient Safety: We Can Only Guard Against What We Are Looking for. J Diabetes Sci Technol 2024;18(3):727-732.
18. Wang X, Luo JF, Qi L, Long Q, Guo J, Wang HH. Adherence to self-monitoring of blood glucose in Chinese patients with type 2 diabetes: current status and influential factors based on electronic questionnaires. Patient Prefer Adherence 2019;13:1269-1282.
19. Lin M, Chen T, Fan G. Current status and influential factors associated with adherence to self-monitoring of blood glucose with type 2 diabetes mellitus patients in grassroots communities: a cross-sectional survey based on information-motivation-behavior skills model in China. Front Endocrinol (Lausanne) 2023;14:1111565.
20. Patton SR. Adherence to glycemic monitoring in diabetes. J Diabetes Sci Technol 2015;9(3):668-675.
21. Rahman SAU. Predicting Factors Affecting Glucose Monitoring Treatment Satisfaction and Drug Attitude Inventory (Adherence) Among Patients with Type 2 Diabetes Mellitus; Cross-sectional Observational Study. Curr Diabetes Rev 2019;15(3):233-239.
22. Emechebe N, Agu N, Malmi M, Zgibor JC. Examining the Association between Treatment Satisfaction and Medication Adherence among Patients with Poorly Controlled Type 2 Diabetes. Diabetes 2018;67.
23. Bakar ZA, Fahrni ML, Khan TM. Patient satisfaction and medication adherence assessment amongst patients at the diabetes medication therapy adherence clinic. Diabetes Metab Syndr 2016;10(2 Suppl 1):139-143.
24. Messer LH, Johnson R, Driscoll KA, Jones J. Best friend or spy: a qualitative meta-synthesis on the impact of continuous glucose monitoring on life with Type 1 diabetes. Diabet Med 2018;35(4):409-418.
25. Messer LH, Berget C, Beatson C, Polsky S, Forlenza GP. Preserving Skin Integrity with Chronic Device Use in Diabetes. Diabetes Technol Ther 2018;20(S2):254-264.
26. Polonsky WH, Fisher L, Hessler D, Edelman SV. Development of a New Measure for Assessing Glucose Monitoring Device-Related Treatment Satisfaction and Quality of Life. Diabetes Technol Ther 2015;17(9):657-663.
27. Lu H, Lu X, Gao H, Gao Y. Reliability and Validity of the Chinese Version of the Glucose Monitoring Satisfaction Survey. Chinese General Practice 2020;23(14):1812.
28. Hermanns N, Ehrmann D, Schipfer M, Kroger J, Haak T, Kulzer B. The impact of a structured education and treatment programme (FLASH) for people with diabetes using a flash sensor-based glucose monitoring system: Results of a randomized

controlled trial. Diabetes Res Clin Pract 2019;150:111-21.
29. Hood KK, Laffel LM, Danne T, et al. Lived Experience of Advanced Hybrid Closed-Loop Versus Hybrid Closed-Loop: Patient-Reported Outcomes and Perspectives. Diabetes Technol Ther 2021;23(12):857-861.
30. Al Hayek A, Al Dawish M, El Jammal M. The Impact of Flash Glucose Monitoring on Markers of Glycaemic Control and Patient Satisfaction in Type 2 Diabetes. Cureus 2021;13(6):e16007.
31. Lukacs A, Szerencsi LB, Barkai L. Continuous glucose monitoring (CGM) satisfaction and its effect on mental health and glycemic control in adults with type 1 diabetes. Physiol Int 2022;109(4):501-510.
32. Bonett DG. Sample size requirements for testing and estimating coefficient alpha. Journal of Educational and Behavioral Statistics 2002;27(4):335-340.
33. WN. A. Sample size calculator (web) 2024 [cited 2024 05.13.2024]. Available from: http://wnarifin.github.io.
34. Eser E, Cevik C, Baydur H, et al. Reliability and validity of the Turkish version of the WHO-5, in adults and older adults for its use in primary care settings. Prim Health Care Res Dev 2019;20:e100.
35. Dorer B. ESS round 6 translation guidelines. Mannheim: European Social Survey, GESIS. 2012;1.
36. Coster WJ, Mancini MC. Recommendations for translation and cross-cultural adaptation of instruments for occupational therapy research and practice. Revista de Terapia Ocupacional da Universidade de São Paulo 2015;26(1):50-57.
37. Beaton D, Bombardier C, Guillemin F, Ferraz MB. Recommendations for the cross-cultural adaptation of the DASH & QuickDASH outcome measures. Institute for Work & Health 2007;1(1):1-45.
38. Davis LL. Instrument review: Getting the most from a panel of experts. Applied nursing research 1992;5(4):194-197.
39. Veneziano L. A method for quantifying content validity of health-related questionnaires. American Journal of Health Behavior 1997;21(1):67-70.
40. Zamanzadeh V, Ghahramanian A, Rassouli M, Abbaszadeh A, Alavi-Majd H, Nikanfar AR. Design and Implementation Content Validity Study: Development of an instrument for measuring Patient-Centered Communication. J Caring Sci 2015;4(2):165-178.
41. Lawshe C. A Quantitative Approach to Content Validity. Personnel psychology/Berrett-Koehler Publishers 1975.
42. Murat YM. Factor analysis and validity in social sciences: Application of exploratory and confirmatory factor analyses. Istanbul Business Research 2017;46(1):74-85.
43. Kilic AF, Doğan N. Comparison of confirmatory factor analysis estimation methods on mixed-format data. International Journal of Assessment Tools in Education 2021;8(1):21-37.
44. Ramsey R. What are reaction time indices of automatic imitation measuring? Conscious Cogn 2018;65:240-254.
45. Chin C-L, Yao G. Convergent Validity. In: Michalos AC, editor. Encyclopedia of Quality of Life and Well-Being Research. Dordrecht: Springer Netherlands; 2014. p. 1275-1276.
46. Ravinder EB, Saraswathi A. Literature review of Cronbach alpha coefficient (α) and McDonald's omega coefficient (Ω). European Journal of Molecular & Clinical Medicine 2020;7(6):2943-2949.
47. de Vet HC, Mokkink LB, Mosmuller DG, Terwee CB. Spearman–Brown prophecy formula and Cronbach's alpha: different faces of reliability and opportunities for new applications. Journal of Clinical Epidemiology 2017;85:45-49.
48. Paulsen J, BrckaLorenz A. Internal consistency statistics. Faculty Survey of Student Engagement; 2017.
49. Behavioral Diabetes Institute. Scales and Measures: Behavioral Diabetes; 2024 [Available from: https://behavioraldiabetes.org/scales-and-measures/#1700007829694-294ec8b1-1535.
50. Johnson B, Christensen L. Educational research (quantitative, qualitative, and mixed approaches, (Çev. Ed. SB Demir). Ankara: Eğiten Kitap. 2014.
51. DeVellis RF, Thorpe CT. Scale development: Theory and applications: Sage publications; 2021.
52. Karagöz Y. SPSS 23 ve AMOS 23 uygulamalı istatistiksel analizler: Nobel Akademik Yayıncılık Ankara; 2016.
53. Kartal M, Bardakçı S. Reliability and validity analysis with SPSS and AMOS applied examples. Ankara, Türkiye: Akademisyen Publishing. 2018.
54. Özdamar K. Scale and test development structural equation modeling. Ankara: Nisan Kitabevi Publishing. 2016:6-286.
55. Tabachnick BG, Fidell LS, Ullman JB. Using multivariate statistics: pearson Boston, MA; 2013.
56. Erkorkmaz Ü, Etikan İ, Demir O, Özdamar K, Sanisoğlu S. Confirmatory factor analysis and fit indices: Review. Turkiye Klinikleri J Med Sci 2013;33(1):210-223.
57. Lam LW. Impact of competitiveness on salespeople's commitment and performance. Journal of Business Research 2012;65(9):1328-1334.
58. Seçer İ. Psychological test development and adaptation process: SPSS and LISREL applications. Ankara: Anı Publishing. 2015.

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The Effect of Antidepressant Use on Weight Loss After One Anastomosis Gastric Bypass: A Retrospective Cohort Study

Antidepresan Kullanımının Tek Anastomoz Gastrik Bypass Sonrası Kilo Kaybına Etkisi: Retrospektif Kohort Çalışması

Recep Aktimur[1] | **Arda Kazım Demirkan**[2]

[1]Samsun Liv Hospital, Department of General Surgery, Samsun, Türkiye
[2]Samsun Liv Hospital, Department of Psychiatry, Samsun, Türkiye

Sorumlu Yazar | Correspondence Author
Arda Kazım Demirkan
ardakazimdemirkan@gmail.com
Address for Correspondence: Samsun Liv Hospital, Hançerli, Fatih Sultan Mehmet Cd No:155, 55020, İlkadım, Samsun, Türkiye.

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The Effect of Antidepressant Use on Weight Loss After One Anastomosis Gastric Bypass: A Retrospective Cohort Study

ABSTRACT

Objective: Antidepressant use is frequently associated with weight gain, yet little is known about its impact on postoperative weight loss following bariatric surgery. This study aimed to examine how antidepressant use—before and/or after surgery—affects weight loss outcomes in patients undergoing one-anastomosis gastric bypass (OAGB).

Material and Method: This retrospective cohort study included 181 patients who underwent OAGB between January 2020 and December 2021. Based on antidepressant use, patients were categorized into four groups: no use (n=87), preoperative use only (n=25), continued use before and after surgery (n=36), and new initiation after surgery (n=33). Weight loss outcomes were assessed using percentage of excess BMI loss (%EBMIL) and total weight loss (%TWL) at 12 months postoperatively. Statistical comparisons were conducted using independent samples t-tests.

Results: There were no significant differences in %TWL between any of the groups (range: 34.54%–37.05%). However, %EBMIL was significantly lower in the continued-use group (82.21%) compared to the no-use group (*p=0.027*) and the preoperative-use-only group (*p=0.0196*). No statistically significant differences were found between other groups. Demographic variables were generally comparable, though hypertension, hyperlipidemia, and gender distribution differed significantly across groups.

Conclusion: Continued antidepressant use after OAGB may negatively affect %EBMIL, despite similar %TWL outcomes. These findings suggest that antidepressant exposure, particularly when continued into the postoperative period, may attenuate the optimal metabolic benefits of bariatric surgery. Future prospective studies with pharmacokinetic monitoring and larger samples are warranted to clarify medication-specific effects.

Keywords: Antidepressants, Bariatric surgery, OAGB, Weight loss, EBMIL, TWL.

ÖZET

Amaç: Antidepresan kullanımı genellikle kilo alımıyla ilişkilendirilmekte olup, bariatrik cerrahi sonrası kilo kaybı üzerindeki etkisi hakkında ise sınırlı bilgi mevcuttur. Bu çalışmada, ameliyat öncesi ve/veya sonrası antidepresan kullanımının, tek anastomozlu gastrik bypass (OAGB) geçiren hastalardaki kilo kaybı sonuçlarına etkisi incelenmiştir.

Gereç ve Yöntem: Bu retrospektif kohort çalışmasına, Ocak 2020 ile Aralık 2021 tarihleri arasında OAGB ameliyatı geçiren 181 hasta dahil edilmiştir. Hastalar antidepresan kullanımına göre dört gruba ayrılmıştır: hiç kullanmayanlar (n=87), sadece ameliyat öncesi kullananlar (n=25), ameliyat öncesi ve sonrasında kullanmaya devam edenler (n=36), ve sadece ameliyat sonrası başlayanlar (n=33). Kilo kaybı sonuçları, ameliyattan 12 ay sonra ölçülen vücut kitle indeksi fazlalığı kaybı yüzdesi (%EBMIL) ve toplam kilo kaybı yüzdesi (%TWL) ile değerlendirilmiştir. İstatistiksel karşılaştırmalar bağımsız örneklem t-testi ile yapılmıştır.

Bulgular: Gruplar arasında %TWL açısından anlamlı bir fark saptanmamıştır (aralık: %34,54–%37.05). Ancak, %EBMIL değeri, antidepresan kullanımını sürdüren grupta (%82,21), hiç kullanmayan gruba (*p=0.027*) ve sadece preoperatif kullanan gruba (*p=0.0196*) kıyasla anlamlı derecede daha düşüktü. Diğer gruplar arasında istatistiksel olarak anlamlı fark bulunmamıştır. Demografik değişkenler genel olarak benzerdi; ancak hipertansiyon, hiperlipidemi ve cinsiyet dağılımı gruplar arasında anlamlı farklılık göstermekteydi.

Sonuç: OAGB sonrası antidepresan kullanımının devam etmesi, %EBMIL üzerinde olumsuz bir etki yaratabilir; bu durum %TWL sonuçlarının benzer olmasına rağmen geçerlidir. Bu bulgular, antidepresan maruziyetinin—özellikle postoperatif dönemde sürdüğünde—bariatrik cerrahinin optimal metabolik faydalarını azaltabileceğini düşündürmektedir. İlaçlara özgü etkilerin netleştirilebilmesi için farmakokinetik izlemi içeren ve daha geniş örneklemlerle yapılacak prospektif çalışmalara ihtiyaç vardır

Anahtar Sözcükler: Antidepresanlar, Bariatrik cerrahi, Kilo kaybı, OAGB, EBMIL, TWL.

Introduction

Obesity has become a global epidemic, with adult obesity rates more than doubling since 1990, according to the latest World Health Organization (WHO) report. In 2022, approximately 890 million individuals—equivalent to 1 in 8 people worldwide—were estimated to have obesity (1).

Bariatric surgery is considered one of the most effective treatments for obesity and its related comorbidities, including type 2 diabetes, hypertension, sleep apnea, and fatty liver disease. The American Society for Metabolic and Bariatric Surgery estimates that approximately 280,000 bariatric procedures were performed in developing countries based on available data. Among these procedures, one anastomosis gastric bypass (OAGB) has emerged as a novel surgical option for treating obesity, accounting for approximately 0.8% of all bariatric surgeries, with its prevalence steadily increasing (2). On average, patients undergoing OAGB experience a reduction of more than 60–90% in excess body weight during the postoperative period (3,4). Although significant weight loss is typically achieved, the extent of weight reduction within the first year after surgery varies considerably between individuals. This variation is influenced by factors such as physical condition, metabolic rate, and dietary habits. Additionally, psychological factors have been identified as important contributors to postoperative weight loss outcomes (5).

Research has highlighted a high prevalence of depression and other psychiatric disorders among individuals with obesity, as well as those who undergo bariatric surgery (6,7). The long-term use of psychotropic medications has shown variable effects on body weight. For instance, commonly prescribed antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have been associated with weight gain, whereas bupropion—a norepinephrine and dopamine reuptake inhibitor (NDRI)—is linked to weight loss (8).

As various classes of antidepressants interact with different metabolic pathways through a range of mechanisms, bariatric surgery may further alter the absorption and efficacy of these medications, potentially influencing both mental health outcomes and weight loss trajectories. However, data on the impact of psychiatric medication on bariatric surgery outcomes remain limited. A recent article on 315 patients with a 22.2% ratio of antidepressant use revealed that patients on antidepressants showed less weight loss at 12 months post-surgery. Another study compared the outcomes of OAGB patients receiving active treatment for depression with those who did not need treatment. The results showed that antidepressant treatment did not have an impact on weight loss or overall health outcomes (9).

The objective of this study was to analyze and compare excess body mass index loss (EBMIL) and total weight loss (TWL) percentages between patients using psychiatric medications and those who are not, to provide valuable information for clinicians in selecting suitable psychiatric treatments and managing care for the at-risk population undergoing bariatric surgery. As a secondary objective, this study aimed to explore the potential influence of psychiatric medication use on postoperative weight loss outcomes within the clinical context, thereby contributing to more informed decision-making in the management of bariatric surgery patients with coexisting psychiatric conditions.

Material and Method

Study Population

Patients who underwent single-anastomosis OAGB surgery at the same institution between January 2020 and December 2021 were included in the study. Individuals who underwent other types of bariatric procedures, revision surgeries, had unknown antidepressant treatment status, or lacked 12-month follow-up data were excluded. Patients who experienced complications or prolonged hospital stays outside the standard postoperative follow-up periods were also excluded. Inclusion criteria were age ≥18 years, ability to understand the benefits and risks of surgery, stable mental and psychological status, and a failure to achieve sufficient weight loss through conservative methods (diet, exercise, or medication). All patients independently opted for surgery based on personal preferences and willingness to proceed.

The study received ethical approval from the local ethical committee of Samsun Training and Research

Hospital (approval date/no: 07.07.2021/2021-13-12), and written informed consent was obtained. All procedures performed in studies involving human participants adhered to the 1964 Helsinki Declaration and its later amendments. Information regarding antidepressant use was obtained from electronic medical records and confirmed through direct patient interviews. Patients with inconsistent or missing data on antidepressant status were excluded. To ensure cohort homogeneity, only patients using antidepressants classified as SSRIs and SNRIs were included. Those prescribed other psychiatric medications (e.g., tricyclic antidepressants, monoamine oxidase inhibitors, mirtazapine, lithium) were excluded.

All surgical procedures were performed by a single surgeon using a standardized laparoscopic technique described in the literature (10). In brief, the operation involved five laparoscopic trocars in the supine position. A gastric pouch was created along the lesser curvature using a 36-Fr tube and 60-mm linear staplers, starting from the distal crow's foot to the His angle. Gastrojejunostomy was performed using a 60-mm linear stapler at a 60-mm anastomotic length on the posterior wall of the pouch, aligned side-to-side with the jejunum. All staple lines, including the gastric pouch and remnant, were reinforced using an invaginating sero-serosal barbed suture (V-Loc 3-0). Postoperatively, all patients received standardized dietary counseling and were followed regularly by the operating surgeon. Demographic and clinical data—such as age, sex, anthropometric measures, medical comorbidities, and use of antipsychotics on the day of surgery and during follow-up—were systematically recorded.

Outcome Measures

Height and weight were recorded at baseline and at 12 months postoperatively. Weight loss was evaluated using the following formulas: %EBMIL = (Preoperative BMI – Follow-up BMI) / (Preoperative BMI – 25) × 100, %TWL = (Preoperative weight – Follow-up weight) / (Preoperative weight) × 100. The most recent follow-up data was used for comparison with preoperative values.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation (SD) and categorical variables as counts and percentages. Normality of distributions was assessed using the Shapiro–Wilk test, and homogeneity of variances with Levene's test. Because distributional assumptions were met, parametric procedures were used throughout. Between-group comparisons were planned a priori to contrast each antidepressant-use group with the reference group (no antidepressant use). Accordingly, independent-samples t-tests were performed for continuous outcomes (postoperative weight, BMI, %EBMIL, and %TWL), using Welch's correction when variance homogeneity was violated. Categorical variables were compared using the χ^2 test or Fisher's exact test when expected cell counts were <5. Two-sided *p-values <0.05* were considered statistically significant, and confidence intervals (CIs) were set at 95%. Given that the analysis plan relied on planned comparisons versus a single reference group and did not involve an omnibus multi-group test, we did not conduct one-way ANOVA or post-hoc procedures, and we did not compute ANOVA-based effect sizes (e.g., η^2) or standardized mean differences (e.g., Cohen's d) for inference. Instead, we report mean differences with 95% CIs to convey the magnitude and precision of group contrasts. To account for potential confounding, a multivariable linear regression model was fitted with %EBMIL as the dependent variable, including antidepressant-use group (categorical; reference = no antidepressant use), age, sex, baseline BMI, diabetes mellitus, hypertension, hyperlipidemia, obstructive sleep apnea syndrome, alcohol intake, and smoking as covariates. Model results are presented as unstandardized coefficients (β) with standard errors (SE), standardized coefficients (β), t statistics, and p values. Regression assumptions (linearity, normality, and homoscedasticity of residuals) were evaluated using residual diagnostics and the Shapiro–Wilk test on residuals. No antidepressant group was the reference category for the groups. Multicollinearity was assessed using variance inflation factors (VIF < 5 considered acceptable). For visualization, %EBMIL and %TWL were displayed with boxplots (median, interquartile range, and whiskers) and complementary mean plots with 95% CIs (Figures II–V) to aid clinical

Table I. Demographic Data of the Study Population

	No antidepressant group (n=87)	Preoperative use of antidepressants (n=25)	Continued use of antidepressants (n=36)	Postoperative use of antidepressants (n=33)
Age (years)	42.24±9.683	42.80±7.887	41.33±12.29	41.00±11.33
Baseline weight (kg)	115.8±20.77	108.6±20.51	125.4±23.39	125.4±31.93
Baseline BMI (kg/m2)	42.30±6.951	39.30±2.431	43.71±4.868	43.66±6.053
M/F	31/56	10/15	16/20	12/21
Diabetes mellitus n (%)	40 (45.9)	10 (40)	20 (55.5)	15 (45.4)
Hypertension n (%)	32 (36.8)	15 (60)	10 (27.7)	6 (18.2)
Hyperlipidemia n (%)	49 (56.3)	15 (60)	24 (66.6)	6 (18.2)
Obstructive sleep apnea syndrome n (%)	31 (35.6)	10 (40)	12 (33.3)	12 (36.4)
Alcohol intake n (%)	26 (29.9)	10 (40)	16 (44.4)	15 (45.4)
Smoking n (%)	44 (50.6)	15 (60)	18 (50)	15 (45.4)

BMI: Body Mass Index; M/F: Male/Female.

interpretability. Statistical analyses were conducted using SPSS for Windows (version 23.0; IBM Corp., Armonk, NY, USA), and plots were generated in Python.

Results

All variables showed normal distribution according to relevant statistical analyses. The demographic and clinical characteristics of the study population are summarized in Table I. A total of 181 patients who underwent OAGB surgery were included in the analysis. Patients were divided into four groups based on their antidepressant use: no antidepressant use (n=87; patients who did not use any antidepressants during both the preoperative and postoperative periods), preoperative use only (n=25; patients who used SSRIs or SNRIs for at least 6 months during the 1-year period prior to surgery but discontinued thereafter), continued use before and after surgery (n=36; patients who used SSRIs or SNRIs for at least 6 months both during the 1-year preoperative period and for at least 6 months during the 1-year postoperative follow-up), and initiated antidepressant treatment postoperatively (n=33; patients who did not use antidepressants preoperatively but initiated SSRI or SNRI treatment for at least 6 months within the 1-year postoperative follow-up period). This classification is summarized in Table II.

The distribution of patients in each group according to antidepressant type was as follows: preoperative use group (20 SSRI, 5 SNRI), continued use group (27 SSRI, 9 SNRI), postoperative use group (27 SSRI, 6 SNRI).

Table II. Patient Groups Based on Timing and Duration of Antidepressant Use

Group	n	Definition
No antidepressant use	87	Patients who did not use any antidepressants during both the preoperative and postoperative periods.
Preoperative use only	25	Patients who used SSRIs or SNRIs for at least 6 months during the 1-year period prior to surgery but discontinued thereafter.
Continued use before and after surgery	36	Patients who used SSRIs or SNRIs for at least 6 months both during the 1-year preoperative period and for at least 6 months during the 1-year postoperative follow-up.
Initiated antidepressant treatment postoperatively	33	Patients who did not use antidepressants preoperatively but initiated SSRI or SNRI treatment for at least 6 months within the 1-year postoperative follow-up period.

There were no statistically significant differences among the groups regarding age, baseline weight, body mass index (BMI), diabetes mellitus, obstructive sleep apnea syndrome (OSAS), alcohol use, or smoking status. However, the prevalence of hypertension and hyperlipidemia differed significantly across groups, ranging from 18.2% to 60% and 18.2% to 66.6%, respectively ($p<0.01$ for both). Additionally, gender distribution also showed a statistically significant difference among groups ($p<0.05$).

