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Relationship Between Hemogram Parameters and HbA1c in Individuals with Iron Deficiency

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ÖZET

Amaç: Demir eksikliği anemisi (DEA) dünyanın birçok bölgesinde ve ülkemizde endemik bir halk sağlığı sorunudur. Demir eksikliği anemisi tanısı hemogram ve demir düzeylerinin analizi ile konulmaktadır. Son yıllarda hemogramdan elde edilen oranlar birçok hastalığın tanısında ve izleminde kullanılmaya başlanmıştır. Bunlardan biri de diyabetes mellitus (DM) tanı kriterlerinde yer alan hemoglobin A1c (HbA1c)'dir. Çalışmamızda demir eksikliği anemisi tanısı konulmuş bireylerin; hemogram sonuçlarından elde edilen parametreler ve oranları analiz edilerek HbA1c ile olan ilişkileri analiz edilmesi amaçlanmıştır.

Gereç ve Yöntemler: Üniversite hastanemiz Hematoloji kliniğine anemi, bulguları ile başvuran ve DEA tanısı alan 119 bireyin hemogram sonuçları laboratuvar bilgi sisteminden alınmış ve bazı hematolojik oranlar hesaplanmıştır. Sonuçlar SPSS 25.0 paket programı ile değerlendirilmiştir.

Bulgular: DEA olan bireylerde HbA1c ile lökosit, nötrofil, monosit sayısı, lenfosit yüzdesi, eritrosit dağılım genişliği ve standart sapması (RDW-SD), immatür granülosit sayısı, monosit lenfosit oranı ve nötrofil lenfosit oranı arasında istatistiksel olarak anlamlı ilişkiler saptanmıştır.

Sonuç: Çalışmamızda demir eksikliği anemisi olan bireylerin, HbA1c düzeyleri ve RDW-SD arasında diğer parametrelere göre daha güçlü pozitif ilişkili saptanmıştır. Aneminin derinleşmesi ile HbA1C düzeylerini öngördürmede hemogram parametre ve oranlarının takibinin önemli olduğunu çalışmamız ortaya koymuştur.

Anahtar Kelimeler: *Hemogram; Hemoglobin A1C; Demir Eksikliği Anemisi*

ABSTRACT

Objective: Iron deficiency anemia (IDA) is an endemic public health problem in many regions and our country. The diagnosis of iron deficiency anemia is made by analysing Hemogram and iron levels. In recent years, the rates obtained from Hemogram have begun to be used in the diagnosis and monitoring of many diseases. One of these is hemoglobin A1c (HbA1c), included in the diagnostic criteria for diabetes mellitus (DM). In our study, individuals diagnosed with iron deficiency anemia It was aimed to analyse the parameters and their ratios obtained from the hemogram results and their relationship with HbA1c.

Material and Methods: The hemogram results of 119 individuals who applied to our university hospital's hematology clinic with anemia symptoms and were diagnosed with IDA were taken from the laboratory information system, and some hematological ratios were calculated. The results were evaluated using the SPSS 25.0 package program.

Results: Statistically significant relationships were detected between HbA1c and leukocyte, neutrophil, monocyte count, lymphocyte percentage, erythrocyte distribution width and standard deviation (RDW-SD), immature granulocyte count, monocyte-lymphocyte ratio and neutrophil-lymphocyte ratio in individuals with IDA.

Conclusion: In our study, HbA1c levels of individuals with iron deficiency anemia were found to be most strongly positively correlated with RDW-SD, one of the hemogram parameters. Our analysis revealed that monitoring hemogram parameters and ratios is essential in predicting HbA1c levels as anemia deepens.

Keywords: *Hemogram; Hemoglobin A1c; Iron Deficiency Anemia*

GİRİŞ

Dünya Sağlık Örgütü'nün tanımlamasına göre demir eksikliği anemisi (DEA); hemoglobinin, 15 yaşın üstünde erkekte 13 g/dL altında, 15 yaşın üstünde ve gebe olmayan kadında 12 g/dL' in altında, gebelerde ise 11 g/dL'nin altında olmasıdır. Demir eksikliği anemisi tanısı klinik ve laboratuvar testleri ile konulmaktadır (1). Demir eksikliği anemisinde ilk azalan ferritin depoları iken, tedavi ile yine en son düzelen ferritin düzeyleridir. Hemogramda hemoglobin ve ortalama eritrosit hacminde (MCV) düşüş ve eritrosit dağılım genişliğinde (RDW) artış tipiktir (2).