Postoperative outcomes based on antidepressant use status are presented in Table III. Postoperative weight and BMI were generally lower in the no-antidepressant group compared to the continued-use

Table III. Comparison of Study Variables between the Groups

Variables	No antidepressant group (n=87)	Preoperative use of antidepressants (n=25)	*p value**	Continued use of antidepressants (n=36)	*p value**	Postoperative use of antidepressants (n=33)	*p value**
Postoperative weight (kg)	74.26±11.71 (51.50 - 107.0)	68.64±12.21 (57.40 - 88.00)	*0.3007*	81.55±14.82 (61.00-118.0)	***0.0238***	78.95±23.01 (57.60-138.0)	*0.2746*
Postoperative BMI (kg/m2)	26.99±3.554 (19.90 - 40.20)	24.92±2.072 (22.70 - 27.50)	*0.2028*	28.46±2.953 (24.70-35.20)	*0.1030*	27.17±4.30 (21.90-37.40)	*0.873*
%EBMIL	91.91±17.16 (52.70-154.3)	100.4±14.68 (82.10-118.3)	*0.2799*	82.21±14.18 (44.10 - 102.4)	***0.0270****	91.40± 18.75 (58.00 - 118.1)	*0.926*
%TWL	35.36±6.701 (19.60-53.70)	36.31±6.759 (29.60 - 45.56)	*0.7578*	34.54±6.867 (16.56 - 43.54)	*0.6373*	37.05±6.720 (27.03 - 48.11)	*0.433*

BMI: Body Mass Index; %EBMIL: Percent Excess Body Mass Index Loss; %TWL: Percent Total Weight Loss; **p* values were based on the comparison with the no antidepressant group; ** Comparison with the preoperative use of antidepressants group: *p=0.0196.*

group. However, the difference reached statistical significance only for BMI in the continued-use group (*p=0.0238*).

Table IV. Multiple Variable Regression Analysis Based on %EBMIL

	Unstandardized coefficients		Standardized coefficients	t	*p*
	Beta	SE	Beta		
Age	0.02	0.03	0.05	0.66	*0.851*
Baseline BMI	-0.45	0.18	-0.26	-3.63	***0.014***
Gender	-1.10	0.85	-0.09	-1.48	*0.145*
Diabetes mellitus	-0.85	0.90	-0.07	-0.94	*0.459*
Hypertension	-0.40	0.82	-0.04	-0.49	*0.710*
Hyperlipidemia	-0.58	0.88	-0.05	-0.62	*0.695*
Obstructive sleep apnea syndrome	-0.96	0.78	-0.08	-1.22	*0.218*
Alcohol intake	-0.41	0.83	-0.06	-0.78	*0.184*
Smoking	-0.30	0.76	-0.03	-0.39	*0.253*
Preoperative use of antidepressants	-1.25	1.10	-0.10	-1.16	*0.357*
Continued use of antidepressants	-2.10	1.00	-0.17	-2.88	***0.041***
Postoperative use of antidepressants	-0.95	1.05	-0.08	-0.90	*0.514*

BMI: Body Mass Index; SE: Standard Error; %EBMIL: Percentage of Excess Body Mass Index Loss.

Furthermore, patients in the continued-use group demonstrated significantly lower %EBMIL (82.21%) compared to those who did not use antidepressants (*p=0.0270*). Similarly, a comparison between the preoperative-only and continued-use groups revealed significantly lower %EBMIL in the latter (*p=0.0196*) (Figure I). (Figure II shows the distribution of percentage excess body mass index loss [%EBMIL] across the four antidepressant use groups, where the central line represents the median, the box indicates the interquartile range, and the whiskers extend to the minimum and maximum values, excluding outliers).

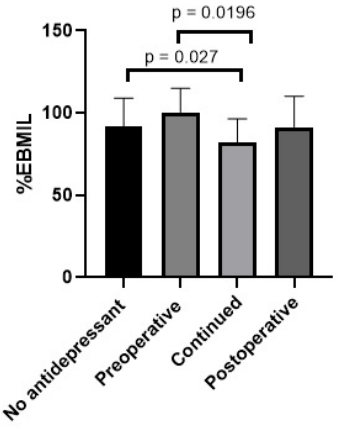

Figure I. Comparison of Study Variables Between the Groups

Other intergroup comparisons for postoperative weight, BMI, and %EBMIL did not yield statistically significant differences. %TWL ranged from 34.54% to 37.05% across all groups, with no statistically significant differences observed. (Figure III presents the distribution of percentage total weight loss [%TWL] across the groups, using the same boxplot format as Figure II).

A multiple linear regression analysis was conducted to examine the association between demographic and clinical variables, taking %EBMIL as the dependent variable. This indicates that higher baseline BMI was associated with a greater effect on the outcome variable (Table IV). Age (*p=0.851*), gender (*p=0.145*), diabetes mellitus (*p=0.459*), hypertension (*p=0.710*), hyperlipidemia (*p=0.695*), OSAS (*p=0.218*), alcohol

intake (*p=0.184*), or smoking (*p=0.253*), were not statistically significant predictors in the model. Figure IV displays the mean %EBMIL for each group with 95% confidence intervals represented by error bars, while Figure V similarly shows the mean %TWL for each group with corresponding confidence intervals. Regarding antidepressant use, continued use of antidepressants was significantly associated with the outcome. This group demonstrated a positive relationship, suggesting that sustained antidepressant therapy may influence the dependent variable even after adjusting for other clinical and demographic factors.

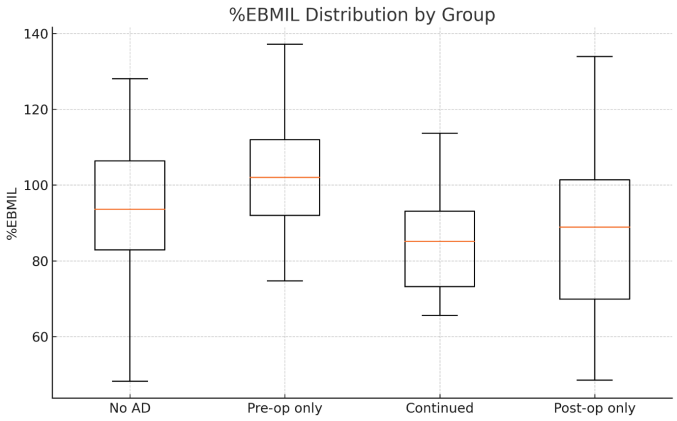

Figure II. Boxplot shows the distribution of percentage excess body mass index loss (%EBMIL) across the four antidepressant use groups. The central line represents the median, the box indicates the interquartile range, and the whiskers extend to the minimum and maximum values, excluding outliers

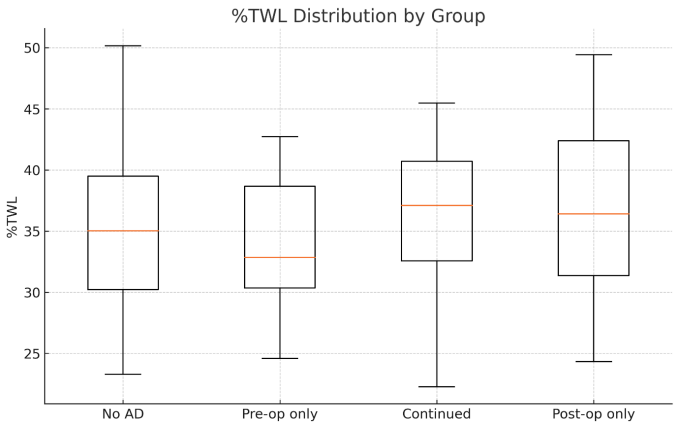

Figure III. Boxplot showing the distribution of percentage total weight loss (%TWL) across the four antidepressant use groups. The central line represents the median, the box indicates the interquartile range, and the whiskers extend to the minimum and maximum values, excluding outliers

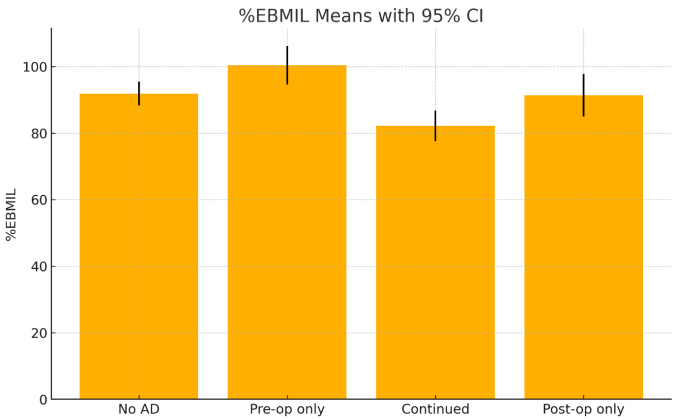

Figure IV. Bar chart displays the mean %EBMIL for each antidepressant use group with 95% confidence intervals represented by error bars

In contrast, preoperative use of antidepressants only (standardized β=0.46, *p=0.357*), postoperative initiation of antidepressants (standardized β=0.35, *p=0.514*), and no antidepressant use (standardized β=0.31, *p=0.174*) were not significantly associated with the outcome. Model fit indices were as follows: R^2=0.18; Adjusted R^2=0.12; F(11, 169) = 3.12, *p=0.001*. All VIF values < 2.0 showing no significant multicollinearity.

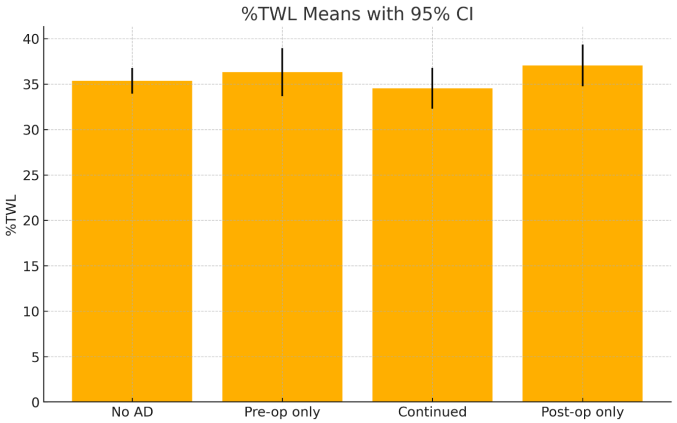

Figure V. Bar chart displays the mean %TWL for each antidepressant use group with 95% confidence intervals represented by error bars

Discussion

Weight gain is a well-known side effect of antidepressants, prompting investigation into their potential impact on postoperative weight loss. While all patients in this study achieved substantial weight loss after OAGB surgery, our findings revealed differential effects based on antidepressant usage. Approximately 19% of patients were on psychiatric medications prior to surgery, and of these, 80% continued using them at least one year postoperatively. We observed no

significant differences in %TWL between groups regardless of antidepressant use before or after surgery, indicating that bariatric surgery can achieve comparable total weight loss outcomes regardless of psychiatric medication status. However, patients who continued using antidepressants postoperatively exhibited significantly lower %EBMIL compared to those who were either not taking antidepressants or discontinued them after the preoperative period.

The weight-related effects of psychiatric medications are well-documented, though the underlying mechanisms remain incompletely understood. Only a limited number of studies have examined this issue specifically in the context of bariatric surgery (11–13).

In a prospective cohort study, Hawkins et al. found no significant differences in %TWL among patients taking varying numbers of psychiatric medications one-year post-surgery, aligning with our findings (11). However, they reported that SNRIs were associated with a higher %TWL than SSRIs (36.4% vs. 27.8%), suggesting that different antidepressant classes may exert distinct effects on postoperative outcomes.

Another large cohort study involving 751 patients undergoing Roux-en-Y gastric bypass (RYGB) reported reductions in both %EBMIL and %TWL among antidepressant users, particularly those taking SNRIs and tricyclic antidepressants (TCAs), independent of metabolic comorbidities (12). Similarly, Arterburn et al. found that preoperative bupropion use was associated with greater initial weight loss compared to SSRIs, though this advantage diminished over a five-year follow-up (13). These findings suggest that bupropion may be a preferable option for patients with obesity preparing for bariatric surgery.

Irrespective of surgical technique, bariatric procedures alter gastrointestinal anatomy and physiology, affecting drug pharmacokinetics and bioavailability. These changes include altered gastric emptying time, reduced absorptive surface area, modified bile acid metabolism, and shortened intestinal transit time. Additionally, bariatric surgery is suggested to affect the gut microbiota, which plays a pivotal role in serotonin and tryptophan metabolism (14,15). Notably, up to 90% of the body's serotonin is synthesized in the gut (16), where it functions not only as a neurotransmitter but also as a regulator of gastrointestinal and systemic processes through 14 distinct receptor subtypes (17). The extent to which SSRI treatment interacts with these serotonin-mediated pathways after bariatric surgery remains unclear due to the profound changes to the gut–brain axis introduced by surgery.

A pharmacokinetic study reported an approximate 25% postoperative decrease in SSRI/SNRI plasma concentrations within the first month following surgery, suggesting the need for early dose adjustments (18). This is clinically important for maintaining antidepressant efficacy in the immediate postoperative period.

The mechanisms by which antidepressants influence weight—whether through gain in general populations or reduced weight loss post-surgery—are likely multifactorial and depend on each drug's specific pharmacological profile. These effects may involve serotonin and alpha-1 adrenergic receptor pathways related to appetite regulation, or reductions in energy expenditure due to sedative and antihistaminic effects (19). The hypothalamic–pituitary–adrenal (HPA) axis, which regulates fat distribution and metabolism, may also be disrupted by abdominal obesity. Interestingly, citalopram has been shown to restore HPA axis dysregulation caused by abdominal adiposity (20,21).

While some studies have reported the heterogeneous effects of antidepressants on postoperative weight outcomes, SNRIs and TCAs appear more likely to attenuate %EBMIL than SSRIs or trazodone (12). In our sample, patients were taking SSRIs, SNRIs, but none used TCAs.

The regression analysis demonstrated that continued use of antidepressants was significantly associated with lower %EBMIL ($p=0.041$). Although the effect sizes of other groups did not reach statistical significance, the consistent signal across both regression and pairwise comparisons strengthen the interpretation that sustained antidepressant exposure may attenuate weight loss. However, given the relatively small sample size, these findings should be interpreted with caution.

Since %EBMIL is a sensitive measure of baseline BMI, the same weight loss may result in lower %EBMIL

in groups with higher baseline BMI. Supportingly, in this study, the group with the lowest %EBMIL was the group with the highest baseline BMI. Studies reported that %EBMIL acceleration in the first three months is strongly correlated with long-term results. Also, a small bougie size and leaving a shorter distance to the pylorus were found to be related to a higher %EBMIL (22,23).

Additionally, studies have linked antidepressant use to reduced rates of diabetes remission following bariatric procedures (12,24). However, these findings are constrained by small sample sizes and limited metabolic profiling. Larger-scale studies including diverse surgical techniques, detailed medication classifications, and extended follow-up are required to evaluate the long-term impact of psychiatric medications on both weight loss and metabolic outcomes.

Our study has several limitations. First, it was retrospective in design, relying on medical records that may lack complete accuracy. However, we attempted to mitigate this by directly verifying medication histories with patients. Second, serum drug levels were not measured, so changes in absorption, bioavailability, and pharmacokinetics could not be assessed. Third, patients were not stratified according to antidepressant subclass or metabolic indicators. Fourth, potential drug–drug interactions involving medications for comorbid conditions were not evaluated. Nonetheless, all psychiatric medications were prescribed and managed by a psychiatrist in accordance with standard treatment protocols. Lastly, clinical measures such as depression severity, psychological well-being, and quality of life were not evaluated in the context of this study.

Conclusion

According to a detailed literature search, this is among the few studies to evaluate the effects of antidepressants on weight loss outcomes specifically in patients undergoing OAGB. In conclusion, this study highlights a potential impact of continued antidepressant use on weight loss outcomes following OAGB surgery, showing significantly lower postoperative weight and %EBMIL in users compared to non-users and preoperative users. While overall weight trends favored non-users, no difference was seen in %TWL. These findings underscore the need for further research to better understand how antidepressants may influence bariatric success.

References

1. World Health Organization (WHO). Obesity and overweight. Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed: 24/03/2024.

2. Clapp B, Ponce J, Corbett J, et al. American Society for Metabolic and Bariatric Surgery 2022 estimate of metabolic and bariatric procedures performed in the United States. Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery 2024;20(5):425–431.

3. Musella M, Susa A, Greco, F et al. The laparoscopic mini-gastric bypass: the Italian experience: outcomes from 974 consecutive cases in a multicenter review. Surgical endoscopy 2014;28(1):156–163.

4. Parmar CD, Bryant C, Luque-de-Leon E, et al. One Anastomosis Gastric Bypass in Morbidly Obese Patients with BMI ≥50 kg/m^2: a Systematic Review Comparing It with Roux-En-Y Gastric Bypass and Sleeve Gastrectomy. Obesity surgery 2019;29(9):3039–3046.

5. Hall KD, Kahan S. Maintenance of Lost Weight and Long-Term Management of Obesity. The Medical Clinics of North America 2018;102(1):183–197.

6. Herstowska M, Przygocka-Pieniążek A, Grabowski K, Kaska Ł. Prevalence of mental disorders in patients with pathological obesity selected for bariatric surgery in the KOS-BAR nationwide multi-centre pilot programme - a preliminary report. Wideochirurgia i inne techniki maloinwazyjne = Videosurgery and other miniinvasive techniques 2023;18(3):502–509.

7. Arhi CS, Dudley R, Moussa O, Ardissino M, Scholtz S, Purkayastha S. The Complex Association Between Bariatric Surgery and Depression: a National Nested-Control Study. Obesity surgery 2021;31(5):1994–2001.

8. Mazereel V, Detraux J, Vancampfort D, van Winkel R, De Hert M. Impact of Psychotropic Medication Effects on Obesity and the Metabolic Syndrome in People with Serious Mental Illness. Frontiers in endocrinology 2020;11:573479.

9. Kozela M, Stepaniak U, Koziara K, Karpińska I, Major P, Matyja M. No association between history of psychiatric treatment and postoperative weight reduction after bariatric surgery. Eating and Weight Disorders 2024;29(1):19.

10. Rutledge R. The mini-gastric bypass: experience with the first 1,274 cases. Obesity surgery 2001 Jun;11(3):276–280.

11. Hawkins M, Leung SE, Lee A, et al. Psychiatric Medication Use and Weight Outcomes One Year After Bariatric Surgery. Psychosomatics 2020;61(1):56–63.
12. Plaeke P, Eede F Van Den, et al. Postoperative Continuation of Antidepressant Therapy is Associated with Reduced Short-Term Weight Loss Following Roux-en-Y Gastric Bypass Surgery. Langenbeck S Archives of Surgery 2019;404(5):621-631
13. Arterburn DE, Maciejewski ML, Berkowitz TSZ, et al. Does Long-Term Post-Bariatric Weight Change Differ Across Antidepressants? Annals of Surgery Open 2022;3(1):e114.
14. Brocks DR, Ben-Eltriki M, Gabr RQ, Padwal RS. The effects of gastric bypass surgery on drug absorption and pharmacokinetics. Expert opinion on drug metabolism & toxicology 2012;8(12):1505–1519.
15. Smith A, Henriksen B, Cohen A. Pharmacokinetic considerations in Roux-en-Y gastric bypass patients. American Journal of Health-System Pharmacy: AJHP, the Official Journal of the American Society of Health-System Pharmacists 2011;68(23):2241–2247.
16. Yano JM, Yu K, Donaldson GP, et al. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell 2015;161(2):264–276.
17. Gershon MD, Tack J. The Serotonin Signaling System: From Basic Understanding to Drug Development for Functional GI Disorders. Gastroenterology 2007;132(1):397–414.
18. Pasi PR, Kröll D, Siegfried A, et al. Plasma Concentrations of SSRI/SNRI After Bariatric Surgery and the Effects on Depressive Symptoms. Frontiers in Psychiatry 2023;14:1132112.
19. Carvalho AF, Sharma MS, Brunoni AR, Vieta E, Fava GA. The Safety, Tolerability and Risks Associated with the Use of Newer Generation Antidepressant Drugs: A Critical Review of the Literature. Psychotherapy and psychosomatics 2016;85(5):270–288.
20. Hainer V, Kabrnová K, Aldhoon B, Kunešová M, Wagenknecht M. Serotonin and Norepinephrine Reuptake Inhibition and Eating Behavior. Annals of the New York Academy of Sciences 2006;1083:252-269
21. Ljung T, Ahlberg AC, Holm, G et al. Treatment of abdominally obese men with a serotonin reuptake inhibitor: a pilot study. Journal of Internal Medicine 2001;250(3):219–224.
22. Philouze G, Voitellier E, Lacaze L, et al. Excess Body Mass Index Loss at 3 Months: A Predictive Factor of Long-Term Result after Sleeve Gastrectomy. Journal of obesity. 2017;2017:2107157.
23. Abd Ellatif ME, Abdallah E, Askar W, et al. Long term predictors of success after laparoscopic sleeve gastrectomy. International journal of surgery (London, England). 2014;12(5):504–508.
24. Thereaux J, Lesuffleur T, Czernichow S et al. Association Between Bariatric Surgery and Rates of Continuation, Discontinuation, or Initiation of Antidiabetes Treatment 6 Years Later. JAMA Surgery. 2018;153(6):526–533.

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Advancing Trends in Electroencephalography Monitoring in Anesthesia: A Bibliometric Analysis from 1980 to 2024

Anestezide Elektroensefalografi Monitörizasyonunda Gelişen Trendler: 1980'den 2024'e Bibliyometrik Analiz

Bülent Meriç Çam[1] | Ahmet Salih Tüzen[2] | Mürsel Kahveci[3] | Muhammet Aydın Akdoğan[1]

[1]Amasya University, Sabuncuoglu Serefeddin Training and Research Hospital, Department of Anesthesiology and Reanimation, Amasya, Türkiye
[2]İzmir Katip Celebi University Ataturk Training and Research Hospital, Department of Anesthesiology and Reanimation, İzmir, Türkiye
[3]Amasya University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Amasya, Türkiye

Sorumlu Yazar | Correspondence Author
Bülent Meriç Çam
bulentmericcam@gmail.com
Address for Correspondence: Göllübağları Mahallesi, Kudret Sokak 8/25 Merkez, Amasya, Türkiye.

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Advancing Trends in Electroencephalography Monitoring in Anesthesia: A Bibliometric Analysis from 1980 to 2024

ABSTRACT

This study examines research trends, productivity, and global academic collaborations related to electroencephalography (EEG) monitoring in anesthesia management. Articles published between 1980 and 2024 were analyzed using bibliometric methods in the Web of Science database. A total of 3,371 articles were identified, with anesthesiology, neuroscience, and clinical neurology being the most active areas. The United States (865 articles) and Germany (433 articles) were the leading contributors. The number of articles strongly correlated with economic indicators such as Gross Domestic Product-Purchasing Power Parity (GDP-PPP) (*r=0.885, p<0.001*). EEG monitoring has become a multidisciplinary field with high citation rates in anesthesiology and neuroscience journals. Key research topics include the bispectral index (BIS), Narcotrend index, entropy-based EEG analyses, and personalized anesthesia management. Developed countries drive innovation in this field, while equipment costs, technological requirements, and data interpretation complexity remain major barriers to widespread adoption of EEG-based anesthesia monitoring.

Keywords: Anesthesia, Bibliometric analysis, Electroencephalogram, Electroencephalography.

ÖZET

Bu çalışma, anestezi yönetiminde elektroensefalografi (EEG) monitörizasyonu ile ilgili araştırma eğilimlerini, üretkenliği ve küresel akademik iş birliklerini incelemektedir. 1980-2024 yılları arasında yayımlanan makaleler, Web of Science veri tabanında bibliyometrik analiz yöntemiyle değerlendirilmiştir. Toplam 3.371 makale tespit edilmiş olup en aktif araştırma alanları anesteziyoloji, sinir bilimleri ve klinik nörolojidir. ABD (865 makale) ve Almanya (433 makale) en fazla katkı sağlayan ülkeler olarak öne çıkmıştır. Makale sayısı, Gayri Safi Yurtiçi Hasıla-Satın Alma Gücü Paritesi (GDP-PPP) gibi ekonomik göstergelerle güçlü bir ilişki göstermiştir (*r=0.885, p<0.001*). EEG izlemi, anesteziyoloji ve sinir bilimi dergilerinde yüksek atıf oranlarıyla çok disiplinli bir alan olarak öne çıkmaktadır. Öne çıkan araştırma konuları arasında Bispektral indeks (BIS), Narcotrend indeksi, entropi temelli EEG analizleri ve EEG verilerine dayalı kişiselleştirilmiş anestezi yönetimi yer almaktadır. Gelişmiş ülkeler bu alanda yeniliklerin öncüsü konumundadır. Ancak ekipman maliyetleri, teknolojik gereksinimler ve veri yorumlamanın karmaşıklığı, EEG tabanlı anestezi izleminin yaygınlaşmasını kısıtlayan temel engeller arasında yer almaktadır.