Glikohemoglobin; glukozun, hemoglobinin amino grubuna nonenzimatik olarak bağlanmış formudur. HbA1c ise glikohemoglobinler arasında spesifik olarak hemoglobinin beta zincirinde N-terminal valin bölgesine bağlanmış formudur. Glikohemoglobinler, hemoglobin kromatografisinde (HPLC) hemoglobin A'dan önce ayrılarak, üç küçük pik oluşturan hızlı hemoglobinler arasında yer alır. Bu fraksiyonda en büyük pik olarak yer alan HbA1c en iyi bilinendir (3,4).

HbA1c'nin bağlı olduğu durumlar bulunduğu eritrositin yaşam süresi ve glikozun kandaki konsantrasyonudur. Eritrosit yaşam süresi ortalama 120 gün olduğu için HbA1c de son 8-12 haftayı gösteren bir değerdir. Eritrosit yapım hızını artıran DEA gibi klinik durumlar HbA1c'nin düzeylerinde değişikliklere yol açacaktır (3,4,5).

Demir eksikliği anemisi olan bireylerin, HbA1c düzeylerinin artışa sebep olduğuna dair çalışmalar literatürde mevcuttur. Bir diğer taraftan da DEA tedavisinin de HbA1c düzeylerinde artış yaptığı öne sürülmektedir (4,5). Son yıllarda inflamasyonu gösterdiği öne sürülen, hemogram parametrelerinden elde edilen monosit lenfosit oranı (MLO), nötrofil lenfosit oranı (NLO), trombosit lenfosit oranı (TLO) gibi oranlar literatürde sıklıkla çalışılmıştır (6).

Ancak DEA kliniği sahip kişilerde, bu oranların HbA1c ile olan ilişkisi henüz tam olarak aydınlatılmamıştır.

Biz de bu amaçla demir eksikliği anemisi olan bireylerde HbA1c düzeylerini değerlendirerek, başka bir inflamatuar belirteci olarak kullanılıp kullanılamayacağını ortaya koymayı amaçladık.

GEREÇ VE YÖNTEMLER

Etik kurul onayının (Karar no: 60116787-020/64497) alınmasının ardından çalışmamıza Pamukkale Üniversitesi Sağlık Uygulama ve Araştırma Hastanesi polikliniklerine ve servislerine Ekim 2022 ve Nisan 2023 tarihleri arasında başvuran 119 hasta dahil edildi. Hastalar ile ilgili detaylı bilgilere veri madencilik prensipleri kullanılarak retrospektif olarak hastane ve laboratuvar bilgi sistemi (HBS, LBS) üzerinden ulaşıldı.

Çalışmaya LBS'den, HbA1c değerleri (mmol/mol ve yüzde olarak), hemogram sonuçları alınmıştır. Hemogram Mindray BC 6800 (Şangay, Çin) otoanalizöründe elektriksel empedans ve optik dansite ile analiz edilirken, HbA1c ise Tosoh G8 HPLC (Japonya) cihazında kromotografik olarak analiz edilmektedir. Hemogramdan elde ettiğimiz monosit, nötrofil, lenfosit ve trombosit sayılarından; MLO, NLO ve TLO oranları hesaplanmıştır.

Ayaktan ya da yatarak hastanemizde takip edilen HBS'ye demir eksikliği anemisi ön tanısı girilmiş Ekim 2022-Nisan 2023 arasında gelen tüm bireyler ve aynı anda HbA1c istemi olan ve en az 1 kez hemogram istenmiş kişiler çalışmamıza dahil edilmiştir. Bu tarihler arasında gelen ayaktan ve yatarak başvuran demir eksikliği anemisi tanısı olup HbA1c istemi olmayanlar ise çalışmamıza dahil edilmemiştir.

Veriler SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)) paket programıyla analiz edilmiştir. Sürekli değişkenler ortalama ± standart sapma, ortanca (25. - 75. yüzdelikler), en küçük ve en büyük değerler verilmiştir. Verilerin normal dağılıma uygunluğunun incelenmesinde Kolmogorov Smirnov testi kullanılmıştır. Sayısal değişkenler arasındaki ilişkilerin incelenmesinde ise Spearman korelasyon katsayısı kullanılmıştır. Buna göre r'nin değeri 0-0,19 arasında iken ilişki yok ya da önemsenmeyecek düzeyde düşük ilişki, 0,2-0,39 arasında ise zayıf (düşük) ilişki, 0,40-0,69 arasında iken orta düzeyde ilişki, 0,70-0,89 arasında kuvvetli (yüksek) ilişki ve 0,90-1 çok kuvvetli ilişkiyi belirtmektedir. Tüm incelemelerde $p<0,05$ istatistiksel olarak anlamlı kabul edilmiştir.