Anahtar Sözcükler: Anestezi, Bibliyometrik analiz, Elektroensefalogram, Elektroensefalografi.

Introduction

The application of electroencephalographic (EEG) monitoring in anesthesia has gained increasing prominence in recent years due to the demand for a more accurate and objective assessment of anesthesia depth (1,2). Traditional monitoring methods, which rely on physiological markers such as heart rate and blood pressure, as well as objective parameters like minimum alveolar concentration (MAC) or target-controlled anesthesia (TCA), are often indirect and may not fully capture the complex effects of anesthetic agents on the brain (3). In contrast, EEG monitoring directly measures electrical brain activity, providing a real-time view of the patient's cerebral status. This allows for more precise titration of anesthetic dosage, reducing the risk of intraoperative awareness or oversedation (4,5).

Various indices derived from EEG signals attempt to quantify anesthetic depth numerically. In this context, commercial systems such as the bispectral index (BIS) and Narcotrend have become increasingly widespread. However, these indices tend to reduce complex brain activity to a single numerical value, which imposes certain limitations (5,6). EEG signals can vary depending on the anesthetic agents used and the individual's unique brain structure (5-7). Advanced methods such as the density spectral array (DSA) reflect this trend (7,8). As a result, recent years have seen a growing emphasis on the direct analysis of raw EEG data and its integration into clinical decision-making (5,7)

EEG monitoring not only enhances intraoperative safety but also has the potential to promote faster postoperative cognitive recovery, facilitate early extubation, and reduce complications (4,5,8,9). In neuroanesthesia, it is indispensable for real-time monitoring of cerebral function during procedures such as epilepsy surgery, tumor resections, and awake craniotomies (10,11).

As EEG monitoring techniques become more refined and widely adopted, they are expected to enhance the standards of perioperative care and improve overall patient outcomes (5). Despite these benefits, several limitations must be considered. A primary challenge is the interpretation of raw EEG data, which is inherently complex and requires a high level of expertise, as signals can vary significantly depending on the anesthetic agent used and the patient's individual cerebral characteristics. Additionally, EEG-derived indices such as BIS can oversimplify the brain's dynamic activity by reducing the raw data to a single number, which may result in less accurate assessments of anesthesia depth (1). Another limitation is the high sensitivity of EEG signals to artifacts from muscle activity, electrical interference, and patient movements.

Given these challenges and considering the potential of EEG monitoring to provide a more accurate reflection of the brain's response to anesthesia, a bibliometric analysis of research in this area is warranted. This study aims to systematically analyze the literature published between 1980 and 2024 in order to evaluate the role of EEG in anesthesiology practice, identify research trends, and map scientific collaborations.

Material and Method

The literature review was conducted using the WoS (Clarivate Analytics, Jersey, USA) database, accessed on 26 September 2024. A bibliometric analysis was conducted on all articles in the WoS database published between 1980 and 2024 that contain the specified search keywords. The search employed the following keywords: 'Electroencephalography' OR 'Electrocorticography' OR 'Electroencephalogram' OR 'Electrocorticogram' OR 'Electroencephalographic' OR 'Electrocorticographic' OR 'EEG' OR 'ECoG' OR 'Alpha Wave' OR 'Alpha Band' OR 'Alpha Activity' OR 'Beta Wave' OR 'Beta Band' OR 'Beta Activity' OR 'Theta Wave' OR 'Theta Band' OR 'Theta Activity' OR 'Delta Wave' OR 'Delta Band' OR 'Delta Activity' OR 'Slow Wave' OR 'Slow Activity' OR 'High Frequency' OR 'Low Frequency' OR 'Suppression Ratio' OR 'Burst Suppression' OR 'Brain Wave' OR 'Frequency Band' OR 'Bispectral index' OR 'Patient State Index' OR 'Narcotrend Index' OR 'Density Spectral Array' OR 'Power Spectral Density' OR 'Spectral Edge Frequency' OR 'Local Field Potential' OR 'Oscillatory' OR 'Oscillation' OR 'Spike' OR 'Amplitude' OR 'Event-Related Potential' OR 'Depth of Anesthesia' OR 'Anesthesia Depth' OR 'Anesthetic depth' (Title) and 'Anesthesia' OR 'Anaesthesia' (Topic); Timespan: 1980-2024. Indexes: A&HCI, BKCI-SSH, BKCI-S, ESCI, CPCI-SSH, CPCI-S, SCI-EXPANDED, SSCI. VOSviewer

(version 1.6.20) software was used to visualize the bibliometric network.

Statistical analyses were conducted using SPSS version 24.0 (IBM Corp, Armonk, NY, USA). Data normality was assessed with the Shapiro–Wilk test. Pearson correlation analysis was used to evaluate the relationship between the number of articles produced by countries and economic and developmental indicators, including gross domestic product (GDP), gross domestic product purchasing power parity (GDP-PPP), and the human development index (HDI). A *p-value of less than 0.05* was considered statistically significant.

Results

The literature screening identified a total of 4,358 published items. Among these, 3,371 were articles, 366 were proceedings papers, 321 were meeting abstracts, 180 were letters, and 141 were reviews. The remaining 116 items include editorial materials, early access publications, corrections, notes, book chapters, retracted publications, and news items. Only 3,371 articles were included in the bibliometric analysis. The 3,371 articles received a total of 44,956 citations, of which 42,210 citations excluded self-citations. The h-index of these articles was 124, and an average of 27.28 citations was received per article. Of these, 96% (n = 3,233) were published in English. The remaining 4% were in other languages: German (n = 76), French (19), Spanish (16), Portuguese (9), Russian (7), Turkish (4), Polish (2), Chinese (1), Japanese (1), Korean (1), Italian (1), and Unspecified (1)

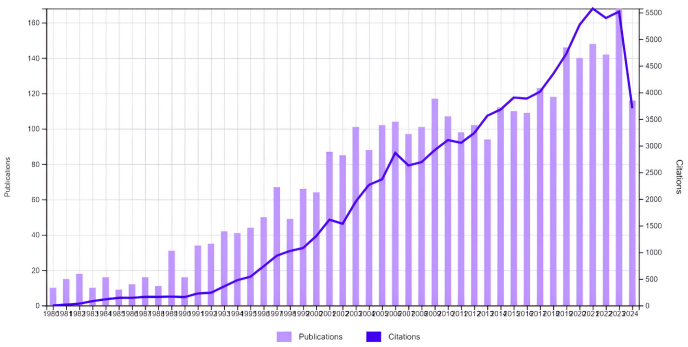

Figure I. Number of Publications and Citations by Years on EEG Studies in Anesthesiology

Research fields: The leading 10 research fields for the published articles were anesthesiology (1,468, 43.5%), neurosciences (578, 17.1%), clinical neurology (329, 9.8%), veterinary sciences (160, 4.7%), engineering biomedical (157, 4.7%), surgery (156, 4.6%), medicine general internal (131, 3.9%), physiology (127, 3.8%), critical care medicine (110, 3.3%), multidisciplinary sciences (108, 3.2%).

Table I. Correlation Analysis

	Record Count			
	n	df	r	p
HDI	73	71	0.279	***0.017***
GDP (million dollar)	73	71	0.884	***0.000***
GDP PPP (million dollar)	71*	69	0.736	***0.000***

GDP: Gross Domestic Product; GDP-PPP: Gross Domestic Product Purchasing Power Parity; HDI: Human Development Index; r: Pearson Correlation coefficient; df: degrees of freedom
* Cuba and Taiwan were excluded from the analysis due to the unavailability of their GDP-PPP data on the official source

As shown in Figure I, the number of publications per year remained low during the 1980s but began to increase significantly starting in the 2000s. The number of publications peaked between 2021 and 2023, with a slight decline observed in 2024.

The number of citations, on the other hand, has increased cumulatively over the years. This trend indicates that EEG monitoring is not only a popular topic but also a field of research that generates high-impact contributions.

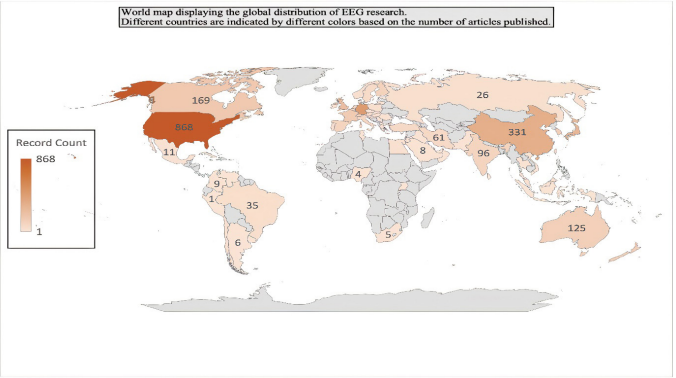

Figure II. World Map for The Publication Productivity of Worldwide Countries on EEG Studies in Anesthesiology

Top countries

Figure II presents the distribution of articles across various countries. The active countries contributing more than 100 articles were the United States of America (USA) (865), Germany (433), China (330),

Japan (274), England (199), Canada (169), France (149), New Zealand (137), Australia (124), South Korea (123), Netherlands (114), Finland (110), Belgium (104), Switzerland (102). A total of 93 countries produced 3,371 articles. Figure III presents the network map illustrating international cooperation among the 38 countries that had published at least 10 articles. Publications originating from the United States show strong collaboration with Germany, Canada, the United Kingdom, and China. Similarly, Germany maintains close ties with Japan, the Netherlands, and the Scandinavian countries. This indicates that both transatlantic and intra-continental collaborations play a prominent role in EEG research (Figure III).

Table II. Active Journals on EEG Studies in Anesthesiology

Journals	RC	C	AC
Anesthesia and Analgesia	246	1,304	5.3
British Journal of Anaesthesia	231	1,159	5.0
Anesthesiology	194	1,179	6.1
Journal Of Clinical Monitoring and Computing	72	281	3.9
Acta Anaesthesiologica Scandinavica	69	373	5.4
European Journal of Anaesthesiology	68	346	5.1
Clinical Neurophysiology	57	471	8.3
Journal of Neurosurgical Anesthesiology	52	268	5.2
Anaesthesia	51	376	7.4
Journal of Neurophysiology	50	618	12.4
Journal of Clinical Anesthesia	44	248	5.7
Pediatric Anesthesia	40	294	7.4
Plos One	38	500	13.2
BMC Anesthesiology	37	215	5.9
Frontiers In System Neuroscience	33	155	4,7
Anaesthesist	32	195	6.1
Anaesthesia and Intensive Care	29	149	5.1
Scientific Reports	29	445	15.3
Neuroscience	28	401	14.3
Journal of Neuroscience	27	808	29.9
IEEE Transactions on Biomedical Engineering	25	180	7.2
Canadian Journal of Anaesthesia Journal Canadien D'Anesthesie	23	146	6.3
Veterinary Anaesthesia and Analgesia	22	128	5.8
Journal of Cardiothoracic and Vascular Anesthesia	21	263	12.5
Korean Journal of Anesthesiology	21	112	5.3
Neuroimage	21	458	21.8

RC: Record Count, C: Number of Citation, AC: Average Citation Per Document.

Correlation analysis

The normality of the data distribution was assessed using the Shapiro-Wilk test (WRC=0.491, WGDP=0.891, WGDP-PPP=0.331, WHDI=0.410). GDP and GDP-PPP data were obtained from the official website of the World Bank using 2023 data, while HDI data were sourced from the official website of the United Nations Development Programme (https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=, https://data.worldbank.org/indicator/NY.GDP.MKTP.PP.KD?locations=, https://hdr.undp.org/data-center/country-insights#/ranks). Statistically significant correlations were observed between the number of articles published by countries on EEG studies in anesthesiology and GDP, GDP-PPP, and HDI, with corresponding *p-values of p<0.001, p<0.001, and p=0.017, respectively* (Table I). These findings indicate that countries with a high level of economic development are more active in producing publications related to EEG.

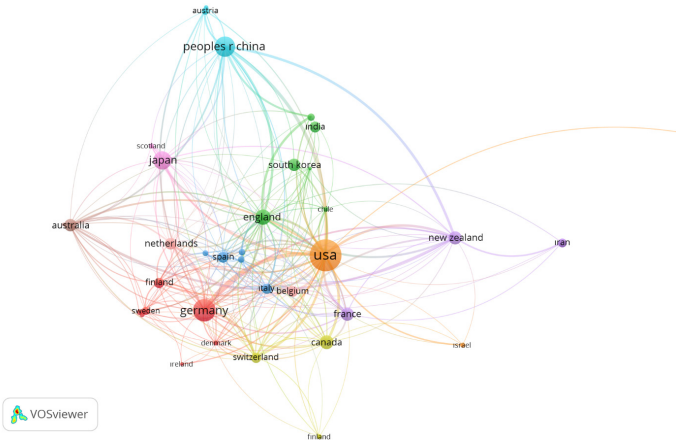

Figure III. Network Visualization Map for International Collaboration of Worldwide Countries on EEG Studies in Anesthesiology

Top journals

The 3,371 articles were published in a total of 1,081 journals. Among these, 26 journals published at least 20 articles on the topic. Table II presents the top 26 journals, which collectively contributed the majority of the articles. The last column of the table displays the total citation count for each journal, along with the average citation number per article. Notably, neuroscience journals such as Journal of Neuroscience and NeuroImage have achieved high average citation counts. The high average citation counts in neuroscience journals, in particular, highlight the multidisciplinary impact of EEG research.

Figure IV presents the journal-based citation density of publications in the field of EEG monitoring.

Among the leading contributors are prestigious journals such as: Anesthesiology, Anesthesia and Analgesia, British Journal of Anaesthesia, Journal of Neuroscience, Journal of Neurophysiology. This indicates that research on EEG is not limited to the field of anesthesia but also maintains strong ties with the neurosciences.

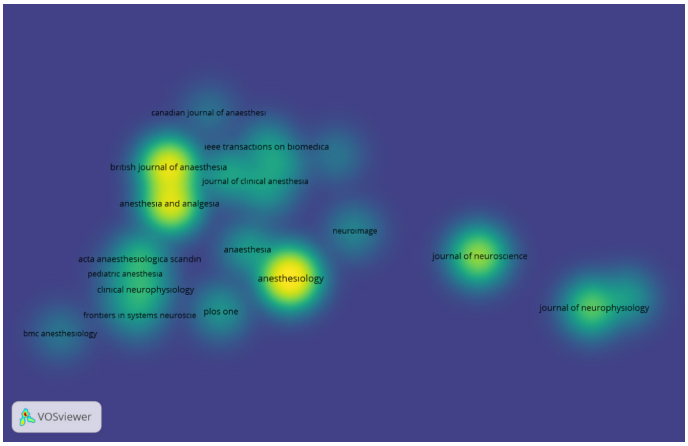

Figure IV. Density Map for Citation Analysis of Active Journals on EEG Studies in Anesthesiology

Top organizations

Table III presents the top 25 contributing institutions based on the number of articles published.

Table III. Active Affiliations on EEG Studies in Anesthesiology

Affiliations	RC	Affiliations	RC
Harvard University	139	Berlin Institute of Health	44
Harvard Medical School	102	Charite Universitatsmedizin Berlin	44
Massachusetts General Hospital	85	Massachusetts Institute of Technology Mit	44
University of California System	83	University of Bonn	41
Technical University of Munich	74	Institut National De La Sante Et De La Recherche Medicale Inserm	40
University of Auckland	57	Laval University	39
Hannover Medical School	53	Ghent University	38
Waikato Hospital	52	University of Pennsylvania	38
Capital Medical University	51	University of London	35
Tampere University	51	University of Michigan	35
Humboldt University of Berlin	47	University of Michigan System	35
Free University of Berlin	46	University of Texas System	35
Washington University Wustl	46		

RC: Record Count

Top authors

The top 15 most prolific authors were: Jamie W. Sleigh (or James W.) (combined total: 77), Gerhard Schneider (51), Matthias Kreuzer (40), Patrick L. Purdon (39), Emery N. Brown (39), Craig B. Johnson (37), Michel R. F. Struys (31), Arvi M. Yli-Hankala (31), Mircea Steriade (27), Jörgen Bruhn (25), Shouzen Fan (25), Michael S. Avidan (24), Darren Hight (24), and Xiaoli Li (24) in descending order.

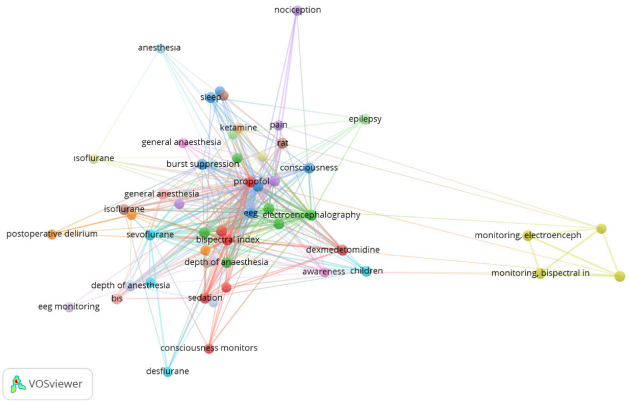

Figure V. Network Visualization Cluster Map for Keyword Analysis on EEG Studies in Anesthesiology

Citation analysis

Table IV presents the 15 most cited articles in the field of anesthesiology, selected by choosing 'anesthesiology' in the citation topic meso category of WoS (13-27). The last column of the table includes the annual citation count for each article. The majority of these articles appear to focus on BIS and the loss and recovery of consciousness. This underscores the dominant position of the BIS index in the scientific literature and the central role of concerns related to intraoperative awareness.

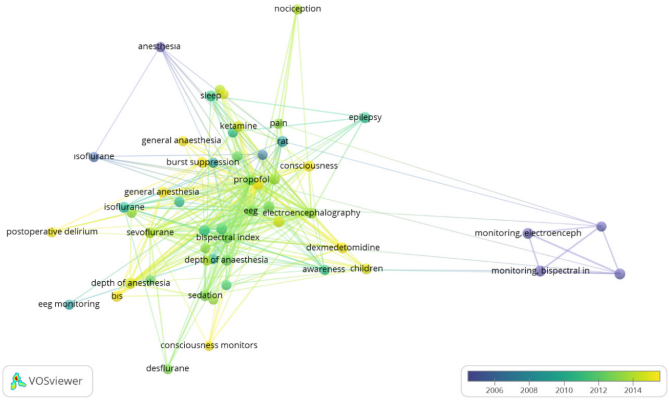

Figure VI. Network Visualization

Table IV. The 15 Most Cited Manuscripts on EEG Studies in Anesthesiology

No.	Article	Author	Journal	PY	TC	AC
1	Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial (13)	Myles PS et al.	Lancet	2004	792	37.71
2	Anesthesia awareness and the bispectral index (14)	Avidan MS et al.	New England Journal of Medicine	2008	564	33.18
3	Electroencephalogram signatures of loss and recovery of consciousness from propofol (15)	Purdon PL et al.	Proceedings of The National Academy of Sciences of The United States of America	2013	541	45.08
4	Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia (16)	Gan TJ et al.	Anesthesiology	1997	464	16.57
5	Measuring the performance of anesthetic depth indicators (17)	Smith WD et al.	Anesthesiology	1996	355	12.24
6	Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation (18)	Liu J et al.	Anesthesia and Analgesia	1997	330	11.79
7	Hospital Stay and Mortality Are Increased in Patients Having a "Triple Low" of Low Blood Pressure, Low Bispectral Index, and Low Minimum Alveolar Concentration of Volatile Anesthesia (19)	Sessler DI et al.	Anesthesiology	2012	318	24.46
8	A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect (20)	Sebel PS et al.	Anesthesia and Analgesia	1997	305	10.89
9	Propofol Anesthesia and Sleep: A High-Density EEG Study (21)	Murphy M et al.	Sleep	2011	279	19.93
10	Titration of volatile anesthetics using bispectral index facilitates recovery after ambulatory anesthesia (22)	Song DJ et al.	Anesthesiology	1997	278	9.93
11	Approximate entropy as an electroencephalographic measure of anesthetic drug effect during desflurane anesthesia (23)	Bruhn J et al.	Anesthesiology	2000	274	10.96
12	Cortical and thalamic cellular correlates of electroencephalographic burst-suppression (24)	Steriade M et al.	Electroencephalography and Clinical Neurophysiology	1994	248	8.00
13	Electroencephalographic derivatives as a tool for predicting the depth of sedation and anesthesia induced by sevoflurane (25)	Katoh T et al.	Anesthesiology	1998	247	9.15
14	Electroencephalographic quantitation of opioid effect-comparative pharmacodynamics of fentanyl and sufentanil (26)	Scott JS et al.	Anesthesiology	1991	243	7.15
15	The Ageing Brain: Age-dependent changes in the electroencephalogram during propofol and sevoflurane general anaesthesia (27)	Purdon PL et al.	British Journal of Anaesthesia	2015	241	24.10

No: Number; PY: Publication Year; TC: Total Citation; AC: Average Citations Per Year

Co-citation analysis

The 3,371 articles referenced a total of 57,724 publications. Among these, 10 publications received more than 150 citations. These publications receiving most citations are, in order, Rampil Ij et al. (1998) (Number of citations: 479), Glass Ps et al. (1997) (338), Myles Ps et al. (2004) (205), Purdon Pl et al. (2015) (203), Gan Tj et al. (1997) (192), Sigl Jc et al. (1994) (189), Johansen Jw et al. (2000) (177), Purdon Pl et al. (2013) (175), Smith Wd et al. (1996) (155) and Brown En et al. (2010) (155) (13, 15-17, 28-33).

Keywords

A total of 5,234 different keywords were identified in the 3,371 articles. The clustering of 53 keywords that appeared in at least 20 publications is presented in Figure V, while their temporal trends are shown in Figure VI. Table V lists the most frequently used terms. Figure V illustrates the clustering of 53 keywords that appeared in at least 20 different publications. In this analysis, core concepts such as EEG, bispectral index, depth of anesthesia, propofol, burst suppression, and consciousness are positioned at the center.

Figure VI presents the temporal trend of these keywords over the years. Terms such as bispectral index and depth of anesthesia show a marked increase after 2005, while in recent years, concepts like propofol, dexmedetomidine, and consciousness monitors have gained prominence. The concepts of Narcotrend and entropy appeared within the same cluster, and this group has shown an increase over

Table V. The Trend Keywords on EEG Studies in Anesthesiology

Keywords	O	Keywords	O	Keywords	O
Bispectral Index	339	Monitoring, Bispectral Index	50	Hippocampus	27
Propofol	292	Remifentanil	49	Nociception	26
Anesthesia	266	Sleep	48	Postoperative Delirium	26
Electroencephalography	252	Epilepsy	46	Midazolam	24
EEG	238	Ketamine	43	Fentanyl	23
Electroencephalogram	209	Depth of Anaesthesia	42	Cardiac Surgery	23
Sevoflurane	139	Entropy	41	Isoflurane	23
Monitoring	117	Monitoring, Electroencephalography	39	Surgery	23
Depth Of Anesthesia	101	Children	37	Bispectral Index Monitoring	22
Anaesthesia	98	Anaesthesia, Depth	36	Narcotrend	21
General Anesthesia	91	Electroencephalogram (EEG)	35	Desflurane	21
Sedation	89	Consciousnees Monitors	32	Halothane	21
Burst Suppression	69	Awareness	30	Spectral Analysis	21
Dexmedetomidine	57	Bispectral Index	29	Anesthesıa	21
Consciousness	53	Cardipulmonary Bypass	29	Seizure	20
BIS	53	General Anaesthesia	29	Electrocorticography	20
Rat	52	Pain	28	EEEG Monitoring	20
Isoflurane	51	Anaesthetics I.V., Propofol	28		

O: number of occurrences.

the past five years.

Discussion

This bibliometric analysis aims to provide a comprehensive overview of publication trends, scientific productivity, and international collaborations in the field of EEG monitoring in anesthesia. Our findings reveal an increasing number of publications focused on the use of EEG to optimize the depth of anesthesia, alongside a shift towards more advanced and sensitive monitoring techniques in perioperative care. In this context, the current literature demonstrates a clear trend away from traditional physiological markers towards real-time brain activity monitoring using EEG-derived indices such as the BIS and the Narcotrend index (2). Despite the limitations associated with BIS, it remains the most frequently cited topic in EEG-related anesthesia research (9,34). In contrast, other EEG-derived indices, such as the Narcotrend index and density spectral array (DSA), receive less attention, despite new evidence suggesting their potential advantages in specific clinical context (35-37). Despite the availability of alternative techniques, the continued preference for BIS monitoring suggests a conservative approach to the adoption of newer methods.

The United States of America and Germany are recognized as leaders in the number of active research centers. This leadership can be attributed to the critical role of substantial economic resources, advanced research institutions, and technological capabilities in generating high-impact research. As demonstrated in previous studies, economically advanced countries with strong financial foundations and higher human development indices tend to contribute more significantly to the global scientific output (38, 39). Our findings align with this trend, showing that nations with higher GDP and GDP-PPP are more productive in EEG-related research, particularly in the field of anesthesia. It can be concluded that economically developed countries with higher GDP and HDI levels make greater academic contributions, particularly in specialized areas such as anesthesia and neuroscience. Similarly, while the United States, Germany, and China lead in terms of publication volume, countries such as Japan and the United Kingdom also produce a substantial number of publications. This further highlights that contributions to specialized academic fields are significant in countries with strong economic foundations. Moreover, it is not surprising that research from these nations also ranks highly in terms of citation counts.

In terms of publication impact, it is evident that

leading journals in the field of anesthesia are also the most significant contributors to the literature on this topic. However, the high citation rates observed in neuroscience journals suggest that EEG monitoring research extends beyond perioperative anesthesia and provides broader insights into brain function. Additionally, our findings point to a growing interest in integrating EEG data with patient-specific cerebral characteristics to develop more personalized anesthesia management systems (40-42). In the future, the use of algorithms with high temporal and spatial resolution to analyze EEG signals may facilitate the development of patient-specific anesthesia protocols. Moreover, the integration of EEG data with other physiological markers—such as hemodynamic parameters, pupillometry, and cerebral oximetry—within multimodal monitoring systems could allow for a more comprehensive assessment of the patient's neurophysiological state during anesthesia. Especially in elderly patients, EEG-guided individualized anesthetic titration may become central to perioperative care strategies aimed at preventing postoperative cognitive dysfunction. Despite these advancements, several challenges continue to hinder the widespread adoption of EEG monitoring, including high equipment costs, limited accessibility, the need for specialized training, and the complexity of interpreting raw EEG data (43,44). Overcoming these barriers is crucial for maximizing the clinical utility of EEG monitoring and improving anesthesia management.

Future research should focus on the development of artificial intelligence-driven clinical decision support tools capable of real-time interpretation of EEG data, and randomized controlled trials should be conducted to evaluate their impact on patient outcomes. Furthermore, studies examining whether EEG-derived indices vary according to age, neurological status, and type of surgery will be essential to inform more refined clinical guidelines. Ultimately, the role of EEG in anesthesia may evolve beyond depth monitoring to become a core component of personalized and goal-directed anesthesia care.

In addition, our study has certain limitations. The analysis was based on data from the WoS database, which may have excluded relevant studies indexed in other databases such as PubMed or Scopus, potentially limiting the scope of this analysis. Furthermore, the study primarily focused on quantitative metrics, such as publication counts and citation rates, without assessing the clinical significance of the findings. Future analyses should incorporate clinical relevance metrics to provide a more comprehensive understanding of the field.

Conclusion

The increasing trend in publications on EEG monitoring in anesthesia highlights the growing interest and use of EEG as a critical tool for enhancing patient safety and optimizing anesthesia practice These findings indicate that the most productive countries in this field are those with higher levels of economic development. Therefore, low-cost EEG solutions should be encouraged for developing countries.

References

1. Sun Y, Wei C, Cui V, Xiu M, Wu A. Electroencephalography: Clinical applications during the perioperative period. Front Med (Lausanne) 2020;7:251.

2. Laferrière-Langlois P, Morisson L, Jeffries S, Duclos C, Espitalier F, Richebé P. Depth of anesthesia and nociception monitoring: current state and vision for 2050. Anesth Analg 2024;138(2):295-307.

3. Bouchez S, Fraipont V, Momeni M, Rex S, De Hert S. Perioperative hemodynamic monitoring techniques: a narrative review. Acta Anaesthesiologica Belgica 2024;75:125-138.

4. Montupil J, Defresne A, Bonhomme V. The raw and processed electroencephalogram as a monitoring and diagnostic tool. J Cardiothorac Vasc Anesth 2019;33 Suppl 1:s3-10.

5. Bonatti G, Iannuzzi F, Amodio S, et al. Neuromonitoring during general anesthesia in non-neurologic surgery. Best Pract Res Clin Anaesthesiol 2021;35(2):255-266.

6. Fleischmann A, Georgii MT, Schuessler J, Schneider G, Pilge S, Kreuzer M. Always assess the raw electroencephalogram: why automated burst suppression detection may not detect all episodes. Anesth Analg 2023;136(2):346-354.

7. Fahy BG, Chau DF. The technology of processed electroencephalogram monitoring devices for assessment of depth of anesthesia. Anesth Analg 2018;126(1):111-117.

8. Shander A, Lobel GP, Mathews DM. Brain monitoring and the depth of anesthesia: another goldilocks dilemma. Anesth

Analg 2018;126(2):705-709.
9. Roche D, Mahon P. Depth of anesthesia monitoring. Anesthesiol Clin. 2021;39(3):477-492.
10. Khoo HM, Hall JA, Dubeau F, et al. Technical aspects of SEEG and its interpretation in the delineation of the epileptogenic zone. Neurol Med Chir (Tokyo) 2020;60(12):565-580.
11. Domingo RA, Vivas-Buitrago T, De Biase G, et al. Intraoperative seizure detection during active resection of glioblastoma through a novel hollow circular electrocorticography array. Oper Neurosurg (Hagerstown) 2021;21(2):e147-152.
12. Larkin CM, O'Brien DF, Maheshwari D. Anaesthesia for epilepsy surgery. BJA Education 2019;19(12):383-389.
13. Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. Lancet 2004;363(9423):1757-1763.
14. Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. N Engl J Med 2008;358(11):1097-1108.
15. Purdon PL, Pierce ET, Mukamel EA, et al. Electroencephalogram signatures of loss and recovery of consciousness from propofol. Proc Natl Acad Sci USA 2013;110(12):E1142-1151.
16. Gan TJ, Glass PS, Windsor A, et al. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. BIS Utility Study Group. Anesthesiology 1997;87(4):808-815.
17. Smith WD, Dutton RC, Smith NT. Measuring the performance of anesthetic depth indicators. Anesthesiology 1996;84(1):38-51.
18. Liu J, Singh H, White PF. Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. Anesth Analg 1997;84(1):185-189.
19. Sessler DI, Sigl JC, Kelley SD, et al. Hospital stay and mortality are increased in patients having a "triple low" of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. Anesthesiology 2012;116(6):1195-1203.
20. Sebel PS, Lang E, Rampil IJ, et al. A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect. Anesth Analg 1997;84(4):891-899.
21. Murphy M, Bruno MA, Riedner BA, et al. Propofol anesthesia and sleep: a high-density EEG study. Sleep 2011;34(3):283-291A.
22. Song D, Joshi GP, White PF. Titration of volatile anesthetics using bispectral index facilitates recovery after ambulatory anesthesia. Anesthesiology 1997;87(4):842-848.
23. Bruhn J, Röpcke H, Hoeft A. Approximate entropy as an electroencephalographic measure of anesthetic drug effect during desflurane anesthesia. Anesthesiology 2000;92(3):715-726.
24. Steriade M, Amzica F, Contreras D. Cortical and thalamic cellular correlates of electroencephalographic burst-suppression. Electroencephalogr Clin Neurophysiol 1994;90(1):1-16.
25. Katoh T, Suzuki A, Ikeda K. Electroencephalographic derivatives as a tool for predicting the depth of sedation and anesthesia induced by sevoflurane. Anesthesiology 1998;88(3):642-650.
26. Scott JC, Cooke JE, Stanski DR. Electroencephalographic quantitation of opioid effect: comparative pharmacodynamics of fentanyl and sufentanil. Anesthesiology 1991;74(1):34-42.
27. Purdon PL, Pavone KJ, Akeju O, et al. The Ageing Brain: Age-dependent changes in the electroencephalogram during propofol and sevoflurane general anaesthesia. Br J Anaesth 2015;115 Suppl 1(Suppl 1):i46-57.
28. Rampil IJ. A primer for EEG signal processing in anesthesia. Anesthesiology 1998;89(4):980-1002.
29. Glass PS, Bloom M, Kearse L, Rosow C, Sebel P, Manberg P. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. Anesthesiology 1997;86(4):836-847.
30. Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical electroencephalography for anesthesiologists: part ı: background and basic signatures. Anesthesiology 2015;123(4):937-960.
31. Sigl JC, Chamoun NG. An introduction to bispectral analysis for the electroencephalogram. J Clin Monit 1994;10(6):392-404.
32. Johansen JW, Sebel PS. Development and clinical application of electroencephalographic bispectrum monitoring. Anesthesiology 2000;93(5):1336-1344.
33. Brown EN, Lydic R, Schiff ND. General anesthesia, sleep, and coma. N Engl J Med 2010;363(27):2638-2650.
34. Vacas S, Hudson AE. Seen and ignored: are we undermining studies of brain health ınterventions before we start? Anesth Analg 2020;131(2):464-465.
35. Chen N, Lu J. Meta-analysis of the prognostic value of narcotrend monitoring of different depths of anesthesia and different bispectral ındex (bıs) values for cognitive dysfunction after tumor surgery in elderly patients. J Healthc Eng 2022;2022:8554188.
36. Ma X, Zhao X, Guo R, Hu Z, Liu J, Nie H. Value of narcotrend anesthesia depth monitoring in predicting POCD in gastrointestinal tumor anesthesia block patients. BMC Anesthesiol 2024;24(1):371.
37. de Heer IJ, Raab HAC, Krul S, Karaöz-Bulut G, Stolker RJ, Weber F. Electroencephalographic density spectral array monitoring during propofol/sevoflurane coadministration in children, an exploratory observational study. Anaesth Crit Care Pain Med 2024;43(2):101342.
38. Kayir S, Kisa A. The evolution of the regional anesthesia: a holistic investigation of global outputs with bibliometric

analysis between 1980-2019. Korean J Pain 2021;34(1):82-93.
39. Asefzadeh S, Jahandideh S, Mousavi A. Relationship between Human Development Index and the number of scientific articles of countries. JQUMS 2013;17(2):33-40.
40. Zhang Y, Yan F, Wang Q, Wang Y, Huang L. Pre-anesthetic brain network metrics as predictors of individual propofol sensitivity. Comput Methods Programs Biomed 2024;257:108447.
41. Liang Z, Lan Z, Wang Y, et al. The EEG complexity, information integration and brain network changes in minimally conscious state patients during general anesthesia. J Neural Eng. 2023;20(6):066030
42. Romagnoli S, Franchi F, Ricci Z. Processed EEG monitoring for anesthesia and intensive care practice. Minerva Anestesiol 2019;85(11):1219-1230.
43. Oliva AM, Montejano J, Simmons CG, Vogel SA, Isaza CF, Clavijo CF. New frontiers in intraoperative neurophysiologic monitoring: a narrative review. Ann Transl Med 2023;11(11):388.
44. Manohara N, Ferrari A, Greenblatt A, et al. Electroencephalogram monitoring during anesthesia and critical care: a guide for the clinician. J Clin Monit Comput 2025;39(2):315-348.

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Non-traditional Topical Negative Pressure Applications

Geleneksel Olmayan Topikal Negatif Basınç Uygulamaları

Said Algan[1] | İhtişam Zafer Cengiz[2]

[1]Gaziosmanpasa Avrasya Hospital, Department of Plastic Reconstructive and Aesthetic Surgery, İstanbul, Türkiye
[2]Atlas University Hospital, Department of Plastic Reconstructive and Aesthetic Surgery, İstanbul, Türkiye

Sorumlu Yazar | Correspondence Author
Said Algan
saidalgan@gmail.com
Address for Correspondence: Department of Plastic Reconstructive and Aesthetic Surgery, Fevzi Cakmak Mh. Hekimsuyu Cd no.26/34 Küçükköy Gaziosmanpasa 34250 Istanbul, Türkiye

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Non-traditional Topical Negative Pressure Applications

ABSTRACT

Topical negative pressure is one of the first treatment methods that comes to mind for chronic wound closure in recent years, and especially in reconstructive surgery, topical negative pressure therapy is a definitive treatment method that is frequently used. The purpose of this article is to compile non-traditional applications in the literature and to prompt scientists to form thoughts on the usability of this method in different areas. Considering the experimental and clinical research conducted for non-traditional topical negative pressure applications, although positive results were obtained in many of them, it is understood that more comprehensive research is required since there are not enough subjects or patients. We think that it can be applied to clinical practice, especially in the experimentally proven hypothermia-induced myocardial infarction and flap delay issues.

Keywords: Negative pressure, Plastic surgery, Topical, Vacuum.

ÖZET

Topikal negatif basınç, son yıllarda kronik yara kapanmasında akla gelen ilk tedavi yöntemlerinden biri olup, özellikle rekonstrüktif cerrahide topikal negatif basınç tedavisi sıklıkla kullanılan kesin bir tedavi yöntemidir. Bu makalenin amacı literatürdeki geleneksel olmayan uygulamaları derlemek ve bilim insanlarını bu yöntemin farklı alanlarda kullanılabilirliği konusunda düşünce oluşturmaya teşvik etmektir. Geleneksel olmayan topikal negatif basınç uygulamaları için yapılan deneysel ve klinik araştırmalar göz önüne alındığında, birçoğunda olumlu sonuçlar elde edilmesine rağmen, yeterli sayıda denek veya hasta olmadığından daha kapsamlı araştırmalara ihtiyaç duyulduğu anlaşılmaktadır. Özellikle deneysel olarak kanıtlanmış hipotermi kaynaklı miyokard enfarktüsü ve flep gecikmesi sorunlarında klinik pratiğe uygulanabileceğini düşünmekteyiz.

Anahtar Sözcükler: Negatif Basınç, Plastik cerrahi, Topikal, Vakum.

Introduction

Wound healing is one of the most important factors affecting patient comfort, hospitalization, and survival. While clean wounds formed after surgery can heal faster and easier within days, chronic wounds may not close for weeks, months, or even years. Topical Negative Pressure (TNP) is one of the first treatment methods that comes to mind for chronic wound closure in recent years, and especially in reconstructive surgery, TNP therapy is a definitive treatment method that is frequently used. Voinchet and Magalon used the term negative pressure-assisted wound and named it vacuum-assisted closure (VAC) (1). Morykwas and Argenta investigated the most comprehensive experimental and clinical applications in the literature regarding TNP (2,3). They proved that TNP increases local blood circulation, accelerates granulation tissue formation, increases survival of random patterned flaps, and reduces the level of bacteria in the wound (2). Since then, TNP has been used frequently in the closure of complicated wounds in plastic surgery, general surgery, orthopedics, and cardiovascular surgery (4–11). These complicated wounds are usually pressure sores, open bone fractures, extremity injuries, wounds with poor circulation, and defects that occur after surgery or trauma. The success of TNP in complicated wounds is known, but scientists have been investigating the beneficial effects of TNP on the body regions and systems for many years. The purpose of this article is to compile Non-Traditional TNP applications in the literature and to prompt scientists to form thoughts on the usability of this method in different areas. Non-traditional TNP applications are summarized in Table I.

Topical Negative Pressure History

Alexander Graham Bell's first son was born prematurely and died several weeks later. He developed the vacuum jacket or Baby Life Saver, aimed to assist breathing in weak or immature babies, and took one of the first steps in neonatal asphyxia. The working principle of this device was to ensure the expansion and contraction of the chest cage in small babies. It was successful in the formation of inspiration and expiration movements. However, since the device was not successful in the study he conducted on a drowning cat, it was not used clinically (12).

In 1928, Drinker and Shaw invented a device called the Iron Lung, which enclosed the entire body except the head and did not leak air to the outside. The Iron Lung was frequently used in polio epidemics in the 20th century. After the 1950s, respiratory ventilation devices were used more frequently instead of this device (13,14).

Table I. Non-traditional topical negative pressure applications

Author	Year	Application	Type
Bell	1989	Chest	Experimental
Drinker	1928	Polio	Clinical
Spalding	1950's	Chest	Clinical
Münster	1999	Cardiovascular Perfusion	Clinical
Greco and Schlenz	2002-2007	Breast Enlargement	Clinical
Kamolz	2004	Burn	Clinical
Lindstedt	2007	Myocardial Infarction	Experimental
Sciortino	2009	Subcutaneous Emphysema	Clinical
Seyfried and Newton	2013-2017	Gastrointestinal Leak	Clinical
Kajihara	2013	Systemic Sclerosis	Clinical
Menezes	2014	Photodynamic Therapy	Clinical
Lee	2015	Fat Graft Survival	Experimental
Aydin	2017	Flap Survival	Experimental
Brown	2021	Flap Survival	Clinical
Liang	2024	Vascular Erectile Dysfunction	Clinical

Non-Conventional Applications of the Topical Negative Pressure

1. Vacuum Assisted Venous Drainage "Hamlet Box"

One of the most common problems with cardiopulmonary bypass is insufficient venous drainage. This problem can contribute to interstitial edema and multiorgan failure, creating serious problems for both the surgeon and the perfusionist. Vacuum-assisted drainage is a system called a "Hamlet Box" with a vacuum regulator. Tested in 54 patients, this system demonstrated effective drainage with smaller catheters, reduced fluid addition, and prevented complications such as hemolysis. Tested both in the laboratory and clinically, it showed no side effects and performed uneventful surgeries. All patients in the study survived and recovered well (15).

2. Non-surgical Vacuum Assisted Breast Augmentation "BRAVA"

A device called BRAVA, which increases breast volume and works with the help of negative pressure, has been described (16). This device has been used in clinical studies by Greco et al. (17). Later, Schlenz and Kaider conducted a detailed study on breast augmentation patients who did not want surgery (18). In this study, the requirement for at least 10 hours of use per day for at least 10 weeks was explained to patients with a body mass index over 18. Standard photographs, breast examination, measurements of breast circumference at nipple height and inframammary fold, and volume measurements of the breasts with the Grossman-Roudner device were obtained periodically at the beginning of treatment, after 6 weeks of use, and up to 14 months after the end of treatment. 40 of the 50 registered women could be evaluated. Ten dropped out of the study for the following reasons: loss of interest and failure to comply with the treatment protocol (n=6), reluctance to attend minimum required follow-up visits (n=3), and greater than 5% weight change (n=1). The median observed volume gain was 155 cc, with a range of 95 to 300 cc. Satisfaction levels varied; 75% of users were satisfied or very satisfied with the results. However, negative situations such as the BRAVA device restricting social life, not being used comfortably while sleeping, patients comparing the results with breast augmentation surgery, and high expectations for it were noted.

3. Use in Superficial Burns

As wound care and treatment for burns improve, morbidity and mortality rates decrease. The most important factor that is a source of infection in a burn wound is exudate. Therefore, methods that can reduce exudate have been continuously investigated. TNP devices have been used as exudate collection containers, and healing has been accelerated, infection rates have decreased, and hospitalization has been shortened (19). TNP is safe and effective for accelerating healing and reducing infection rates in burn wounds (20). TNP has also been used to reduce swelling and increase perfusion in non-full-thickness and superficial burn injuries (21). However, no statistically significant results were found in these studies. Furthermore, high-quality research, including well-designed, adequately powered multicenter trials, is needed to evaluate the effects of TNP on healing times, costs, and patient quality of life (22).

4. Use in Hypothermia-Induced Myocardial Infarction

It is known that hypothermia limits myocardial infarction. Interesting results were found in a study investigating the effects of different levels of TNP on microvascular blood flow in the myocardium reperfused during hypothermia (23). The study used a porcine model, specifically seven domestic terrier pigs, to investigate the effects of TNP on microvascular blood flow during hypothermia. Median sternotomy was performed, and cardiopulmonary bypass (CPB) was established to facilitate the measurement of microvascular blood flow using laser Doppler velocimetry. After hypothermia was induced to 31°C, microvascular blood flow was recorded before and after application of various levels of TNP (50, 75-, 100-, 125-, and 150-mm Hg). Following a 40-minute occlusion of the left anterior descending artery, measurements were made at depths of 6 to 8 mm in the epicardium and myocardium. The study concluded that a TNP of -50 mm Hg significantly increased microvascular blood flow in both the epicardium and myocardium of reperfused hypothermic myocardium. However, TNP levels of -75 mm Hg and above did not significantly alter microvascular blood flow, and pressures of -100 mm Hg to -150 mm Hg resulted in a significant decrease in blood flow. These findings may have implications for improving outcomes in the treatment of myocardial infarction by optimizing TNP administration.

5. Use for Subcutaneous Emphysema

Intrathoracic infection is a serious life-threatening condition. TNP has been successfully applied for a variety of severe intrathoracic infections, including postresectional empyema, necrotizing lung, intrathoracic esophageal leaking empyema, and mediastinitis. It has been stated that it may be an alternative to open thoracostomy for severe infections (24). A 70-year-old man with a history of bullous emphysema developed severe subcutaneous emphysema due to repeated needle decompression

attempts. A chest tube was placed, and a "vent" incision was made to relieve subcutaneous air. TNP was applied because of the ongoing subcutaneous emphysema. After 48 weeks of this treatment, the subcutaneous emphysema was found to have significantly decreased, and the results were supported by computed tomography (25).

6. Use of Gastrointestinal Surgery Leaks

Gastric leaks after bariatric surgery, such as Roux-en-Y gastric bypass, are serious complications that require expert management. Traditional surgical reinterventions are often ineffective due to the inflamed and damaged tissue surrounding the leak, making closure difficult. In a 41-year-old woman who developed a large gastric leak after Roux-en-Y gastric bypass surgery, previous attempts to close the leak with covered metal stents had failed due to stent migration (26). Endoluminal negative pressure therapy successfully sealed the leak within a week, and the patient showed complete recovery without stenosis on follow-up.

A review of the literature on esophageal perforations found that 163 out of 179 patients recovered, with a mortality rate of 12.8% (27). Although sample sizes are small, TNP results are better than traditional treatments, with most patients recovering in an average of four weeks, compared to the typical 6-8 weeks for stents.

Rectal resection is an important treatment for rectal cancer. Anastomotic leakage may lead to decreased long-term survival and increased tumor recurrence. Endoscopic Vacuum Therapy (EVT) shows 79.7-100% success rates in various surgeries (28).

7. Use in Systemic Sclerosis

Systemic sclerosis is a condition characterized by vascular involvement, such as skin ulcers, gangrene, and fissures, that are often resistant to conventional medical treatments and can significantly impact patients' quality of life, leading to long treatment periods and, in severe cases, amputation. TNP therapy supplemented with split-thickness grafts (STSG) was applied to two patients, aged 64 and 73, who had a history of amputation and fistula. The combination of TNP and STSG was effective in both patients, leading to complete wound healing and preventing the need for further amputation (29).

8. Optimization of Photodynamic Therapy

To treat and diagnose various cancers and skin diseases, it is important to increase the formation of protoporphyrin IX (PPIX), and for this purpose, Photodynamic therapy (PDT) with 5-Aminolevulinic acid (5-ALA) is used. However, the penetration of 5-ALA through the skin is limited, which affects its efficacy. Menenez et al. aimed to improve topical photodynamic therapy using TNP with 5-ALA cream (30). The study applied 20% 5-ALA cream to a 9 cm^2 skin area and then applied an occlusive dressing to protect from light. They used fluorescence spectroscopy and wide-field fluorescence imaging to measure PPIX production on the skin surface after 7 and 24 hours. A vacuum device was used to induce negative pressure, which is assumed to increase PPIX production and distribution. They applied 200 mmHg for 4 minutes, using alternating continuous and pulsed modes, while monitoring skin temperature changes hourly with an infrared thermometer. TNP therapy was found to significantly increase PPIX production, distribution, and elimination compared to the control group. PPIX formation was approximately 30% greater in the deeper skin layers and 20% greater in the surface layers. The therapy also accelerated the elimination of PPIX by reducing skin photosensitivity, which is beneficial for PDT treatment.