BULGULAR

Çalışmamıza 119 bireyin sonuçları dahil edilmiştir. HbA1c mmol/mol olarak seviyesi ve yüzde ifadesi ile istatistiksel anlamlılık gösteren hemogram parametrelerinin korelasyon ilişkisi tablo 1 de ayrıntılı olarak verilmiştir. Çalışmada lökosit sayısı ile HbA1c

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Tablo 1. HbA1c mmol/mol olarak seviyesi ve yüzde ifadesi ile istatistiksel anlamlılık gösteren hemogram parametrelerinin korelasyon tablosu

		HbA1c mmol/mol (% HbA1c)
Lökosit sayısı /mm³	r	0,204
	p	0,027*
RDW-SD	r	0,314
	p	0,001*
RDW	r	0,268
	p	0,003*
NLO	r	0,199
	p	0,031*
Nötrofil yüzdesi	r	0,192
	p	0,037*
Nötrofil sayısı /mm³	r	0,246
	p	0,007*
Monosit sayısı /mm³	r	0,233
	p	0,011*
Lenfosit yüzdesi	r	-0,200
	p	0,030*
IMG yüzdesi	r	0,269
	p	0,003*
IMG sayısı /mm³	r	0,269
	p	0,003*
MLO	r	0,227
	p	0,014*

RDW (eritrosit dağılım genişliği), RDW-SD (eritrosit dağılım genişliği dağılım aralığı), NLO (Nötrofil lenfosit oranı), IMG: İmmatür granülosit, MLO (Monosit lenfosit oranı) Korelasyon r ile ifade edilirken, *p<0,05 anlamlı kabul edilmiştir.

arasında anlamlı bir ilişki (p=0,02) bulunmuşken bu ilişkinin zayıf olduğu (r:0,204) görülmüştür. HbA1c ile MLO arasında anlamlı (p=0,010) ama düşük düzeyde güçlü (r=0,227) bir ilişki olduğu görülmüştür. HbA1c ile RDW arasında anlamlı bir ilişki (p=0,003) bulunmuşken bu ilişkinin zayıf (r=0,268) olduğu görülmüştür. Aynı zamanda eritrosit dağılım genişliğinin standart sapması (RDW-SD) arasında anlamlı bir ilişki (p=0,001) bulunmuş ancak bu ilişkinin zayıf (r=0,314) olduğu görülmüştür.

HbA1c ile nötrofil lenfosit oranı (NLO) arasında anlamlı bir ilişki (p=0,031) bulunmuşken bu ilişkinin zayıf (r=0,199) olduğu görülmüştür. HbA1c ile nötrofil sayısı arasında anlamlı (p=0,007) ama düşük düzeyde bir ilişki (r=0,246) bulunmuştur. Ayrıca HbA1c ile nötrofil yüzdesi arasında da anlamlı (p=0.037) ama düşük düzeyde bir ilişki (r=0,192) bulunmuştur. HbA1c ile monosit sayısı arasında da anlamlı (p=0,011) ama düşük düzey bir ilişki (r=0,233) bulunmuştur. Lenfosit yüzdesi ile HbA1c arasında anlamlı (p=0,03) ama (r=-0,200) düşük ve ters yönlü bir ilişki bulunmuştur. İmmatür granülosit (IMG) ile HbA1c arasında anlamlı (p=0,03) ama düşük düzeyde (r=0,269) bir ilişki bulunmuştur. IMG yüzdesi (IMG%) ile ise yine aynı şekilde anlamlı (p=0,03) ve düşük düzeyde (r=0,269) bir ilişki bulunmuştur.

Çalışmamızda baktığımız parametrelerden olan eritrosit sayısı, platelet, ortalama platelet hacmi, ortalama eritrosit hacmi, ortalama eritrosit hemoglobin konsantrasyonu, ortalama eritrosit hemoglobini, hematokrit, eozinofil ve bazofil sayısı ile hesaplanmış TLO ile HbA1c arasında istatistiksel bir anlamlılık saptanmamıştır (p>0,05).