9. Use to Improve Fat Graft Survival

Fat grafting is widely used for soft tissue augmentation, but due to the low ischemic tolerance of fat tissues, early revascularization is crucial for graft survival. An experimental study was conducted using 20 New Zealand male white rabbits that were subjected to negative pressure of -125 mm Hg on the left or right dorsal ear for one week before fat grafting (31). Fat was grafted onto the dorsal perichondrium, and various parameters such as fat weight, microvessel density, and glycerol release were measured one week and three months after grafting. Microvessel density in the study was evaluated using a standard immunohistochemical method and Laser Doppler Flow measurement

for tissue perfusion. The experimental group that received negative pressure preconditioning showed significantly higher microvessel density in both skin and fat tissues compared to the control group. Skin perfusion and fat survival rates were also significantly higher in the experimental group, indicating improved vascularity and graft viability. The study proved that TNP therapy increased angiogenesis, which is crucial for the survival of transplanted fat tissues.

10. Use for Flap Survival

As an alternative to the traditional surgical flap delay method, the effectiveness of non-invasive TNP-assisted flap delay was investigated experimentally (32). 3 groups were formed as the Control group, the Surgical delay group, and the TNP-assisted group. A total of 30 experimental animals were used, 10 New Zealand breed rabbits in each group. The experiment was performed using a 25x5 cm random flap in the lateral thoracic region. In the TNP-assisted group, flaps were lifted after applying 80 mmHg pressure for one week. The obtained parameters, total flap area and necrotic flap areas, necrosis rate, vascular density, and neovascularization markers (CD31/CD34), were measured with Laser Doppler flowmeter images and contrast-enhanced Computed Tomography. In all measured parameters, the TNP-assisted group showed equivalent results to surgical delay and was superior to the control group. The necrosis rate was significantly lower in the TNP group (19.58%) compared to the control group (65.56%) and the surgical delay group (37.31%). This result proved that TNP-assisted flap delay is a good alternative to surgical flap delay. Thus, reconstructive surgeons have the opportunity to reduce surgeries to a single operation by using TNP-assisted methods instead of a two-stage surgical flap delay. However, this study needs to be reinforced with clinical studies. In a related clinical study in the literature, Brown et al. applied a free anterolateral tight flap to two patients and applied -125 mmHg TNP to the donor area for 6 days. Although the flaps were huge, approximately 22x9 cm, the flaps survived completely, and no partial or complete necrosis was reported (33). Postoperative flap survival is also one of the most important issues for reconstructive surgery. In a large-scale systematic review, flap survival with TNP was as high as 97.1% and complications were found to be as low as 5.7% (34).

11. Use for Vascular Erectile Dysfunction

The clinical effects of Traditional Chinese Medicine topical irrigation combined with TNP irrigation and tadalafil for the treatment of vascular erectile dysfunction (ED) have been investigated (35). Arterial ED means there is a problem with blood flow to the penis, while intravenous ED means there is a problem with blood flow from the penis. There were 43 patients in total in the observation group. This group included 22 arterial ED patients and 21 intravenous ED patients. There were also 43 patients in the control group, including 21 arterial ED patients and 22 intravenous ED patients. The observation group received oral tadalafil along with traditional Chinese medicine TNP irrigation for four weeks. The control group received only oral tadalafil for the same period. Significant improvements were observed in the observation group in terms of IIEF-5 (International Index of Erectile Function-5), EHS (Erection Hardness Score), GAD (Generalized Anxiety Disorder) scores, PSV (Peak Systolic Velocity), EDV (End Diastolic Volume), and RI (Resistance Index) compared to before treatment. Although the results in this study are positive, larger groups and more detailed studies are needed since there is no control group that did not receive Tadalafil.

12. Recent Studies of the TNP

Recent studies have shown that this method not only serves drainage purposes but also provides regenerative, hemostatic, and vascular modulatory effects. Tan et al. reported that the application of TNP combined with fish skin-derived acellular dermal matrix in diabetic foot ulcers significantly reduced infection rates and healing time. This study demonstrates that TNP can be considered not only a mechanical drainage tool but also a platform that supports biological regeneration (10). Currie et al. reported that complications such as seroma and skin necrosis, which may occur after lymphadenectomy, were significantly reduced with the combination of topical tranexamic acid, TNP, and long-term drainage. This finding suggests that TNP can be considered a proactive tool in preventing surgical complications

by supporting vascular stability and tissue integrity (36). Pelham et al. reported that TNP both provides infection control and helps protect the implant in the treatment of infected and exposed orthopedic implants. This study demonstrates that TNP may support regenerative processes by increasing antibiotic penetration at the bone-implant interface (37). TNP has been frequently reported in head and neck surgery, infected and exposed implants, intrathoracic surgery, cardiac surgery, spinal surgery, gynecological problems, burns, congenital problems, donor site closure, lymphadenectomy, and extremity salvage (36–40).

Conclusion

This study emphasized rare applications, as opposed to TNP therapy, which has traditionally been used for wound closure in clinics. Considering the experimental and clinical research conducted for non-traditional TNP applications, although positive results were obtained in many of them, it is understood that more comprehensive research is required since there are not enough subjects or patients. We think that it can be applied to clinical practice, especially in the experimentally proven hypothermia-induced myocardial infarction and flap delay issues.

References

1. Voinchet V, Magalon G. Vacuum assisted closure. Wound healing by negative pressure. Ann Chir Plast Esthet 1996;41(5):583–589.
2. Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-Assisted Closure: A New Method for Wound Control and Treatment: Animal Studies and Basic Foundation. Ann Plast Surg 1997;38(6):553–562.
3. Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. Ann Plast Surg 1997;38(6):563–576.
4. Hallberg H, Holmström H. Vaginal construction with skin grafts and vacuum-assisted closure. Scand J Plast Reconstr Surg Hand Surg 2003;37(2):97–101.
5. Erdmann D, Drye C, Heller L, Wong MS, Levin SL. Abdominal wall defect and enterocutaneous fistula treatment with the Vacuum-Assisted Closure (V.A.C.) system. Plast Reconstr Surg 2001;108(7):2066–2068.
6. Attinger C, Cooper P. Soft tissue reconstruction for calcaneal fractures or osteomyelitis. Orthop Clin North Am 2001;32(1):135–170.
7. Tang AT, Okri SK, Haw MP. Vacuum-assisted closure to treat deep sternal wound infection following cardiac surgery. J Wound Care 2000;9(5):229–230.
8. Bludau M, Fuchs HF, Herbold T, et al. Results of endoscopic vacuum-assisted closure device for treatment of upper GI leaks. Surg Endosc 2018;32(4):1906–1914.
9. Greer SE, Longaker MT, Margiotta M, Mathews AJ, Kasabian A. The use of subatmospheric pressure dressing for the coverage of radial forearm free flap donor-site exposed tendon complications. Ann Plast Surg 1999;43(5):551–554.
10. Tan APP, Chng JK. Fish Skin Acellular Dermal Matrix Combined With Negative Pressure Wound Therapy for Diabetic Foot Ulcers. Cureus. 2025;17(3):e80488.
11. Schlatterer DR, Hirschfeld AG, Webb LX. Negative Pressure Wound Therapy in Grade IIIB Tibial Fractures: Fewer Infections and Fewer Flap Procedures Clin Orthop 2015;473(5):1802–1811.
12. Baskett TF. Alexander Graham Bell and the vacuum jacket for assisted respiration. Resuscitation 2004;63(2):115–117.
13. Spalding JM, Opie L. Artificial respiration with the Tunnicliffe breathing-jacket. Lancet 1958;1(7021):613-615.
14. Shneerson JM. Assisted ventilation. 5. Non-invasive and domiciliary ventilation: negative pressure techniques. Thorax 1991;46(2):131–135.
15. Münster K, Andersen U, Mikkelsen J, Pettersson G. Vacuum assisted venous drainage Perfusion 1999;14(6):419–423.
16. Mustoe T. A. The mechanical bra for breast enlargement. Aesthet Surg J 2000;20(2):176–178.
17. Greco RJ. Nonsurgical breast enhancement--fact or fiction Plast Reconstr Surg 2002;110(1):337–339.
18. Schlenz I, Kaider A. The Brava External Tissue Expander: Is Breast Enlargement without Surgery a Reality Plast Reconstr Surg 2007;120(6):1680–1689.
19. Baudoin J, Jafari P, Meuli J, Applegate LA, Raffoul W. Topical Negative Pressure on Burns: An Innovative Method for Wound Exudate Collection. Plast Reconstr Surg Glob Open 2016;4(11):e1117.
20. Lin D, Kao Y, Chen C, Wang H, Chiu W. Negative pressure wound therapy for burn patients: A meta-analysis and systematic review. Int Wound J 2021;18(1):112–123.
21. Kamolz LP, Andel H, Haslik W, Winter W, Meissl G, Frey M. Use of subatmospheric pressure therapy to prevent burn wound progression in human: first experiences. Burns 2004;30(3):253–258.
22. Wasiak J, Cleland H. Topical negative pressure (TNP) for partial thickness burns. Cochrane Database Syst Rev 2007;(3):CD006215.

23. Lindstedt S, Malmsjö M, Ingemansson R. The effect of different topical negative pressures on microvascular blood flow in reperfused myocardium during hypothermia. Innov Phila Pa 2007;2(5):231–236.
24. Saadi A, Perentes JY, Gonzalez M, et al. Vacuum-Assisted Closure Device: A Useful Tool in the Management of Severe Intrathoracic Infections. Ann Thorac Surg 2011;91(5):1582–1589.
25. Sciortino CM, Mundinger GS, Kuwayama DP, Yang SC, Sussman MS. Case report: treatment of severe subcutaneous emphysema with a negative pressure wound therapy dressing. Eplasty 2009;9:e1.
26. Seyfried F, Reimer S, Miras AD, et al. Successful treatment of a gastric leak after bariatric surgery using endoluminal vacuum therapy. Endoscopy 2013;45 Suppl 2 UCTN:E267-268.
27. Newton NJ, Sharrock A, Rickard R, Mughal M. Systematic review of the use of endo-luminal topical negative pressure in oesophageal leaks and perforations. Dis Esophagus Off J Int Soc Dis Esophagus 2017;30(3):1–5.
28. Kollmann C, Kusnezov B, Kollmann L, et al. The effects of endoscopic vacuum therapy for non-operative treatment of anastomotic leakage on oncological outcomes in rectal cancer patients. Langenbecks Arch Surg 2025;410(1):107.
29. Kajihara I, Jinnin M, Yamada S, et al. Successful treatment of skin fistulas in systemic sclerosis patients with the combination of topical negative pressure therapy and split-thickness skin grafting. Mod Rheumatol 2014;24(2):374-376.
30. Menezes PFC, Requena MB, Bagnato VS. Optimization of photodynamic therapy using negative pressure. Photomed Laser Surg 2014;32(5):296–301.
31. Lee JW, Han YS, Kim SR, Kim HK, Kim H, Park JH. A rabbit model of fat graft recipient site preconditioning using external negative pressure. Arch Plast Surg 2015;42(2):150–158.
32. Aydin OE, Algan S, Tan O, Demirci E, Keles ON, Kantarci A. A novel method for flap delay vacuum assisted flap delay: an experimental study in rabbits. J Plast Surg Hand Surg 2019;53(4):208–215.
33. Brown CA, Ghareeb PA. Early Experience with External Negative Pressure Delay in Free Anterolateral Thigh Perforator Flap Reconstruction. Plast Reconstr Surg - Glob Open 2021;9(6):e3606.
34. Yu P, Yu N, Yang X, Jin X, Lu H, Qi Z. Clinical Efficacy and Safety of Negative-Pressure Wound Therapy on Flaps: A Systematic Review. J Reconstr Microsurg 2017;33(05):358–366.
35. Liang K, Ke Z, Huang J, Fei X, Qi L, Wang J. Analysis of vacuum negative pressure therapy and traditional Chinese medicine lavage in combination with tadalafil for vascular erectile dysfunction. Front Reprod Health 2024;6:1335239.
36. Currie RV, Durand CJ, Bond J. Reducing the incidence of problematic seroma formation and skin necrosis post-lymphadenectomy: Triple action of topical tranexamic acid, negative pressure wound therapy, and prolonged drainage. J Plast Reconstr Aesthet Surg 2024;94.54–61.
37. Pelham FR, Kubiak EN, Sathappan SS, Di Cesare PE. Topical negative pressure in the treatment of infected wounds with exposed orthopaedic implants. J Wound Care 2006;15(3):111–116.
38. Satteson ES, Crantford JC, Wood J, David LR. Outcomes of Vacuum-Assisted Therapy in the Treatment of Head and Neck Wounds. J Craniofac Surg 2015;26(7):e599–602.
39. Goon PKY, Dalal M. Limb-Threatening Extravasation Injury: Topical Negative Pressure and Limb Salvage. Plast Reconstr Surg 2006;117(3):1064–1065.
40. Hou S, Shi Z, Li X, Yang R, Song Y, Zeng Z. Combined negative pressure wound therapy with new wound dressings to repair a ruptured giant omphalocele in a neonate: a case report and literature review. BMC Pediatr 2025;25(1):44.

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Nodular Lymphoid Hyperplasia of the Gastrointestinal Tract with Selective IgA Deficiency in an Adult Patient: A Case Report

Selektif IgA eksikliği Olan Erişkin Hastada Gastrointestinal Nodüler Lenfoid Hiperplazi: Olgu Sunumu

Arzu Hazal Aydın[1] | Mustafa Ergin[2] | Seda Tas Ayçicek[1]

[1]Aksaray Training and Research Hospital, Department of Pathology, Aksaray, Türkiye
[2]Aksaray Training and Research Hospital, Department of Gastroenterology, Aksaray, Türkiye

Sorumlu Yazar | Correspondence Author
Arzu Hazal Aydın
arzu.hazal.aydin@gmail.com
Address for Correspondence: Aksaray Eğitim ve Araştırma Hastanesi, Tıbbi Patoloji Bölümü, Aksaray, Türkiye.

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Nodular Lymphoid Hyperplasia of the Gastrointestinal Tract with Selective IgA Deficiency in an Adult Patient: A Case Report

ABSTRACT

Nodular lymphoid hyperplasia (NLH) of the gastrointestinal tract is a rare and benign condition which may accompany immunodeficiency. Although benign, it carries a risk for intestinal and extraintestinal lymphoma. There is no specific and definitive treatment for NLH. Thus, treatment is dependent on the management of the associated conditions. Duodenal and terminal ileal biopsies from a 54-year-old woman with multiple mesenteric lymphadenopathies and gastrointestinal lymphoid hyperplasia revealed nodular lymphoid hyperplasia as well as a paucity of plasma cells. Based on histopathological findings and laboratory results, a diagnosis of selective IgA deficiency was made. It is important to evaluate patients with nodular lymphoid hyperplasia for additional histopathological findings due to the association with possible immune deficiency, such as absence or scarcity of plasma cells.

Keywords: Gastrointestinal tract, Nodular lymphoid hyperplasia, Selective IgA deficiency.

ÖZET

Gastrointestinal kanalın nodüler lenfoid hiperplazisi (NLH) nadir ve benign bir durum olup immün yetmezlikler ile ilişkili olabilir. Benign bir durum olmasına rağmen artmış intestinal ve ekstraintestinal lenfoma riski söz konusudur. NLH'nın kesin ve spesifik bir tedavisi yoktur. Bu nedenle, NLH'nin tedavisi ilişkili durumların yönetimine bağlıdır. Multiple mezenterik lenfadenopati ve gastrointestinal traktta diffüz lenfoid hiperplazi tespit edilen 54 yaşında kadın hastada duodenal ve terminal ileum biyopsilerinde nodüler lenfoid hiperplazi yanı sıra plazma hücrelerinde belirgin azalma tespit edilmiştir. Histopatolojik bulgular ve laboratuvar sonuçları esas alınarak selektif IgA eksikliği tanısı almıştır. Gastrointestinal trakt biyopsilerinde nodüler lenfoid hiperplazi bulguları izlenen hastalarda ilişkili olabilecek antiteler açısından plazma hücre azlığı gibi diğer histopatolojik bulguların da değerlendirilmesi önemlidir.

Anahtar Sözcükler: Gastrointestinal trakt, Nodüler lenfoid hiperplazi, Selektif IgA eksikliği.

Introduction

Nodular lymphoid hyperplasia (NLH) of the gastrointestinal tract is characterized by multiple small nodules distributed along the tract. The size of the nodules usually varies between 2-10 mm. While it is often asymptomatic, it can cause abdominal pain, chronic diarrhea, intestinal obstruction, or bleeding.

The pathogenesis is still unknown. Although it can affect all age groups, it primarily occurs in children and young adults with or without immunodeficiency. It has been reported that cases associated with common variable immunodeficiency, selective IgA deficiency, celiac disease, besides infectious diseases such as *H. pylori, Giardia,* and *Human Immunodeficiency Virus (HIV)* (1,2).

We herein present an adult patient with immunodeficiency who had nodular lymphoid hyperplasia in duodenal and terminal ileum biopsies.

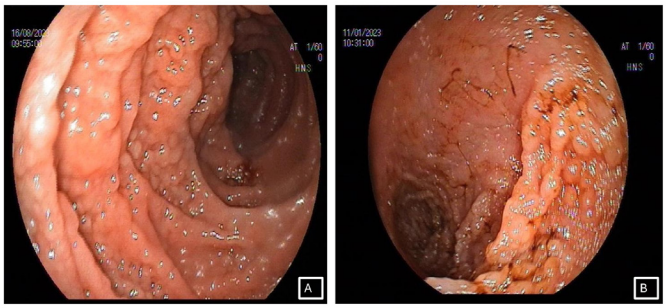

Figure I. Esophagogastroduodenoscopy (EGD) and colonoscopy of the patient showed numerous diffuse mucosal nodular lesions in the duodenum (A) and terminal ileum (B)

Case Report

A 54-year-old woman with complaints of chronic diarrhea applied to the gastroenterology clinic. She also had night sweating and weight loss. Multiple mesenteric lymphadenopathies were defined in computed tomography (CT). In esophagogastroduodenoscopy and colonoscopy, linear erosions in the stomach and cracked soil appearance in the duodenum were described, and biopsies were taken. Terminal ileum mucosa was seen as edematous and nodular (Figure I). In microscopic examination of biopsies, findings were compatible with *H. pylori* gastritis in the stomach samples. The biopsies from the duodenum and terminal ileum showed nodular lymphoid hyperplasia (Figure II). In higher magnification, almost no plasma cells were detected in the lamina propria (Figure III). *Giardia* and *H. pylori* were not detected in the duodenal biopsy. It was recommended to investigate the possible presence of immunodeficiency in the case with the current histomorphological findings. Serum IgA was extremely low (0.065 g/L; normal 0.7–4.0 g/L), and serum IgE was decreased (<1.00 IU/mL; normal 1.9–170 IU/mL). Serum IgG and IgM ratios were within normal limits. Based on the laboratory results, the patient was diagnosed with selective IgA deficiency, and intravenous immunoglobulin (IVIG) treatment was given. Symptoms of the patient regressed. Surveillance of the patient continues at regular intervals. Written informed consent was obtained from the patient for publication of this case report.

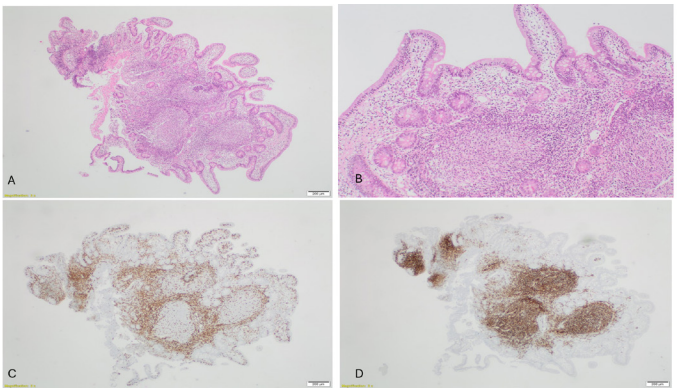

Figure II. (A) and (B). Duodenal and terminal ileal biopsies demonstrated nodular lymphoid hyperplasia (H&E x4), (C) and (D). Immunohistochemical staining in reactive lymphoid hyperplasia with CD3 and CD20, respectively (x4).

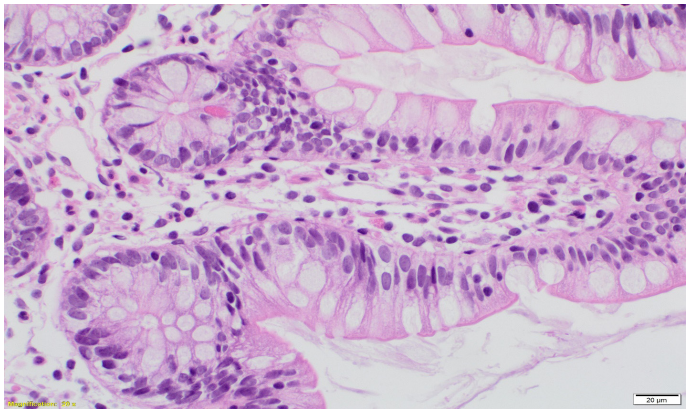

Figure III. In higher magnification, nearly zero plasma cells were detected in the lamina propria of the duodenum (H&E x20)

Discussion

During endoscopic imaging, nodular lymphoid hyperplasia (NLH) is seen as nodules ranging in size from 2 to 10 mm along the gastrointestinal tract. Nodular lymphoid hyperplasia primarily involves the small intestine, but it can also involve the colon and stomach (1). Lymphoid nodules localized in the colon may appear as red macules, as circumferential target lesions (halo sign), or as raised papules (2). Nodular lymphoid hyperplasia can be observed in a focal or diffuse form. In children, it is usually limited to the rectum, colon, and terminal ileum, has a mild clinical course, and often shows spontaneous regression. Cases associated with refractory constipation, viral infection, and food allergies have been reported (3). It has been emphasized that prognosis determination is more uncertain in adults (4). Although case reports and series have increased in the last years, there is no epidemiological data to determine incidence and prevalence (1,2).

Pathogenesis is largely unknown. However, there are some theories explaining the condition according to the presence/ absence of immunodeficiency. It is thought that in the case of immune deficiency, the accumulation of plasma cells and their precursors due to maturation defects of B lymphocytes occurs during the compensation of functionally inadequate intestinal lymphoid tissue (1). It is believed that NLH in the absence of immunodeficiency may be related to repetitive immune stimulation of gastrointestinal lymphoid tissue (2,3).

Chiaramonte et al suggested that NLH could be a transitional stage in the development of malignancy (5). It has been emphasized that NLH carries a risk for intestinal and extraintestinal lymphoma (1,2). Considering the risk of malignant transformation, regular endoscopic control becomes important (1). Although the duration and interval of these controls are not defined, it has been reported that a biopsy should be taken from growing lymphoid nodules to exclude transformation (2).

The treatment of NLH is directed to associated conditions (1). The diagnosis of NLH requires histopathological confirmation following endoscopic imaging or contrast barium examination. This is necessary to distinguish entities that may be confused with NLH and to prevent overtreatment resulting from misdiagnosis.

In conclusion, although NLH is a rare and benign condition, it is clinically important due to its associated conditions and possible complications such as malignant transformation. Therefore, detecting the underlying causes and monitoring these patients are necessary for treatment and prevention of complications. It is important to keep in mind the possible associated conditions in a patient with nodular lymphoid hyperplasia and to evaluate all possibilities in the differential diagnosis.

References

1. Elkholy S, Albitar A, Elfadel S, Farag A, Roshdy A. Diffuse Nodular Lymphoid hyperplasia with Selective IgA Deficiency Syndrome Presenting with Intestinal Lymphoma. MOJ Clin Med Case Rep 2016;4(5):116-118.

2. Albuquerque A. Nodular lymphoid hyperplasia in the gastrointestinal tract in adult patients: A review. World journal of gastrointestinal endoscopy 2014;6(11):534.

3. Khuroo MS, Khuroo NS, Khuroo MS. Diffuse duodenal nodular lymphoid hyperplasia: a large cohort of patients etiologically related to Helicobacter pylori infection. BMC Gastroenterology 2011;11:1-12.

4. Ward E, Wolfsen H. The non-inherited gastrointestinal polyposis syndromes. Alimentary pharmacology & therapeutics 2002;16(3):333-342.

5. Chiaramonte C, Glick SN. Nodular lymphoid hyperplasia of the small bowel complicated by jejunal lymphoma in a patient with common variable immune deficiency syndrome. AJR American journal of roentgenology 1994;163(5):1118-1119.