TARTIŞMA

Çalışmamız DEA'lı bireylerde hemogram parametreleri

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ve parametrelerden elde edilen oranların bazılarının HbA1c ile istatistiksel olarak anlamlı ilişkide olduğunu ortaya koymuştur. Veri madenciliği yaptığımız çalışmamızda, HbA1c ile diğerleri içinde en güçlü ilişki gösteren RDW-SD idi. Benzer olarak Tanburoğlu ve arkadaşının 310 diyabetik hasta ve 328 sağlıklı kontrol üzerinde yaptığı çalışmada, Diyabetik grubunun RDW'sinin, kontrol grubuna göre anlamlı derecede yüksek olduğu ortaya konulmuştur. Çalışmacılar eritrosit sayısının dolaşımdaki düzeyine bağlı değişen olan RDW'nin inflamasyon göstergesi olduğunu ve yüksek HbA1c düzeyleri ile ilişki olabileceğini öne sürmüştür (7).

Veysel ve ark. yapmış olduğu çalışmada açlık glukozu ve hemoglobin A1c düzeyleri referans aralık içinde bulunan ve diyabet hikayesi bulunmayan bireylerde demir eksikliği anemisinin hemoglobin A1c düzeylerine etkisi olup olmadığını araştırmış ve demir eksikliği anemisi, referans aralıklarda seyreden hemoglobin A1c düzeylerini anlamlı artış yönünde etkilediği sonucuna varılmıştır (5). Benzer bulguyu çalışmamızda biz de ortaya koyduk.

Sinha ve ark. yapmış olduğu çalışmada demir eksikliği anemisinin HbA1c düzeyleri üzerindeki etkisini analiz ederek demir eksikliği anemisi tedavisinin HbA1c düzeylerini etkileyip etkilemediğini araştırmışlar ve DEA tedavisiyle HbA1c düzeylerinin ve mutlak HbA1c düzeylerinin arttığı sonucuna varılmıştır (8). Bizim çalışmamız retrospektif olduğundan tedavi konusunda yeterli bilgimizin olmayışı kısıtlılığımızdır. Yine, İmdat ve ark. yapmış oldukları çalışmada demir eksikliği anemisi tanısı konulan hastalarda eritrosit indeksleri, hemogram sonuçları ve etyolojik nedenleri incelemişler ve DEA olan bireylerde RDW değeri, ortalama değerinin üstünde bulunmuştur (9).

Akarsu ve ark. yaptıkları çalışmada çocukluk yaş gruplarında DEA'nin Hb alt tipleri üzerine etkisini araştırmışlar ve DEA gibi eritrosit yaşam süresini kısaltan durumların HbA1c düzeylerinde yanıltıcı olarak düşüklüğe sebep olduğunu saptamışlardır (10). Çalışmamız RDW-SD değerinin HbA1C ile pozitif ilişkisini gösterdiğinden Saadet ve ark aksi olarak yaşam süresinin bu parametreyi doğrudan etkilediğini öne sürüyoruz. Oğuz ve ark. yaptıkları çalışmada normoglisemik hasta grubunda DEA'nin HbA1c düzeylerine olan etkisini incelemişler ve DEA olan ve sağlıklı grup arasında HbA1c düzeyleri açısından anlamlı bir fark bulamamışlardır. Demir eksikliği anemisinde eritrosit yaşam oranının değişmediği ve bununla ilişkili olarak HbA1c düzeylerinin de etkilenmediği sonucuna ulaşmışlardır (11).

İnflamatuvar oranlar NLO ve PLO'nun son yıllarda farklı klinik patolojilerde ve hasta gruplarında yapılan çalışmalarda sık tercih edildiğini görmekteyiz. Ancak diğer birçok hastalıkta olduğu gibi demir eksikliği ön tanılı hastalarda da yapılan çalışmalarda elde edilen sonuçlar görece yetersiz ve tartışmaya açıktır.