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Pneumatosis Intestinalis with Thyroid Hormone Abnormality: An Interesting Case

Tiroid Hormon Anormalliği ile Birlikte Pneumatozis İntestinalis: İlginç Bir Olgu

Betül Güzelyüz[1] | Ali Mert Özdoğan[2] | Sefa Ergün[2]

[1]Hassa State Hospital, Department of General Surgery, Hatay, Türkiye
[2]Istanbul University Cerrahpaşa Faculty of Medicine, Department of General Surgery, İstanbul, Türkiye

Sorumlu Yazar | Correspondence Author
Betül Güzelyüz
b.gzlyz1994@gmail.com
Address for Correspondence: Hassa State Hospital, Department of General Surgery, Kahramanmaraş, Türkiye.

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Pneumatosis Intestinalis with Thyroid Hormone Abnormality: An Interesting Case

ABSTRACT

Pneumatosis intestinalis is characterized by the presence of gas in the intestinal wall. Although its clinical findings and etiology are not clear, a delay in diagnosis is associated with high morbidity and mortality. Therefore, in cases where pneumatosis in the bowel wall is detected radiologically, aggressive laparotomy is recommended in the presence of a negative prognostic disease. Then, the current approach recommended in the guidelines is second-look laparotomies, in which bowel viability will be re-evaluated before a definitive resection decision is made. This approach is emphasized as an extremely useful option in terms of prognosis and survival in cases of thyroid hormone abnormalities, in cases with underlying diseases such as heart failure, in conditions such as hemodynamic instability and sepsis, where even small changes in the reference range are known to affect systemic vascular resistance and oxygen demand and lead to many cardiovascular effects. In this case report, a patient with a complex history who wasn't detected to have ischemia in the first surgery performed due to pneumatosis intestinalis but was observed to have intestinal ischemia in the second-look laparotomy; the complicated and negative prognosis process, accompanied by a newly diagnosed thyroid hormone abnormality, is presented.

Keywords: Mesenteric ischemia, pneumatosis intestinalis, second-look operation, thyroid hormone.

ÖZET

Pneumatosis İntestinalis, bağırsak duvarında gaz varlığı ile karakterizedir; klinik bulguları ve etiyolojisi net olmamakla birlikte tanıda gecikme yüksek morbidite ve mortalite ile ilişkilidir. Bu nedenle, radyolojik olarak bağırsak duvarında pneumatosis saptanan olgularda, negatif prognostik hastalık varlığında agresif laparotomi önerilir. Daha sonra, kılavuzlarda önerilen güncel yaklaşım, kesin rezeksiyon kararı verilmeden önce bağırsak canlılığının yeniden değerlendirileceği ikinci bakış laparotomileridir. Bu yaklaşım; referans aralığındaki küçük değişikliklerin bile sistemik vasküler direnç ile oksijen talebini etkileyip pek çok kardiyovasküler etkiye yol açtığı bilinen tiroid hormon anormalliklerinde, altta yatan başta kalp yetmezliği gibi hastalıkları olan olgularda, hemodinamik instabilite ve sepsis gibi durumlarda; prognoz ve sağkalım açısından son derece yararlı bir seçenek olarak vurgulanmaktadır. Bu olgu sunumunda, pneumatosis intestinalis nedeniyle yapılan ilk cerrahide iskemi saptanmayan, ancak ikinci bakış laparotomisinde bağırsak iskemisi gözlenen, kompleks bir özgeçmişi olan hastanın; yeni saptanan tiroid hormon anormalliğinin da eşlik ettiği komplike ve kötü prognozla seyreden süreci sunulmaktadır.

Anahtar Sözcükler: Mezenter iskemi, pnömatozis intestinalis, ikincil-bakı operasyon, tiroid hormonu.

Introduction

Pneumatosis intestinalis is a rare entity characterized by the presence of gas in the intestinal wall. Although the etiology isn't clear, there is usually an underlying cause such as inflammation, malignancy, or autoimmune-endocrine events. While it may be the precursor lesion of intestinal ischemia, it may also remain only as a radiological finding without any clinical findings, and diagnosis may be delayed; it is associated with high mortality (1,2). Therefore, aggressive laparotomy is recommended in cases where pneumatosis is detected radiologically in the intestinal wall and in cases of ischemia. After the primary operation, routine re-evaluation of bowel viability with second-look laparotomies before a definitive resection decision is made, as is the current approach recommended in the guidelines (3,4). This approach, in the presence of thyroid abnormalities, underlying cardiovascular and hemodynamic instability, which are known to affect systemic vascular resistance and oxygen demand and cause many vascular effects, even small changes in the reference range, is extremely important for prognosis and survival (5,6).

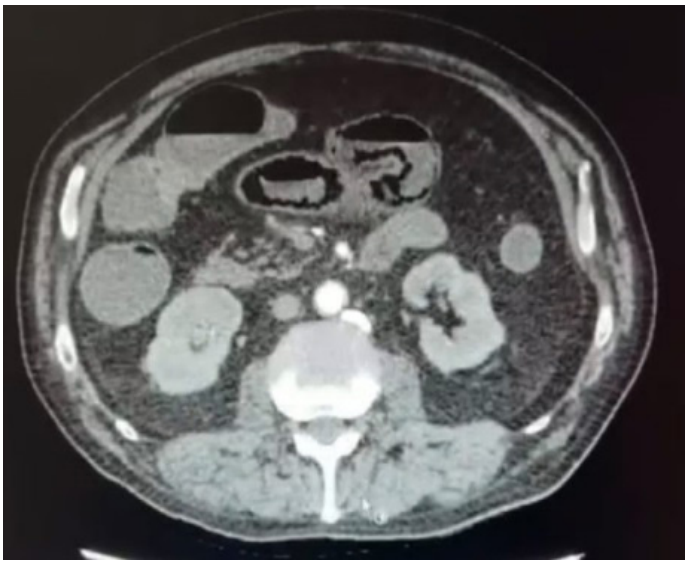

Figure I. CT section with intravenous contrast; diffuse air densities in the small intestine walls, compatible with pneumatosis intestinalis.

In this case report, a patient with a complex history who wasn't detected to have ischemia in the first surgery performed due to pneumatosis intestinalis but was observed to have intestinal ischemia in the second-look laparotomy; the complicated and negative prognosis process, accompanied by a newly diagnosed thyroid hormone abnormality, is presented.

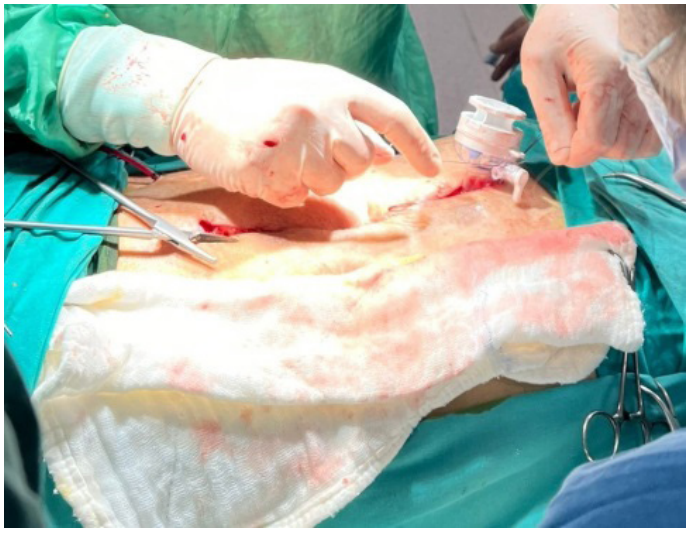

Figure II. The end of the first surgery; Since second-look was planned, a trocar was placed cranial to the median incision for laparoscopy, taking into account the hemodynamic suitability of the patient in the second surgery and the possibility, albeit low, of not encountering any complicated findings during exploration.

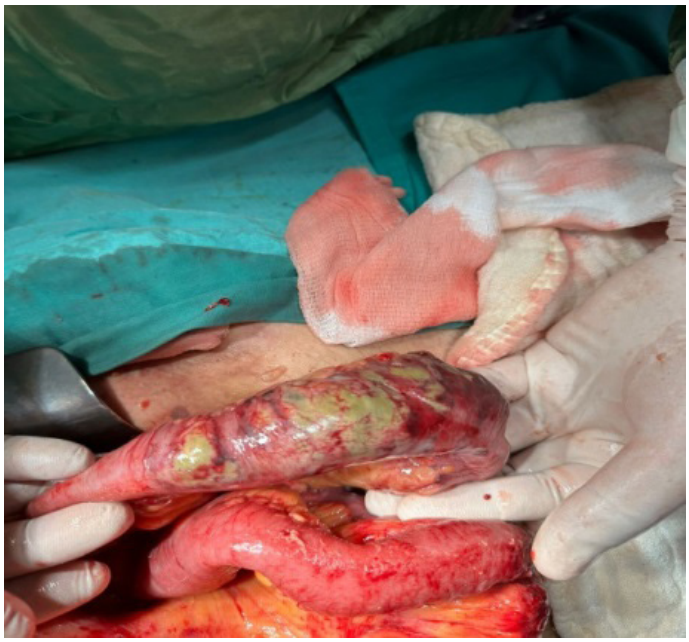

Figure III. Second-look operation; 45 cm necrotic small intestine segment observed 140 cm distal to the ligament of Treitz.

Case Report

A 71-year-old male patient with a medical history of hypertension, coronary artery disease, type 2 diabetes mellitus, chronic renal failure, benign prostatic hyperplasia, rectal cancer, small cell lung

Table I. Laboratory Findings

	WBC (x10^9/L)	CRP (mg/dL)	D-dimer (mg/L)	pH	HCO_3 (mmol/L)	Lac (venous) (mmol/L)	fT_3 (pg/mL)	fT_4 (ng/dL)	TSH (µIU/ml)
Normal range	*(4-10)*	*(<5)*	*(0-0.5)*	*(7.35-7.45)*	*(22-26)*	*(0.5-2.2)*	*(2-4.4)*	*(0.93-1.7)*	*(0.27-4.2)*
8 years ago							**2.59**	**1.31**	**1.59**
4 years ago							**2.34**	**1.49**	**1.6**
1 year ago							**2.72**	**1.45**	**0.816**
On arrival	**0.5**	**128**	**6.68**	**7.45**	**21**	**1.8**			
48 hours later	**1.6**	**382**	**6.81**	**7.32**	**22.4**	**4.1**	**0.98**	**2.21**	**1.36**

cancer; coronary angiography and two stents 10 years ago, coronary bypass surgery 20 years ago, numerous abdominal surgeries, the last of which ended with an end colostomy 6 years ago; oral antiplatelet, insulin, and chemotherapy due to lung cancer 1 week ago. He was admitted to the emergency department with complaints of abdominal pain that started 4 days ago and had worsened over the last 4-5 hours, and diarrhea. On arrival, his vital signs were within normal limits, and on examination, the abdomen was tender to palpation, and there was guarding and rebound tenderness. White blood cell (WBC) 0.5×10^9/L, C-reactive protein (CRP) 128mg/dL, D-dimer 6.68 mg/L, pH 7.45, HCO_3 21 mmol/L, venous lactate (lac) 1.8mmol/L (Table I). The electrocardiogram and abdominal X-ray were normal. Intravenous contrast-enhanced computed tomography (CT) revealed air in the portal vein, diffuse air densities in the small intestine walls, and an appearance consistent with pneumatosis intestinalis (Figure I). An emergency laparotomy was performed; there was widespread venous congestion in the middle ileal loops, and no ischemic findings were observed; a 10 mm trocar was left in the midline incision to monitor intestinal viability with second-look before definitive abdominal closure, and he was taken to the intensive care unit (ICU) after the surgery (Figure II). As the patient's hemodynamic parameters were worsening, noradrenaline was started; WBC 1,6×109/L, CRP 382 mg/dl, D-dimer 6.81 mg/L, pH 7.32, HCO_3 22.4 mmol/L, and lactate 4.1 mmol/L were detected. In addition, in the tests performed on the same day, fT_3 0.98pg/mL, fT_4 2.21ng/dL, TSH 1.36µIU/mL. It was determined through a retrospective examination of approximately 8 years that there was no known history of thyroid disease and that his thyroid hormone levels had always been within the normal range in his previous tests (Table I). Second-look operation was performed 48 hours later; the surgery was started with laparoscopy by creating pneumoperitoneum through the trocar in the midline incision, but relaparotomy was performed due to inadequate exploration due to hemodynamic instability. On exploration, a 45 cm small intestine segment 140 cm distal to the ligament of Treitz was found to be necrotic (Figure III). Resection-ileostomy was performed. However, mortality occurred after 13 days due to ongoing hemodynamic instability. Pathological examination reported transmural infarction, ischemia findings, submucosal edema, and amyloid deposition in the vascular walls in the segmental small bowel resection material.

Discussion

Pneumatosis intestinalis is an entity associated with gastrointestinal diseases, immune suppression, rheumatological, and metabolic events. Although clinical findings are not clear, symptoms such as abdominal pain and diarrhea may occur. A complicated table is mostly associated with inflammatory bowel diseases, lung diseases, some specific medications, and immunosuppression. In addition, although intestinal toxicity and pneumatosis intestinalis due to chemotherapeutics are rare in cancer patients, the condition is usually fulminant in these cases and requires urgent surgical intervention (7). It is important to confirm the diagnosis as soon as possible in order to prevent progression to ischemia; gas bubbles are observed in the intestinal wall on CT, and gas is also found in the portal vein in approximately 25% of cases (1,5,8). Although there are some studies showing that pneumatosis intestinalis has a good prognosis with conservative treatments, a mortality of up to 80% is observed in patients with concomitant gas detected in the portal vein (Liu et al, 2022); it was stated that surgical intervention

should be performed urgently (2,7,8). In a study on portomesenteric venous thromboembolism (Uludağ, 2021), it was concluded that conservative treatment is essential, treatment for the underlying cause is absolutely necessary, and surgical intervention is essential for small bowel necrosis (9). In the patient discussed in this study, cardiovascular, metabolic, pulmonary and gastrointestinal diseases, as well as immunosuppression and recent chemotherapy history were present; although his complaints at the time of admission were nonspecific abdominal pain and diarrhea, it was important to clarify the diagnosis as soon as possible, and emergency laparotomy became the only option in this case with a complicated history, upon detection of pneumatosis intestinalis in the computed tomography. In addition, in a study examining prognosis and mortality in patients without laparotomy and after laparotomy, it is mentioned that effective management of mesenteric ischemia requires early treatment of the underlying disease; monitoring of blood gas and hemodynamic parameters; although there is no specific treatment protocol, planned second-look surgery is recommended in current guidelines after 24-48 hours of observation in the ICU (5). Although the hemodynamic parameters were normal at the time of admission and there were no ischemic findings and no findings other than venous congestion in the intestinal loops in the first laparotomy, second-look surgery was planned due to the presence of multiple comorbidities and many negative prognostic factors for pneumatosis intestinalis. Indeed, the patient's hemodynamics began to deteriorate in the period leading to the planned second-look 48 hours later, and an ischemic bowel segment was encountered in the relaparotomy, and resection was required.
In pathology, in addition to the classical findings of ischemia, amyloid deposition was found in the vascular wall of the resected segment, but it wasn't specifically detailed. It is known that reactive amyloidosis can often occur secondary to chronic inflammation, infection, and neoplasms, and some studies have shown that small intestine involvement is most common when the gastrointestinal system is affected by amyloid (10).

In this case, which contains many of the possible etiological and predisposing factors and negative prognostic factors of pneumatosis intestinalis, a thyroid hormone abnormality that wasn't present before was also detected. It is known that thyroid hormone abnormalities and even emergencies aren't uncommon in intensive care patients. However, it is said that most of these are due to a known thyroid disease, and a small number of them are unknown because they are not examined before admission to the ICU (11). In this case, whose previous thyroid levels were normal, and there was no history of thyroid disease, the cause of this condition couldn't be clarified because of the mortality that occurred. Iodine is an essential trace element absorbed in the small intestine. Decreased iodine intake may result in decreased thyroid hormone synthesis. This may be due to the patient's newly detected thyroid hormone abnormality as a result of diarrheal symptoms (12). Although the cause is not clear, thyroid hormone abnormality may be associated with a negative prognosis and outcome. Because it is known that thyroid hormones protect vascular homeostasis with their positive effects on endothelial and vascular smooth muscle cells, and that when thyroid hormone levels are low, blood and oxygen delivery are impaired, and target organs are affected (13). Moreover, in a study examining whether correction of thyroid dysfunction results in improved cardiovascular outcomes, even the presence of subclinical thyroid disease was associated with increased vascular risk and mortality (14). New studies and a small number of cases have begun to appear in the literature on the association of intestinal microbiota with thyroid diseases through some mechanisms (15). This suggests that thyroid hormone abnormalities may influence intestinal ischemia through the vascular system, as well as other mechanisms.

Conclusion

It is known that cardiovascular diseases and endocrine and metabolic abnormalities in diseases associated with intestinal ischemia lead to high mortality rates. The cardiac and vascular effects of thyroid hormone abnormalities have also been demonstrated, even in the absence of clinical thyroid disease findings. However, further studies are needed

to determine whether thyroid hormone abnormalities can directly affect prognosis in pneumatosis intestinalis and mesenteric ischemia cases.

References

1. Tropeano G, Di Grezia M, Puccioni C et al. The spectrum of pneumatosis intestinalis in the adult. A surgical dilemma. World J Gastrointest Surg 2023;15(4): 553-565.
2. Suzuki T, Murata S, Tsunoyama T, et al. Recanalization using direct stenting before bowel resection for acute-on-chronic superior mesenteric artery occlusion: A case report, International Journal of Surgery Case Reports 2020;68:92-95.
3. Nakamura F, Yui R, Muratsu A, et al. A strategy for improving the prognosis of non-occlusive mesenteric ischemia (NOMI): a single-center observational study. Acute Medicine & Surgery 2019;6:365-370.
4. Acosta S, Kärkkäinen J. Open abdomen in acute mesenteric ischemia. Anaesthesiology Intensive Therapy 2019;51(2):159-162.
5. Murata T, Yamaguchi N, Shimomoto Y, et al. Preoperative prognostic predictors and treatment strategies for surgical procedure focused on the Sequential Organ Failure Assessment score in nonocclusive mesenteric ischemia: A multicenter retrospective cohort study. Int J Surg 2023;109(12):4119-4125
6. Razvi, S. Novel uses of thyroid hormones in cardiovascular conditions. Endocrine 2019;66:115-123.
7. Liu H, Hsieh CT, Sun JM. Pneumatosis intestinalis after systemic chemotherapy for colorectal cancer: A case report. World J Clin Cases 2022;10(16):5337-5342.
8. Ling F, Guo D, Zhu L. Pneumatosis cystoides intestinalis: a case report and literature review. BMC Gastroenterol 2019;19(1):176.
9. Uludağ S. Non-Operative Management of Portomesenteric Venous Thromboembolism After Laparoscopic Sleeve Gastrectomy and the Importance of Long-Term Anticoagulant Prophylaxis. Turk J Diab Obes 2021; 5(1): 19-24.
10. Wu J, Wang Y, Wang C. Amyloidosis: An Unusual Cause of Intestinal Pseudo-Obstruction. Clin Gastroenterol Hepatol 2018;16(5):e53-e54.
11. Bourcier S, Coutrot M, Kimmoun A, et al. Thyroid Storm in the ICU: A Retrospective Multicenter Study. Crit Care Med 2020;48(1):83-90.
12. Shahid MA, Ashraf MA, Sharma S. Physiology, Thyroid Hormone. 2023 Jun 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
13. Gluvic ZM, Zafirovic SS, Obradovic MM, et al. Hypothyroidism and Risk of Cardiovascular Disease. Current Pharmaceutical Design 2022;28(25):2065-2072.
14. Cappola AR, Fried LP, Arnold AM, et al. Thyroid status, cardiovascular risk, and mortality in older adults. JAMA 2006;295(9):1033-1041.
15. Zhu X, Zhang C, Feng S, He R, Zhang S. Intestinal microbiota regulates the gut-thyroid axis: the new dawn of improving Hashimoto thyroiditis. Clin Exp Med 2024;24(1):39.

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Case Report: Successful Drug Desensitization to Ustekinumab in an Adult Patient with Crohn's Disease

Vaka Raporu: Crohn Hastalığı Olan Yetişkin Bir Hastada Ustekinumab'a Karşı Başarılı İlaç Desensitizasyonu

Selma Yeşilkaya

Samsun Training and Research Hospital, Department of Respiratory Medicine, Division of Immunology and Allergy, Samsun, Türkiye

Sorumlu Yazar | Correspondence Author
Selma Yeşilkaya
selmayesilkaya@hotmail.com
Address for Correspondence: Samsun Training and Research Hospital, Division of Immunology and Allergy, İlkadım, 55000, Samsun, Türkiye

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Case Report: Successful Drug Desensitization to Ustekinumab in an Adult Patient with Crohn's Disease

ABSTRACT

Ustekinumab is a biological agent used in the treatment of inflammatory diseases. Since biological therapies are targeted therapies, their use is increasing, and the incidence of related reactions is increasing accordingly. We present this case because we successfully desensitized a patient who experienced a ustekinumab reaction. An adult Crohn's disease patient who experienced an adverse reaction to the fifth subcutaneous dose of Ustekinumab was evaluated in our Immunology and Allergy clinic. The patient was successfully treated using the stepwise rapid drug desensitization protocol. We present this case to emphasize the importance and awareness of desensitization in managing drug reactions in clinics such as Dermatology, Rheumatology, and Gastroenterology, where the drug is widely used.

Keywords: Bbiological therapy, Crohn's Disease, desensitization, Ustekinumab.

ÖZET

Ustekinumab, inflamatuar hastalıkların tedavisinde kullanılan biyolojik bir ajandır. Biyolojik tedaviler hedefli tedaviler olduğundan, kullanımları artmakta ve buna bağlı olarak ilgili reaksiyonların görülme sıklığı artmaktadır. Bu olguyu, ustekinumab reaksiyonu yaşayan bir hastayı başarıyla duyarsızlaştırdığımız için sunuyoruz. Ustekinumab'ın beşinci subkutan dozuna karşı olumsuz reaksiyon yaşayan yetişkin bir Crohn Hastalığı hastası, İmmünoloji ve Alerji kliniğimizde değerlendirildi. Hasta, kademeli hızlı ilaç duyarsızlaştırma protokolü kullanılarak başarıyla tedavi edildi. Bu olguyu, ilacın yaygın olarak kullanıldığı Dermatoloji, Romatoloji ve Gastroenteroloji gibi kliniklerde ilaç reaksiyonlarının yönetiminde duyarsızlaştırmanın önemini ve farkındalığını vurgulamak için sunuyoruz.

Anahtar Sözcükler: Biyolojik tedavi, Crohn Hastalığı, duyarsızlaştırma, Ustekinumab.

Introduction

Ustekinumab is a fully human monoclonal antibody that targets the p40 subunit shared by interleukin (IL)-12 and IL-23 (1). It is approved for the treatment of psoriasis, psoriatic arthritis, and inflammatory bowel disease. In 2016, both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) approved Ustekinumab for adults (≥18 years) with moderately to severely active Crohn's disease who have failed or are intolerant to immunomodulators, corticosteroids, and tumor necrosis factor (TNF) antagonists (2,3). Biological therapies are increasingly used to treat oncologic, immunologic, and inflammatory conditions as targeted therapies (4). Psoriasis is believed to result from a dysregulated type 1 immune response, characterized by elevated cytokines such as IL-12 and IL-23. These cytokines activate IL-17-producing T cells, which play a role in inflammation leading to joint damage in psoriatic arthritis. Ustekinumab acts by blocking this interleukin activity (5). Ustekinumab exerts its effect in arthritis by blocking this interleukin. Hypersensitivity reactions to biologic agents are categorized into seven types based on clinical phenotype, underlying endotype, and biomarkers: infusion reactions, type I (IgE and non-IgE mediated), cytokine release syndrome, mixed reactions, and type II, III, and IV hypersensitivity reactions (6). Infusion-related and cytokine-release reactions can occur with the first infusion, though the former tends to self-limit with repeated exposure and premedication (7). A study conducted in two tertiary hospitals examined acute infusion reactions to Ustekinumab and suggested they were not immune-mediated, as the reactions occurred on first exposure, resolved with premedication, and most patients tolerated subsequent subcutaneous (SC) injections (8).

This case report presents the successful use of a desensitization protocol in an adult Crohn's Disease patient who experienced a hypersensitivity reaction to Ustekinumab.