Bir diğer çalışmada sağlıklı, prediyabetik ve diyabetik gruplarda, HbA1c ile NLO ve TLO ile CRP ve sedimantasyon arasındaki ilişki araştırılmış ve HbA1c ile NLO, TLO ve sedimantasyon arasında bir ilişki saptanamazken, CRP ile HbA1c değerleri arasında ilişki saptanmıştır (12). Çalışmamızın bir diğer kısıtlılığı inflamasyon parametrelerinin çalışmaya dahil edilememesiydi. Çünkü bireylerin çoğunda bu test istemi gerçekleşmemişti. Ancak bu çalışmanın aksine bulgularımız orta derecede olsa da inflamasyon oranları ile HbA1c düzeylerini anlamlı ilişkili bulmuştur. Özetle çalışmamızda HbA1c ile inflamasyon hücreleri ve oranlar arasında anlamlı ama düşük düzeyde korelasyonlar saptanmıştır; güçlü bir korelasyon saptanmamıştır. Veri analizinin devamlılığı bu hastalarda ilerleyen dönemlerde anemi takiplerinde etkili olabileceği çalışmamızda sunulmuştur.

SONUÇ

Veri madenciliği analizi ile elde ettiğimiz veriler; DEA kliniğine sahip bireylerin takibinde farklı belirteçler ile inflamasyon süreçlerinin takip edilebileceğini bize göstermiştir. Laboratuvar verilerinden yararlanılarak daha fazla testin hastalık tanı ve takibinde daha kullanışlı olacağını düşünmekteyiz.

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PARANEOPLASTİK NÖROLOJİK SENDROMLAR: KLİNİK SPEKTRUM VE ÖZELLİKLERİNİN DEĞERLENDİRİLMESİ

Paraneoplastic Neurological Syndromes: Evaluation of The Clinical Spectrum and Features

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ÖZET

Amaç: Paraneoplastik nörolojik sendromlar (PNS) genellikle altta yatan tümör tarafından tetiklenen immün yanıtların aracılık ettiği bir grup sendromu ifade etmekte olup, sinir sisteminde her düzeyi etkileyebilecek farklı klinik spektrumları kapsamaktadır. Bu nedenle hastalarda tanıda zorluklara neden olmaktadır. Bu çalışmada PNS ile değerlendirilen hastaların klinik ve laboratorur özelliklerinin ve hasta yönetimlerinin retrospektif olarak değerlendirilmesi ve tartışılması amaçlanmıştır.

Gereç ve Yöntemler: Bu çalışmada Başkent Üniversitesi Hastanesi'nde 2012-2023 yılları arasında nöroloji polikliniği, nöroloji servisi yada yoğun bakımda izlemi yapılmış PNS ile uyumlu klinik bulguları olan ve antikor pozitifliği saptanan hastaların verisi retrospektif olarak değerlendirilmiştir. PNS ön tanısı olan toplam 342 hasta verisi incelendi. Bireylerin demografik verileri, serum ve beyin omurilik sıvısı sonuçları, beyin manyetik rezonans görüntüleme tetkik sonuçları, elektroensefalografi ve elektromyografi değerlendirilmeleri, uygulanan tedavi türleri, taburculuk tedavi yanıtı ve takip verileri incelendi. Veriler SPSS programı kullanılarak analiz edildi.

Bulgular: Dışlama kriteri sonrasında toplam 21 hastanın verisi retrospektif olarak değerlendirildi. Hastaların %57.1' i (n=12) erkek cinsiyetindeydi ve yaş ortalamaları 69.57 ± 11.18 yıldı. Hastalarda en sık limbik ensefalit (n=6, %28.6) ve hızlı progresif serebellar sendrom (n=6, %28.6) saptandı. Anti- amfifizin, CASPR2 ve Yo antikorları en sık saptanan antikorlardı. 8 hastada (%38.1) başvuru, tedavi ve takip süresince malignite izlenmedi. İntravenöz pulse steroid tedavisi ile intravenöz immunglobin tedavisi en sık uygulanan tedavi yöntemleriydi. Takip süreci içinde 5 hastada (%23.8) ölüm gözlendi.

Sonuç: PNS nadir görülen, tanısı zor olan sendromlar olup, sıklıkla hastaya yanlış tanı konulur yada tanı atlanabilir. Hastalarda semptom ve bulgularının erken tanınması ve uygun tanı ve tedavi planının zamanında belirlenmesi için farklı merkezden PNS ilişkili verilere ihtiyaç vardır.

Anahtar Kelimeler: *Paraneoplastik Nörolojik Sendrom; Limbik Ensefalit; Onkonöral Antikor; Serebellar Sendrom*

ABSTRACT

Objective: Paraneoplastic neurological syndromes (PNS) refer to a group of syndromes generally mediated by immune responses triggered by the underlying tumor and cover different clinical spectrums that can affect every level in the nervous system. Therefore, it causes difficulties in diagnosis for patients. This study aimed to evaluate and discuss the clinical and laboratory characteristics and patient management of patients with PNS retrospectively.