Case Report

A 48-year-old female patient had been under follow-up for 13 years due to Rheumatoid Arthritis (RA) and for 2 years due to Crohn's Disease. She was also being monitored for uveitis. The patient had no history of smoking and no known drug allergies. Additionally, she had not been diagnosed with asthma or rhinitis. She was receiving Leflunomide 20 mg for RA. For her Crohn's Disease, the patient had previously been treated with corticosteroids, Methotrexate, and subsequently Infliximab. During the fourth infusion of Infliximab, she experienced mild shortness of breath, and during the fifth infusion, she reported a sensation of throat tightness, shortness of breath, palpitations, and loss of sensation in her legs. These symptoms resolved with treatment, and she was monitored for three hours post-infusion. Following this, her treatment was switched to Ustekinumab by the Gastroenterology department. The initial dose was administered via intravenous infusion, after which she transitioned to subcutaneous (SC) dosing. The fourth SC dose was administered uneventfully. However, during the administration of the fifth SC dose in the emergency room, the patient returned five minutes later with complaints of shortness of breath and palpitations. Her symptoms improved during follow-up. She was referred to our clinic due to her adverse reactions to both infliximab and Ustekinumab. She expressed a desire to continue Ustekinumab treatment due to its therapeutic benefits.

During evaluation, the symptoms were considered adverse drug reactions and scored as 7 on the Naranjo algorithm (9). The patient was desensitized using the subcutaneous protocol adapted from Cohen et al. (10). Written informed consent was obtained from the patient on 19/08/2024. At follow-up, the patient remained asymptomatic. Four additional SC doses, administered every eight weeks, were given using the same protocol with no further adverse reactions, confirming both reproducibility and efficacy.

Discussion

Crohn's Disease is a chronic inflammatory bowel disease that can affect the entire gastrointestinal tract, from the mouth to the anus (11). Some patients with Crohn's Disease may experience treatment failure or develop significant side effects. Biological agents, such as Ustekinumab, are generally preferred for patients who do not respond to conventional treatments for chronic diseases. Clinical studies have demonstrated that Ustekinumab possesses a

Table I. Intravenous and Subcutaneous Ustekinumab Desensitization Protocols

#	Solution, mg/mL, formulation	Rate, mL/h for IV formulation	Time, min	Volume, mL administered	Dose administered with this step, mg	Cumulative Dose, mg
1	0.010 IV	2.5	15	0.63	0.00625	0.00625
2	0.010 IV	5	15	1.25	0.01250	0.01875
3	0.010 IV	10	15	2.50	0.02500	0.04375
4	0.010 IV	20	15	5.00	0.05000	0.09375
5	0.104 IV	5	15	1.25	0.13000	0.2275
6	0.104 IV	10	15	2.50	0.26000	0.4875
7	0.104 IV	20	15	5.00	0.52000	1.0075
8	0.104 IV	40	15	10.00	1.04000	2.0475
9	1.032 IV	10	15	2.50	2.5795	4.6270
10	1.032 IV	20	15	5.00	5.1591	9.7861
11	1.032 IV	40	15	10.00	10.3181	20.1042
12	1.032 IV	80	174.375	232.50	239.8958	260.0000
SC Ustekinumab Desensitization (90 mg/mL)						
1	90 SC	N/A	0	0.05	4.5	4.5
2	90 SC	N/A	15	0.1	9	13.5
3	90 SC	N/A	15	0.2	18	31.5
4	90 SC	N/A	15	0.25	22.5	54
5	90 SC	N/A	15	0.4	36	90
IV: intravenous, SC: subcutaneous						

favorable safety profile in the treatment of patients with Crohn's Disease. In the pilot studies UNITI-1 and UNITI-2, the prevalence of adverse events was reported at 65.9% and 55.6%, respectively, which was not significantly different from the placebo groups, which reported 64.9% and 54.3% (12). Furthermore, the incidence of serious adverse events was comparable between patients treated with Ustekinumab and those receiving a placebo. In a case report by Thomas PWA et al., three patients were presented, all of whom experienced immediate reactions to the first dose of IV treatment. Two of these patients attempted to continue treatment via subcutaneous administration, but their medications were ultimately discontinued due to the recurrence of reactions (13). Conversely, in the case report by Cleveland NK et al., no reaction was observed during the first IV infusion in a patient who had previously experienced a reaction. The authors attributed this lack of reaction to the presence of Ethylenediaminetetraacetic Acid (EDTA) in the IV formulation, which was absent in the SC formulation (14).

In the aforementioned cases, reactions were noted during the first IV infusion. However, in our patient, the reaction occurred during the fifth dose and following SC administration. Therefore, we did not classify this as a typical infusion reaction; rather, we considered it to be an IgE-mediated reaction or a mixed reaction.

Although we initially planned to conduct a skin test due to the high cost of the medication, we opted for direct desensitization to ensure that the patient would not have to forgo treatment for an additional two months, particularly given that her physician indicated she was benefiting from the drug.

Drug desensitization is indicated when there are no viable alternatives to the medication or when alternatives are less effective. It involves the administration of gradually increasing doses of the drug under controlled conditions to induce temporary tolerance (15,16).

Given the absence of a standardized desensitization protocol for Ustekinumab, we initially adopted the successful desensitization regimen employed by Cohen et al. in a 9-year-old Crohn's Disease patient, as described in the literature (10). In that case, a 12-step desensitization was performed via IV infusion, followed by subcutaneous administration in subsequent doses, which proved effective and well tolerated.

In conclusion, we report a successful subcutaneous desensitization procedure in an adult Crohn's Disease patient who experienced an adverse reaction to

Ustekinumab. This case underscores the importance of desensitization protocols in enabling the continued use of essential biologics when no alternatives are available. Implementing such protocols can improve patient safety, broaden therapeutic options, and reduce treatment discontinuation due to hypersensitivity.

References

1. Ryan C, Thrash B, Warren RB, et al. The use of ustekinumab in autoimmune disease. Expert Opin Biol Ther. 2010;10:587–604.
2. Johnson & Johnson. Content Lab. U.S. FDA Approves STELARA® [Ustekinumab] for Treatment of Adults with Moderately to Severely Active Crohn's Disease. https://www.jnj.com/media-center/press-releases/fda-approves-stelara-ustekinumab-for-treatment-of-adults-with-moderately-to-severely-active-crohns-disease (Accessed: September 4, 2021.)
3. European Medicines Agency. Stelara®.2018. https://www.ema.europa.eu/en/medicines/human/EPAR/stelara (Accessed: September 4, 2021.)
4. Yang BC, Castells MC. The who, what, where, when, why, and how of drug desensitization. Immunol Allergy Clin North Am 2022;42(2):403-420.
5. Murphy CA, Langrish CL, Chen Y, et al. Divergent pro- and anti-inflammatory roles for IL-23 and IL-12 in joint autoimmune inflammation. J Exp Med 2003;198(12):1951-1957.
6. Bavbek S, Pagani M, Alvarez-Cuesta E, et al. Hypersensitivity reactions to biologicals: an EAACI position paper. Allergy 2022;77(1):39-54.
7. Picard M, Galvao VR. Current knowledge and management of hypersensitivity reactions to monoclonal antibodies. J Allergy Clin Immunol Pract 2017;5:600-9.
8. Spencer EA, Kinnucan J, Wang J, et al. Real-World Experience with Acute Infusion Reactions to Ustekinumab at 2 Large Tertiary Care Centers. Crohns Colitis 360 2020 Apr 10;2(2):otaa022.
9. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30(2):239-245.
10. Cohen B, Tomer G, Gavrilova T. Successful drug desensitization to ustekinumab in a patient with Crohn's disease. Case Rep Gastroenterol 2021;15(2):657–661.
11. Torres J, Mehandru S, Colombel JF, et al. Crohn's disease. Lancet 2017;389:1741–1755.
12. Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med 2016;375(20):1946-1960.
13. Thomas PWA. Immediate infusion reaction to intravenous ustekinumab in three Crohn's disease patients: a case report and review of the literature. J Crohns Colitis 2021;15(1):162–164.
14. Cleveland NK, Masching A, Rubin DT. Hypersensitivity to IV ustekinumab but tolerance to subcutaneous ustekinumab in a patient with Crohn's disease. Am J Gastroenterol 2018;113:1167–1168.
15. Yang BC, Castells MC. Rituximab hypersensitivity and desensitization: a personalized approach to treat cancer and connective tissue diseases. Ann Allergy Asthma Immunol 2019;123(1):11–15.
16. Yang BC, Castells M. Medical algorithm: Diagnosis and treatment of drug hypersensitivity reactions to biologicals. Allergy 2020;75(12):3293-3296.

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A Rare Case of Cervical Rhabdomyosarcoma in Adults

Yetişkinlerde Ender Görülen Servikal Rabdomiyosarkom Vakası

Celal Akdemir[1] | Halil İbrahim Yıldız[2] | Mücahit Furkan Balcı[3] | Özgür Erdoğan[1] Duygu Ayaz[4] | Esra Canan Kelten Talu[4] | Muzaffer Sancı[1]

[1]İzmir City Hospital, Department of Gynecologic Oncology, İzmir, Türkiye
[2]University of Health Sciences Tepecik Training and Research Hospital, Department of Medical Oncology, İzmir, Türkiye
[3]İzmir City Hospital, Department of Obstetrics and Gynecology, İzmir, Türkiye
[4]University of Health Sciences Tepecik Training and Research Hospital, Department of Pathology, İzmir, Türkiye

Sorumlu Yazar | Correspondence Author
Celal Akdemir
akdemircelal@gmail.com
Address for Correspondence: Department of Gynecologic Oncology, İzmir City Hospital, İzmir, Türkiye

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A Rare Case of Cervical Rhabdomyosarcoma in Adults

ABSTRACT

Cervical embryonal rhabdomyosarcoma is a rare mesenchymal solid tumor that accounts for less than 1% of all cervical neoplasms in the female genital system. There is no standardized protocol for the treatment of cervical embryonal rhabdomyosarcoma, and the literature primarily consists of case reports and series. Treatment options described in the literature range from conservative, fertility-preserving approaches to radical surgery in combination with chemotherapy and radiotherapy. A combined approach involving surgery, chemotherapy, and radiotherapy is believed to yield better outcomes for the disease. In this article, we present a case of cervical embryonal rhabdomyosarcoma in a 45-year-old female patient presenting with a polypoid cervical mass. Histopathological and immunohistochemical examination confirmed that the localized mass in the cervix was of cervical origin and consistent with embryonal rhabdomyosarcoma. Following total abdominal hysterectomy, the patient was administered a combination treatment of adjuvant chemoradiotherapy, and she has remained disease-free for a period of 23 months.

Keywords: Cervical Cancer, Mesenchymal tumor, Rhabdomyosarcoma.

ÖZET

Servikal embriyonel rabdomyosarkom, kadın genital sistemindeki tüm servikal neoplazmların %1'inden azını oluşturan nadir görülen mezenkimal kaynaklı solid bir tümördür. Bu tümörün tedavisine yönelik standartlaştırılmış bir protokol bulunmamaktadır ve mevcut literatür büyük ölçüde olgu sunumları ve olgu serilerinden oluşmaktadır. Literatürde tanımlanan tedavi seçenekleri, fertilite koruyucu konservatif yaklaşımlardan, kemoterapi ve radyoterapi ile kombine edilen radikal cerrahiye kadar geniş bir yelpazeye yayılmaktadır. Cerrahi, kemoterapi ve radyoterapiyi içeren kombine tedavi yaklaşımının hastalığın seyrinde daha iyi sonuçlar sağladığı düşünülmektedir. Bu yazıda, servikste polipoid bir kitle ile başvuran 45 yaşında kadın hastada görülen bir servikal embriyonel rabdomyosarkom olgusunu sunmaktayız. Yapılan histopatolojik ve immünohistokimyasal incelemeler, servikste lokalize olan kitlenin servikal kökenli olduğunu ve embriyonel rabdomyosarkom ile uyumlu olduğunu doğrulamıştır. Hastaya total abdominal histerektomi uygulanmasının ardından adjuvan kemoradyoterapi kombinasyon tedavisi uygulanmış, tedavinin ardından hasta 23 aydır hastalıksız olarak izlenmektedir.

Anahtar Sözcükler: Mezenkimal tümör, Rabdomyosarkom, Serviks Kanseri.

Introduction

Rhabdomyosarcomas are primitive mesenchymal soft tissue sarcomas that are predominantly rare in adults and mainly seen in the prepubertal age group. Due to the frequent occurrence of rhabdomyosarcomas in pediatric age groups, there is no standardized treatment approach for adult patients. Treatment selection in adults often relies on the risk groups and treatment protocols established for the pediatric population.

This mesenchymal tumor originates from immature striated muscle myocytes and can arise in various locations such as the head, neck, lymph nodes, extremities, retroperitoneum, and any part of the body. The genitourinary system is the second most commonly affected region after the head and neck. Embryonal RMS typically affects the vagina or bladder in infants and the uterus and cervix in reproductive-aged females (1). In adults, the prognosis is generally poor due to the rarity of the disease and the absence of a standardized treatment protocol (2,3).

Embryonal rhabdomyosarcoma of the uterine cervix typically manifests with symptoms such as irregular vaginal bleeding, postcoital bleeding, and a polypoid cervical mass on vaginal examination (4). Embryonal rhabdomyosarcoma of the cervix has been shown to respond positively to a combination of surgery, radiotherapy and chemotherapy. In a single-centre experience of 20 patients over 19 years of age diagnosed with RMS, the use of concurrent chemoradiotherapy and extended chemotherapy was found to improve disease-free survival (DFS) and overall survival (OS) outcomes (5). The 5-year overall survival rate for patients diagnosed with rhabdomyosarcoma of the cervix is estimated to be approximately 82% (6). Preserving fertility and sexual dysfunction are important challenges that influence treatment selection. In cases of localized rhabdomyosarcoma of the cervix, alternative options to radical hysterectomy include polypectomy and cervical conization, which can be applied. In selected cases, radical trachelectomy has been reported to preserve the patient's fertility potential while ensuring local control of the disease (7,8).

In the adult population, cases of RMS frequently present as case reports. Treatment studies in RMS have been conducted with consideration for risk groups, stages, and anatomical localization.

Case Presentation

A 45-year-old female patient was admitted to the gynecology clinic, reporting an increase in vaginal bleeding following sexual intercourse for a period of three months. During the vaginal examination of the patient, two polypoid lesions measuring 2.5x1.5 cm and 1x1.5 cm were observed at the 6-9 and 9-12 o'clock positions of the cervix, respectively. Subsequently, polypectomy was performed on the patient under local anesthesia.

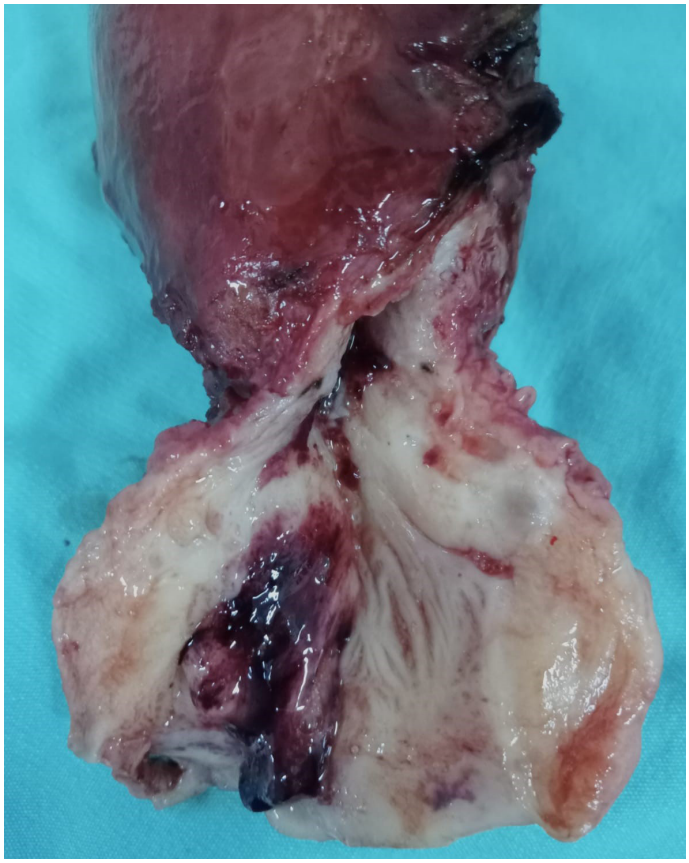

Figure I. Hysterectomy Material, Tumor in the Endocervical Canal

Tissues exhibiting a polypoid morphology were subjected to pathological evaluation based on both histopathological findings and immunohistochemical staining. The predominant interpretation was consistent with embryonal rhabdomyosarcoma. Subsequent magnetic resonance imaging (MRI) revealed that the anterior wall of the cervix exhibited mild heterogeneous signal characteristics without evidence of a distinct mass lesion. Additionally, the distal vaginal walls appeared thickened, and no significant diffusion restriction was noted. Positron

emission tomography-computed tomography (PET-CT) demonstrated mild physiological FDG uptake in the uterine cavity. Symmetrical, centimetric-sized follicular cysts were observed in both adnexal regions without increased FDG avidity. The distribution of F-18 FDG uptake across the scanned body regions was within physiological limits, and no findings suggestive of primary malignancy or distant metastasis were detected.

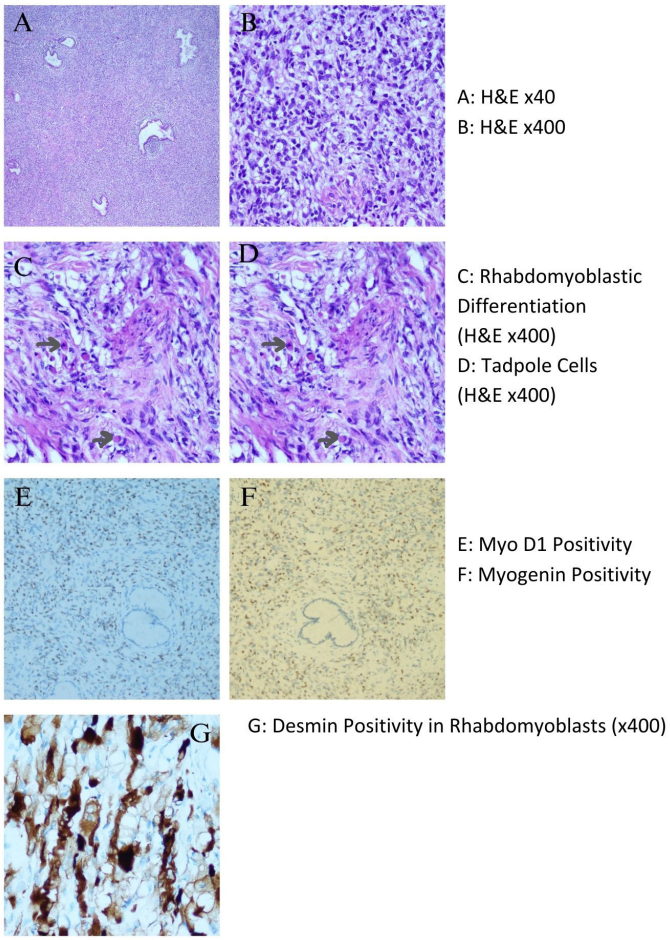

Figure II. Immunohistochemical and Pathological Examination of the Case

A. Primitive mesenchymal cells are observed in the stroma between the endocervical glands. Tumor cells are concentrated around the glands. (H&E, ×40)

B. The tumor cells have spindle-shaped, oval, and occasionally stellate morphology with narrow cytoplasm; nucleoli are not prominent. (H&E, ×400)

C. Tumor cells show abundant eosinophilic cytoplasm and eccentrically located nuclei, indicating rhabdomyoblastic differentiation. (H&E, ×400)

D. Cytoplasmic eosinophilic striations (tadpole-like cells) are observed. (H&E, ×400)

E. MyoD1 positivity in tumor cells. (×200)

F. Myogenin positivity in tumor cells. (×200)

G. Desmin positivity in rhabdomyoblasts. (×400)

In light of the prevailing pathological diagnosis and findings, the patient underwent evaluation by a multidisciplinary gynecologic oncology council. Given the patient's age, a decision was made to perform a hysterectomy. The patient underwent a laparotomic hysterectomy. When the uterus was opened along the endocervical canal, a tumor measuring 3.5x1.5x1 cm was observed on the right lateral wall of the cervix, filling the endocervical canal and displaying a polypoid appearance with bleeding (Figure I). Histopathological examination of the tumor samples revealed an infiltrating tumor starting from beneath the surface epithelium and diffusely infiltrating the stroma, with a concentration around the endocervical glands (Figure IIA). The tumor consisted of spindle-oval-shaped cells with narrow cytoplasm and mild pleomorphism (Figure IIB). Additionally, cells with broad eosinophilic cytoplasm and eccentric nuclei (Figure IIC), as well as cells showing cytoplasmic striations (Figure IID), were observed. Immunohistochemical analysis showed that the tumor cells were negative for EMA and AE1/AE3, while they stained positively for vimentin, myo-D1 (Figure IIE), myogenin (Figure IIF), desmin (Figure IIG). Based on these findings, a diagnosis of botryoid-type rhabdomyosarcoma was made. The tumor had invaded two-thirds of the cervical wall, with a depth of invasion of 0.6 cm and a distance from the parametrium of 0.6 cm. Lymphovascular invasion was detected.

No neoplasm was observed in the endometrium or the right and left fallopian tubes. In accordance with the staging criteria established by the Intergroup Rhabdomyosarcoma Study Group (IRSG), the patient was designated as Group I and Stage I. After a period of convalescence devoid of complications, the patient was referred to the relevant departments for the administration of chemotherapy and radiotherapy. Prior to discharge, the patient was provided with comprehensive information, and informed consent was obtained in accordance with standard practice. The patient was classified as a low-risk case based on clinical and pathological findings. Since no preoperative treatment was administered, adjuvant therapy was initiated following surgery. The patient received four cycles of VAC chemotherapy (vincristine, actinomycin D, and cyclophosphamide). This was followed by CT-

based high-dose-rate (HDR) brachytherapy targeting the vaginal cuff, delivered as 300 cGy twice daily over seven fractions, for a total dose of 2100 cGy. During radiotherapy, the patient also received two additional cycles of concurrent chemotherapy. The treatment was completed in March 2023, and the patient has remained disease-free for 23 months.

Discussion

Uterine cervical embryonal rhabdomyosarcoma accounts for approximately 0.4-1.0% of cervical cancers (9). Epidemiological data indicate that up to 90% of cases occur in women under the age of 25, and approximately 70% occur in children under the age of 12 (10). Perimenopausal women are less affected, but the prognosis in this age group is worse. RMS cases typically occur sporadically, and no specific risk factors have been identified. Among the histological subtypes that affect the female genital system, embryonal rhabdomyosarcomas are the most common, comprising 60% of all cases (10).

MRI is the gold standard for determining the location and invasion of the tumor, and it is useful in demonstrating the spread of the tumor to adjacent structures. The IRSG has proposed a staging system based on tumor size, involvement of the primary site, local invasion, lymph node involvement, and distant metastasis. This staging system helps in determining the stage of the tumor (10). There is no consensus on the management protocol for embryonal rhabdomyosarcoma. However, it has been observed that a multimodal approach to treatment improves patient outcomes. The multimodal approach consists of a combination of surgery, systemic chemotherapy, and radiation therapy. Given that the affected patients are predominantly young, preserving fertility and addressing postoperative sexual dysfunction in cases of surgical menopause pose significant challenges that influence treatment selection (7).

Localized rhabdomyosarcomas in the cervix can be treated with adjuvant chemotherapy along with fertility-preserving procedures such as polypectomy and simple or radical trachelectomy (11). In cases of isolated cervical and uterine involvement, simple total hysterectomy that preserves the ovaries may be recommended (4). Radical surgery has been found to not provide survival benefits in patients with superficial lesions and local recurrence. Lymphadenectomy is not routinely recommended for all patient groups, but it may be considered for those with high-risk clinical features (12). Considering the patient's age and the preoperative imaging showing a mildly heterogeneous signal in the anterior wall of the cervix without any significant mass lesion, a simple hysterectomy was performed on the patient.

In conclusion, the treatment of cervical rhabdomyosarcoma differs from other cervical tumours, especially in terms of the radicality of surgical and chemotherapy regimens, making accurate diagnosis crucial for a good prognosis. The ideal treatment for these tumors has not yet been established. However, based on current knowledge, a combined treatment approach including surgery, chemotherapy, and radiotherapy has been shown to yield favorable outcomes for cervical rhabdomyosarcoma.

References

1. Ibrahim U, Saqib A, Mohammad F, et al. Embryonal rhabdomyosarcoma of the cervix: a rare disease at an uncommon age. Cureus 2017;9(11):e1864.

2. Sultan I, Qaddoumi I, Yaser S, Rodriguez-Galindo C, Ferrari A. Comparing adult and pediatric rhabdomyosarcoma in the surveillance, epidemiology and end results program, 1973 to 2005: an analysis of 2,600 patients. J Clin Oncol 2009;27(20):3391–3397.

3. Fletcher CDM, Bridge J, Hogendoorn PCW, Mertens F. WHO Classification of Tumours of Soft Tissue and Bone. Lyon: IARC Press; 2013.

4. Behtash N, Mousavi A, Tehranian A, Khanafshar N, Hanjani P. Embryonal rhabdomyosarcoma of the uterine cervix: case report and review of the literature. Gynecol Oncol 2003;91(2):452–455.

5. Liu YT, Wang CW, Hong RL, Kuo SH. Prognostic factors and treatment outcomes of adult patients with rhabdomyosarcoma after multimodality treatment. Anticancer Res 2019;39(3):1355–1364.

6. Sardinha MGP, Ramajo FM, Ponce CC, et al. Uterine cavity embryonal rhabdomyosarcoma. Autops Case Rep 2019;9(3):e2019103.

7. Buruiana FE, Gupta B, Singh K. Rhabdomyosarcoma of the cervix in teenagers: is fertility preservation a feasible option?

Gynecol Oncol Rep 2020;34:100677.
8. Hermoza AD, de Macêdo Matsushita G, dos Santos MH, Schmidt RL, dos Reis R, da Cunha Andrade CEM. Botryoid embryonal rhabdomyosarcoma of the cervix: a case report. Int J Surg Case Rep 2023;102:107858.
9. Mousavi A, Akhavan S. Sarcoma botryoides (embryonal rhabdomyosarcoma) of the uterine cervix in sisters. J Gynecol Oncol 2010;21(4):273–275.
10. Raney RB, Maurer HM, Anderson JR, et al. The Intergroup Rhabdomyosarcoma Study Group (IRSG): major lessons from the IRS-I through IRS-IV studies as background for the current IRS-V treatment protocols. Sarcoma 2001;5(1):9–15.
11. Elsebaie MA, Elsayed Z. Is fertility-preservation safe for adult non-metastatic gynecologic rhabdomyosarcoma patients? Systematic review and pooled survival analysis of 137 patients. Arch Gynecol Obstet 2018;297(3):559–572.
12. Li C, Yang S, Hua K. Nomogram predicting parametrial involvement based on the radical hysterectomy specimens in the early-stage cervical cancer. Front Surg. 2021;8:489.

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Posterior Hysterotomy for Uterine Torsion at Term: Report of Two Cases with Long-term Follow-up

Term Gebeliklerde Uterin Torsiyonun Yönetiminde Posterior Histerotomi: Uzun Dönem Takipli İki Olgu Sunumu

Ayşe Topcu Akduman | Gizem Işık Solmaz | Özhan Özdemir

University of Health Sciences, Ankara Gülhane Training and Research Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

Sorumlu Yazar | Correspondence Author
Ayşe Topcu Akduman
drayse58@gmail.com
Address for Correspondence: University of Health Sciences, Gülhane Training and Research Hospital, Department of Obstetrics and Gynecology, Ankara, Türkiye

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Posterior Hysterotomy for Uterine Torsion at Term: Report of Two Cases with Long-term Follow-up

ABSTRACT

Uterine torsion is defined as a rotation of the uterus exceeding 45° around its longitudinal axis. In this report, we present two cases of uterine torsion diagnosed during cesarean delivery. In both cases, the babies were delivered through a transverse incision made in the lower posterior segment of the uterus. Both mothers and their newborns had an uneventful postoperative recovery and were discharged in good condition. During follow-up of the first case, a cesarean scar defect was observed, whereas complete uterine healing was noted in the second case. The potential complications and long-term outcomes associated with a posterior hysterotomy scar in future pregnancies remain uncertain.

Keywords: Cesarean delivery, Cesarean scar defect, Posterior hysterotomy, Uterine torsion.

ÖZET

Uterin torsiyon, uterusun longitudinal aksı etrafında 45°'yi aşan rotasyonu olarak tanımlanmaktadır. Bu çalışmada, sezaryen sırasında tanı konulan iki uterin torsiyon olgusu sunulmaktadır. Her iki olguda da bebekler, alt posterior uterin segmentten yapılan transvers insizyon ile doğurtulmuştur. Hem anneler hem de yenidoğanlar sorunsuz bir şekilde iyileşerek taburcu edilmiştir. Birinci olgunun takip sürecinde sezaryen skar defekti saptanırken, ikinci olguda uterusun tamamen iyileştiği gözlemlenmiştir. Gelecek gebeliklerde posterior histerotomi skarına bağlı gelişebilecek olası komplikasyonlar ve uzun dönem sonuçları henüz netlik kazanmamıştır.

Anahtar Sözcükler: Posterior histerotomi, Sezaryen doğum, Sezaryen skar defekti, Uterin torsiyon.

Introduction

Uterine torsion (UT) is a rare but potentially serious condition in obstetric practice. First described by Virchow in 1863, it is defined as a rotation of the uterus greater than 45° around its longitudinal axis (1). In most cases, the rotation reaches 180° and typically occurs in a dextrorotatory direction, although it can extend up to 360°. The exact prevalence remains unknown, as UT can occur at any age, in women of any parity, and at any stage of pregnancy (2). Although its etiology is not fully understood, known risk factors include uterine fibroids, congenital uterine anomalies, fetal malpresentation, pelvic adhesions, and laxity of the abdominal wall or ligaments. However, UT has also been reported in the absence of any predisposing factors (2,3).

Clinically, uterine torsion may present with non-specific symptoms such as abdominal pain, gastrointestinal or urinary complaints, uterine hypertonicity, or vaginal bleeding. However, in some cases, it may remain entirely asymptomatic, with the diagnosis made incidentally during cesarean section (4). In a 2021 review of 38 cases, Ferrari et al. reported that approximately one-third of uterine torsion cases were diagnosed intraoperatively during cesarean delivery without any prior clinical suspicion. This highlights the diagnostic challenges associated with this rare condition (2).

Uterine torsion can impair uterine blood flow, compromise placental perfusion, and lead to fetal distress (5). Furthermore, although rare, it has also been associated with intrauterine growth restriction or fetal hypoxia due to impaired uteroplacental perfusion. However, further studies are needed to clarify this potential relationship (2,6).

Here, we present two cases of uterine torsion diagnosed incidentally during cesarean section in women with term singleton pregnancies. The aim of this report is to contribute to the current understanding of the diagnosis and management of UT during pregnancy. This case report is presented in accordance with the SCARE 2023 criteria (7). Written informed consent was obtained from both patients prior to inclusion in this report.

Case 1

A 37-year-old woman (gravida 2, para 1) at 38 weeks of gestation with a singleton pregnancy was admitted due to an unreliable non-stress test and acute lower abdominal pain. Her previous cesarean section (CS), performed for cephalopelvic disproportion, had been uncomplicated. The prenatal course, including fetal growth, was within normal limits.

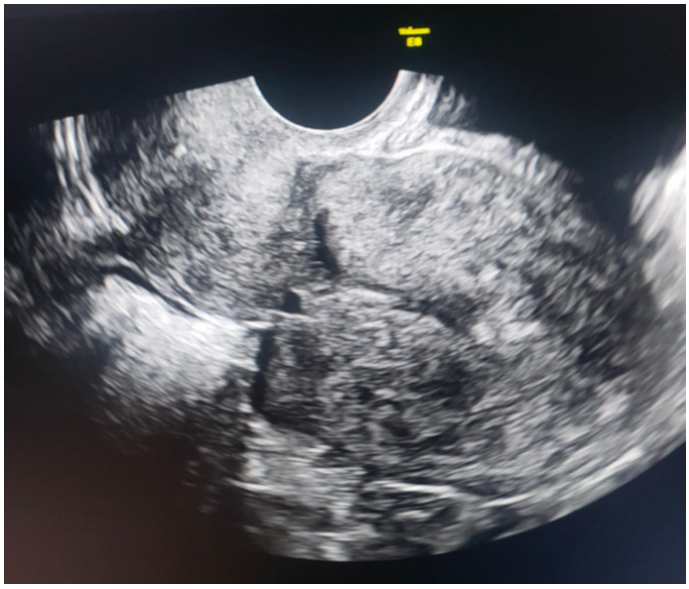

Figure I. (Case 1) Postoperative US image: The incision of the posterior wall of the uterus had recovered with a cesarean scar defect

Upon admission, her vital signs and laboratory test results were normal. Ultrasound revealed a fetal weight of 2800 g, a posterior placenta, and a normal volume of amniotic fluid.

A cesarean section was performed under spinal anesthesia via a Pfannenstiel incision. Intraoperatively, the uterus was found to be levorotated 180°, with the left adnexa located on the right and the right adnexa on the left; both adnexal structures appeared normal. The uterovesical peritoneal fold was absent. A transverse hysterotomy was performed in the lower uterine segment, and the baby was delivered in a cephalic presentation. The placenta and membranes were completely removed. Following delivery, the uterus was detorted, and the hysterotomy was closed in two layers using Vicryl sutures. Forty units of intravenous oxytocin were administered according to protocol. Bilateral tubal ligation was also performed. Intraoperative excessive bleeding was attributed to uterine atony, which was managed successfully with medical treatment. The hemorrhage

was controlled with uterotonic agents and blood component therapy, including two units of packed red blood cells and one unit of platelet concentrate. A Jackson-Pratt drain was placed in the Douglas pouch.

The newborn weighed 2750 g and had Apgar scores of 5 at 1 minute and 8 at 5 minutes. Postoperative recovery was uneventful, and the patient was discharged on postoperative day four. Three years later, she presented with postmenstrual spotting. A transvaginal ultrasound revealed a cesarean scar defect (Figure I).

Case 2

The patient was a 32-year-old woman (gravida 2, para 1) at 38 weeks of gestation with a singleton pregnancy. Her obstetric history included a CS performed 12 years earlier due to labor arrest, although no medical records were available for that procedure. The current pregnancy progressed without complications. Her medical history was notable for gestational diabetes mellitus.

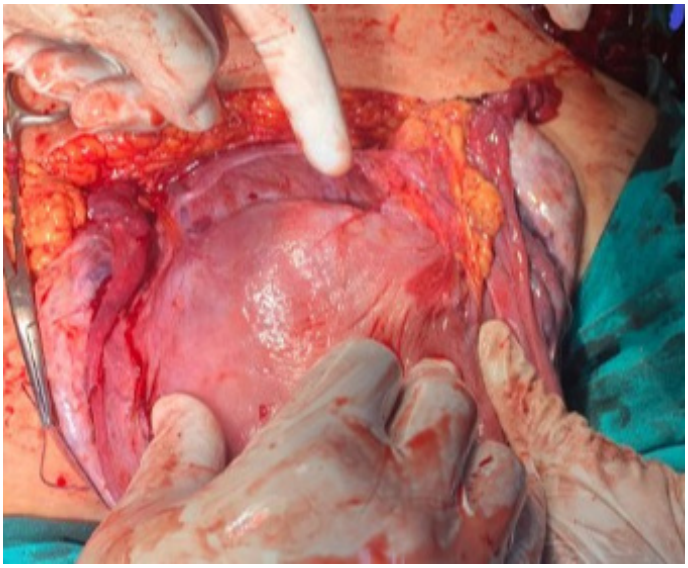

Figure II. (Case 2) Intraoperative image: The uterine incision is a transverse incision of the posterior lower uterine segment.

A planned CS was scheduled at 38 weeks due to the previous CS. Upon admission, the patient was in good general condition, with normal vital signs and laboratory test results. Clinical examination and routine investigations were unremarkable. Ultrasonography revealed an estimated fetal weight of 4000 g and an anterior placenta.

The CS was performed under spinal anesthesia. The baby was delivered successfully. As per hospital protocol, 40 units of intravenous oxytocin were administered following delivery of the anterior shoulder. After the delivery, the uterus was noted to be twisted 180° to the right, and the incision was identified on the posterior wall of the uterus. The hysterotomy repair was uneventful and was performed in two layers (Figure II). The remainder of the surgery proceeded without complications. A Jackson-Pratt drain was placed in the Douglas pouch.

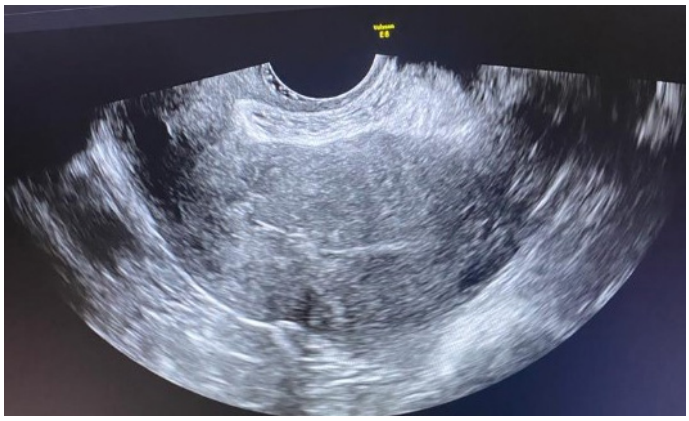

Figure III. (Case 2) Postoperative US image: The incision of the posterior wall of the uterus had recovered well, the myometrium was continuous, and the intrauterine line was clear.

The female neonate weighed 3840 g and had Apgar scores of 7 at 1 minute and 9 at 5 minutes. The patient had an uncomplicated postoperative course and was discharged in stable condition on postoperative day two.

One year later, a gynecological examination and transvaginal ultrasound were both normal (Figure III). Postoperative imaging demonstrated complete healing of the posterior uterine wall incision, with continuous myometrium and a clearly defined endometrial stripe.

Discussion

UT is a rare condition during pregnancy but carries significant risks for both maternal and fetal outcomes. It typically presents with symptoms such as acute abdominal pain in the third trimester and can be challenging to diagnose. A literature review encompassing 149 cases from 146 publications

reported a maternal mortality rate of 2% and a perinatal mortality rate of 38.2% (8). Although the exact etiology of UT remains unclear, several predisposing factors have been identified, including uterine asymmetry due to myomatous changes or Müllerian anomalies, pelvic adhesions, and ligamentous laxity. Notably, 16% of cases have no identifiable cause (2). Here, we presented two term pregnancies complicated by uterine torsion in the absence of any predisposing factors, both managed via posterior hysterotomy.

The preoperative diagnosis of UT is challenging, as clinical manifestations vary depending on the degree and duration of torsion and may sometimes be asymptomatic. In certain cases, symptoms mimic other obstetric emergencies, such as placental abruption, appendicitis, or adnexal torsion. In most instances, UT is diagnosed intraoperatively during CS. While fetal ultrasound is the primary diagnostic tool, its role is largely supportive when clinical suspicion exists. Notably, prenatal diagnosis may be aided by identifying unexpected changes in placental location, such as a shift from anterior to posterior (3).

Several studies have reported the need for CS via posterior hysterotomy in cases of UT. However, whenever feasible, detorsion should be attempted before making the uterine incision, in order to minimize complications related to inappropriate incision placement, especially in future pregnancies. The risk of uterine rupture following a posterior hysterotomy remains uncertain, and only a limited number of cases have documented pregnancy and delivery outcomes following this procedure (9,10).

Clinically significant pelvic adhesions and cesarean scar defects (CSDs) are potential risks after uterine surgery. The European Niche Taskforce defines a CSD, or niche, as an indentation of at least 2 mm in the myometrium at the site of the cesarean scar (11). While CSDs are more commonly observed after anterior hysterotomy, they may also occur following posterior hysterotomy. Associated complications include cesarean scar pregnancy, postmenstrual spotting, pelvic pain, dysmenorrhea, dyspareunia, and uterine rupture (12). Although anterior uterine rupture has been well documented, reports of posterior uterine rupture are rare. Importantly, the literature does not clearly distinguish the clinical outcomes between anterior and posterior hysterotomy scars (13).

In conclusion, UT is an extremely rare obstetric emergency that can result in serious maternal and fetal complications. It should be considered in pregnant patients presenting with acute abdominal pain. Peritoneal signs such as rebound tenderness and guarding should never be dismissed as normal findings during pregnancy. In cases of unexpected UT, a CS with a transverse incision in the lower posterior uterine segment is a safe and viable surgical option. Following a posterior hysterotomy, the surgeon should document the incision site clearly in the operative note and inform the patient that the long-term consequences and potential complications of a posterior uterine scar in future pregnancies remain uncertain and these two cases contribute to the limited body of literature on uterine torsion by providing detailed intraoperative findings and long-term follow-up outcomes.

References

1. Biswas MK, Summers P, Schultis SA, Herrera EH, Pernoll ML. Torsion of the gravid uterus: a report of two cases. J Reprod Med 1990;35(2):194-197.

2. Ferrari F, Ferrari FA, Negri B, et al. Uterine torsion and intrauterine growth restriction: Case report and systematic literature review. J Obstet Gynaecol Res 2021;47(12)4224-4231.

3. Sparic R, Lazovic B. Inevitable cesarean myomectomy following delivery through posterior hysterotomy in a case of uterine torsion. Med Arch 2013;67(1):75-76.

4. Liu S, Zhou L, Song B, et al. Uterine torsion complicated by severe placental abruption in the second trimester: a case report and literature review. BMC Pregnancy Childbirth 2023;23(1):51.

5. Salani R, Theiler RN, Lindsay M. Uterine torsion and fetal bradycardia associated with external cephalic version. Obstet Gynecol 2006;108:820-822.

6. LaHood J, You W. Uterine torsion and subsequent rupture in a gravid bicornuate uterus associated with an elevated alpha-fetoprotein. BMJ Case Rep 2018;2018:bcr2018224388.

7. Sohrabi C, Mathew G, Maria N, Kerwan A, Franchi T, Agha RA. The SCARE 2023 guideline: updating consensus surgical CAse REport (SCARE) guidelines. Int J Surg 2023;109(5):1136–1140.

8. Zahar AZ, Mazrin Nur MA. Uterine torsion in pregnancy: a case report and systematic review. Med J Malaysia 2025;80:245-257.

9. Kime KM, Bazzett-Matabele L, Nassali MN, Hofmeyr GJ.

Posterior lower uterine segment caesarean hysterotomy, an innovative surgical technique to avoid classical hysterotomy: Case report and discussion. SAGE Open Med Case Rep 2024;12:2050313X241284037.
10. Boogaerts M, Wuyts K, Joos H. Two successive cesarean deliveries through separate posterior and anterior hysterotomy due to asymptomatic uterine torsion. A case report. Case Rep Womens Health 2022;36:e00435.
11. Jordans IPM, de Leeuw RA, Stegwee SI, et al. Sonographic examination of uterine niche in non-pregnant women: a modified Delphi procedure. Ultrasound Obstet Gynecol 2019;53(1):107-115.
12. Bij de Vaate AJ, van der Voet LF, Naji O, et al. Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review. Ultrasound Obstet Gynecol 2014;43:372-382.
13. Verberkt C, Lemmers M, de Vries R, Stegwee SI, de Leeuw RA, Huirne JAF. Aetiology, risk factors and preventive strategies for niche development: A review. Best Pract Res Clin Obstet Gynaecol 2023;90:102363.

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Editöre Mektup: "Anestezistlerin Pratikte Premedikasyon Uygulamalarının Değerlendirilmesi" Üzerine Yorum

Semin Turhan

Hitit University, Erol Olçok Training and Research Hospital, Department of Anesthesiology and Reanimation, Çorum, Türkiye

Sorumlu Yazar | Correspondence Author
Semin Turhan
smnondr@hotmail.com
Address for Correspondence: Hitit University Erol Olçok Training and Research Hospital, Department of Anesthesiology and Reanimation, Çepni Dist. İnönü Str. No:176, Çorum, Türkiye

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Dear Editor,

We have read with great interest the article titled "Anestezistlerin Pratikte Premedikasyon Uygulamalarının Değerlendirilmesi" (1) published in Hitit Medical Journal. The study provides valuable insights into the clinical practice of anesthetists regarding premedication administration. However, after reviewing the current literature, we believe that some critical aspects require further discussion.

One of the key findings of the study is that premedication practices were often incomplete and that standardized forms were not fully completed. This aligns with previous studies indicating a gap between guidelines and actual clinical practice (2). A similar issue was highlighted in the study by Melesse et al., where 100% of anesthesia records contained a premedication form, yet none of these forms were fully completed according to predefined criteria (2). This suggests that the issue may not only stem from individual practitioners but also from systemic documentation challenges.

Additionally, the study does not discuss why dexmedetomidine was not included as a premedication option, despite its well-documented sedative and analgesic effects in balanced anesthesia (3). Although its cardiovascular effects necessitate cautious use, dexmedetomidine has been shown to reduce opioid consumption and improve postoperative outcomes in multiple studies (2). Clarifying the selection criteria for premedication agents would provide a more comprehensive understanding of current practices. Another limitation is the lack of assessment of patient anxiety levels before surgery. It is well established that preoperative anxiety can impact patient outcomes, and alternative approaches such as psychological preparation and patient communication have been found to be as effective as pharmacological premedication in certain cases (4). Interestingly, Melesse et al. reported that non-pharmacologic anxiolytic methods were used in 63.3% of cases, whereas pharmacologic premedication was applied in only 16.7% of cases (2). This discrepancy raises questions about whether anesthesia providers are relying more on communication-based approaches rather than pharmacologic intervention.

Finally, while antiemetics such as metoclopramide were administered in 80% of cases (2), analgesic premedication (e.g., paracetamol) was underutilized. Given the known benefits of preemptive analgesia in reducing postoperative pain (4), future studies should explore the rationale behind this preference. In conclusion, while this study provides important data on premedication practices, addressing these limitations in future research could enhance its clinical applicability. We appreciate the authors' contributions and look forward to further discussions on this topic.

References

1. Altınbas A. Premedication Applications of Anesthesiologists in Practice Evaluation. Hitit Med J 2023;5(3):156-161.

2. Melesse DY, Agegnehu AF, Kassahun HG. The assessment of the practice of premedication before anesthesia, 2020: a cross-sectional study. J Anesth Clin Res 2020;11(11):978.

3. Pan S-Y, Liu G, Lin J-H, Jin Y-P. Efficacy and safety of dexmedetomidine premedication in balanced anesthesia: a systematic review and meta-analysis in dogs. Animals (Basel) 2021;11(11):3254.

4. Blunt MC, Barber N. Principles of anesthesia: premedication. Surgery 2002;20(3):58-61.

Response from Author

Dear Editor, we would like to express our sincere thanks to the reviewer for their valuable comments and contributions regarding our article titled "Evaluation of Anesthetists' Practices in Premedication." The primary aim of our study is to present the current clinical practice of premedication based on field data and to describe the discrepancies in this area. The comments received will significantly contribute to further in-depth discussions of the topic. As emphasized in our study, the incomplete filling of premedication forms and the lack of standardization in practices are related not only to individual practitioner preferences but also to deficiencies in systemic documentation and monitoring processes. This issue, as highlighted in similar studies, is not unique to our country but is encountered globally, and the literature supporting this claim further strengthens our findings and provides an international perspective on the matter. The selection of premedication agents was addressed in our study based on frequency data, and the exclusion of agents such as dexmedetomidine is acknowledged as one of the factors that limited

the scope of our work. However, this can be clarified through more advanced comparative or interventional studies. The lack of assessment of anxiety levels is due to the descriptive nature of our study. In future prospective studies, it is important to comparatively evaluate the efficacy of both pharmacological and non-pharmacological anxiolysis methods as an emerging area of research. Finally, the limited use of analgesic premedication may be shaped by practice habits specific to individual clinics and patient profiles. However, it is evident that further research is needed to explore the effects of this practice on postoperative pain management. We would like to once again thank the reviewers for their interest in our study and constructive feedback, and we believe that future multidisciplinary research will add significant value to this field.

Sincerely,
Dr. Ali ALTINBAŞ