Material and Methods: In this study, the data of patients with clinical findings compatible with PNS and antibody positivity who were followed up in the neurology outpatient clinic, neurology service or intensive care unit at Baskent University Hospital between 2012 and 2023 were evaluated retrospectively. Totally 342 patients with a preliminary diagnosis of were investigated. Demographic data, serum and cerebrospinal fluid results, brain magnetic resonance imaging examination results, electroencephalography and electromyography evaluations, types of treatment, treatment response and follow-up data were examined. Data were analyzed using the SPSS program.

Results: After the exclusion criteria, the data of a total of 21 patients were evaluated. 57.1% (n=12) of the patients were male and the mean age of the patients was 69.57 ± 11.18 years. Limbic encephalitis (n=6, 28.6%) and rapidly progressive cerebellar syndrome (n=6, 28.6%) were most frequently detected in patients. Anti-amphiphysin, CASPR2 and Yo antibodies were the most commonly detected antibodies. No malignancy was observed in 8 patients (38.1%) during admission, treatment and follow-up. Intravenous pulse steroid therapy and intravenous immunoglobulin therapy were the most frequently applied treatment methods. Death was observed in 5 patients (23.8%) during the follow-up period.

Conclusion: PNS is a rare syndrome that is difficult to diagnose and the patient is often misdiagnosed or the diagnosis may be missed. PNS related data from different centers are needed for early recognition of symptoms and determination of the appropriate diagnosis or treatment plan.

Keywords: *Paraneoplastic Neurological Syndrome; Limbic Encephalitis; Onconeural Antibody; Cerebellar Syndrome*

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GİRİŞ

Paraneoplastik nörolojik sendromlar (PNS) genellikle altta yatan tümör tarafından tetiklenen immün yanıtların aracılık ettiği, metastaz, infeksiyon, iskemi, metabolik bozukluklar yada kanser tedavi yan etkisi ilişkili olmayan bir grup sendromu ifade eder (1-3). PNS, merkezi veya periferik sinir sisteminin herhangi bir seviyesini etkileyebilir (2). PNS nadir görülmekte olup, yaklaşık insidansı 100.000 kişi-yıl başına 0,8-0,89'dur (4). 'Paraneoplastik' terimi ilk kez 1949'da ortaya atılmış olup, uterus neoplazmının metastazlarından kaynaklanan multipl kranial ve radiküler nöropatileri olan bir hastanın ayırıcı tanısını tartışmak için kullanılmıştır (3). Otoantikorların keşfi PNS araştırmalarında bir dönüm noktasını oluşturmuştur (3). 1980'li yıllarda over kanseri ve akciğer kanseri gibi kanser hastalarının serumlarında art arda antikorlar keşfedilmeye başlanmış ve 1985 yılında Graus ve ark. , bu vakalardan bazılarının serumlarında nöron çekirdeklerini etkileyen farklı bir antikor bulunduğunu tespit etmişlerdir (3, 5).

Hastalarda klinik, kognitif bozukluklar ve ensefalitten, nöromusküler hastalıklar ve periferik sinir hastalıklarına kadar her düzeyi etkileyebilecek farklı spektrumları kapsamakta ve bu hastaların tanısında zorluklara neden olmaktadır (4). Tüm PNS'lerin erken tanı ve teşhisi, etkili tedavi için kritik öneme sahiptir ve sendromlar nadir olduğundan, yeni onkonöral antikorları ve yeni sendromları tanımlamak için farklı merkezlerden gelen verileri bir araya toplayabilmek önemlidir. Bu nedenle, bu çalışmada PNS ile değerlendirilen hastaların klinik ve laboratuvar özellikleri ile hasta yönetimlerinin retrospektif olarak değerlendirilmesi ve tartışılması amaçlanmıştır.

GEREÇ VE YÖNTEM

Bu çalışmada, Başkent Üniversitesi Hastanesi'nde 2012-2023 yılları arasında nöroloji polikliniği, nöroloji servisi yada yoğun bakımda izlemi yapılmış PNS ile uyumlu klinik bulguları olan ve antikor pozitifliği saptanan 18 yaş üstü hastaların verisi retrospektif olarak değerlendirildi. PNS ön tanısı olan toplam 342 hasta verisi incelendi. Antikor pozitifliği olan ancak kliniği uygun olmayan hastalar ve antikor sonucu negatif olarak değerlendirilen hastalar çalışma dışı bırakıldı.

Merkezimiz serum paraneoplastik antikor paneli anti-Hu, Yo, CV2/ collapsin response mediator protein (CRMP) 5, Ma2, Ri, recoverin, SOX, titin, tr/ Delta/Notch-like epidermal growth factor-related reseptör (DNER), amfifizin, zic ve glutamic acid decarboxylase 65 (GAD65) antikor incelemelerini içermekteydi. Limbik ensefalit ön tanısı olan hastalarda ise serumda anti- Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) 1-2, contactin-associated protein-like 2 (CASPR 2), leucine-rich glioma inactivated 1 (LGI-1), gamma-aminobutyric acid B (GABA B) ve N-methyl-D-aspartate (NMDA) antikorları çalışılmaktaydı. Beyin omurilik sıvı (BOS) analizinde ise anti-Hu, Yo, Ri ve tr antikorları çalışılmaktaydı. Bütün antikor incelemeleri aynı laboratuvar ve teknik kullanılarak sonuçlandırıldı. BOS ve serum limbik ensefalit panel incelemelerinde immunfloresans metodu ve paraneoplastik antikor serum incelemelerinde immunoblot yöntemi kullanıldı. Bu antikorlardan biri pozitif yada zayıf pozitif olan hastalar çalışmaya dahil edildi.

Paraneoplastik nörolojik sendrom tanısı için Graus ve ark. tarafından bildirilen kriterler kullanıldı (6). Hastalarda limbik ensefalit tanısı Gültekin ve ark. tarafından bildirilen tanı kriterleri doğrultusunda koyuldu (7).

Hastaların demografik verileri, rutin serum ve tam kan tetkikleri, serum ve BOS sonuçları, beyin manyetik rezonans (MR) görüntüleme tetkik sonuçları, elektroensefalografi (EEG) ve elektromyografi (EMG) değerlendirilmeleri incelendi. BOS değerlendirilmelerinde protein normal aralığı 15-45 mg /dl ve BOS'ta 5/mm3 üstü hücre pleositoz olarak değerlendirildi. Hastalara uygulanan tedavi türleri, dozları ve taburculuk tedavi yanıtı ve takip verileri kaydedildi. Hastaların malignite açısından taramaları, sonuçları ve ölüm oranları saptandı. Veriler SPSS paket programı kullanılarak analiz edildi. Kategorik veriler sayı (%) şeklinde, normal dağılıma sahip sayısal veriler ortalama (ort) ± standart sapma (SS) şeklinde gösterilirken, normal dağılıma sahip olmayan sayısal veriler medyan (interquartil range (IQR)) olarak belirtildi. Çalışma için Başkent Üniversitesi Tıp ve Sağlık Bilimleri Araştırma Kurulu tarafından onay alındı (Proje no: KA 24/247, Ankara, Türkiye).

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BULGULAR

Dışlama kriterleri sonrası toplam 21 hastanın verisi retrospektif olarak değerlendirildi. Hastaların %57,1' i (n=12) erkek cinsiyetindeydi ve yaş ortalamaları 69,57 ± 11,18 yıl olarak bulundu. Başvurularında 7 hastada (%33,3) sistemik hastalık öyküsü yoktu. Sistemik hastalığı bulunanların hastalıklarının dağılımı Tablo 1.'de gösterilmiştir.

Hastalarda semptom başlangıcı ile hastane başvuru arası geçen süre medyan 45,00 (IQR: 133) gün olup, hastaların çoğunluğu (n=10, %47,6) 2-8 hafta içerisinde başvurmuştu. Hastaneye başvuru ile PNS tanısı arası geçen süre medyan 10 (IQR: 17) gün olarak saptandı (Tablo 1.).

Hastaların başvuru semptomları değerlendirildiğinde hastalar en sık yürüme güçlüğü şikayeti ile (n=10, %47,6), takibinde dengesizlik (n=6, %28,6) ve ekstremitelerde kuvvetsizlik (n=5, %23,8) veya ekstremitelerde kasılma (n=5,%23,8) şikayeti ile başvurmuştu. Hastaların başvuru şikayetlerinin dağılımı Tablo 1.' de belirtilmiştir. Hastaların başvuru değerlendirilmelerinde 4 hastada (%19,0) nöbet saptandı. Muayenelerinde 6 hastada (%28,6) ataksi, 4 hastada (%19,0) nistagmus, 4 hastada (%19,0) quadriparezi, 2 hastada (%9,5) paraparezi, 2 hastada (%9,5) bulbar güçsüzlük, 2 hastada (%9,5) hipoestezi, 1 hastada (%4,8) myoklonus ve 1 hastada (%4,8) oftalmoparezi mevcuttu. Klinik fenotiplerin dağılımları incelendiğinde hastalarda en sık limbik ensefalit (LE) (n=6, %28,6) ve hızlı progresif serebellar sendrom (HPSS) (n=6, %28,6) bulunmaktaydı (Tablo 2.). Hastalarda en sık %19,0 oranı (n=4) ile anti- amfifizin antikorları mevcuttu. Takibinde en sık anti-CASPR2 antikoru, anti-Yo ve anti-tr antikorları izlendi.. Dört hastada birden fazla antikorun eş zamanlı pozitifliği mevcuttu. Hastalarda PNS ilişkili saptanan antikorların dağılımı Tablo 2.' de sunulmuştur.

BOS incelemesi yapılan 16 hastadan 4'ünde (%19,0) pleositoz ve 10 hastada (%47,6) protein yüksekliği

Tablo 1. Hastaların başvuru ve demografik özellikleri

Yaş , yıl, ort ±SS	69,57 ± 11,18
Erkek, n (%)	12 (%57,1)
Sistemik hastalık , n (%)	
Hipertansiyon	13 (%61,9)
Diyabetes Mellitus	4 (%19,0)
Hiperlipidemi	2 (%9,52)
Koroner Arter Hastalığı	1 (%4,76)
Kronik Obstruktif Akciğer Hastalığı	1 (%4,76)
Hipotiroidi	1 (%4,76)
Sistemik Lupus Eritamatozus	1 (%4,76)
Sistemik hastalık bulunmayan	7 (%33,3)
Semptom başlangıcı – başvuru arası süre, gün, medyan (IQR)	45.00 (133)
Başvuru- tanı arası süre, gün, medyan (IQR)	10 (17)
Başvuru semptom, n (%)	
Yürüme güçlüğü	10 (%47,6)
Dengesizlik	6 (%28,6)
Kognitif Etkilenim	3 (%14,3)
Konfüzyon	1 (%4,8)
Konuşma bozukluğu	4 (%19,0)
Ekstremitelerde kuvvetsizlik	5 (%23,8)
Ekstremitelerde uyuşukluk-duyu kaybı	1 (%4,8)
Ekstremitelerde kasılma	5 (%23,8)
İstemsiz hareket	2 (%9,5)
Çift görme	2 (%9,5)

Ort: Ortalama, SS: Standart sapma, IQR: interquartile range

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Tablo 2. İncelenen hastaların detaylı klinik profili

Hasta no	Cinsiyet	Yaş	PNS	Serum Antikor	BOS Antikor	BOS Protein	BOS pleositoz	Bilinen Malignite Türü	Yeni Tanı Malignite Türü	Tedavi	Ölüm
1	E	70	LE	LGI-1	LGI-1	Yüksek	-	-	-	Pulse steroid+IVIg+ PF	+
2	E	67	LE	CASPR2	NA	NA	NA	Mesane	KHAK	Pulse steroid	+
3	E	78	LE	CASPR2	NA	Yüksek	+	Meme	-	Pulse steroid+IVIg	+
4	E	68	LE	Anti-Hu	NA	Yüksek	-	KHAK	-	Oral steroid	+
5	E	75	LE	Anti-sox	NA	NA	NA	KHAK	-	Pulse steroid	+
6	E	77	LE	Anti-zic	NA	Normal	-	-	-	Pulse steroid	-
7	K	63	HPSS	Anti-Yo	Anti-Yo	Normal	-	-	Over	Pulse steroid+IVIg+oral steroid	-
8	K	46	HPSS	Anti-Yo	Anti-Yo	Yüksek	+	-	Over	Pulse steroid+IVIg+oral steroid	-
9	K	73	HPSS	Anti-amfifizin	NA	Yüksek	+	-	KHAK	Pulse steroid+IVIg	-
10	E	50	HPSS	Anti-tr	NA	NA	NA	HL	-	-	-
11	E	73	HPSS	Anti-zic ve sox	NA	NA	NA	KHAK	-	IVIg	-
12	K	81	HPSS	Anti-zic,sox,hu	Anti-Hu	Yüksek	-	-	KHAK	-	-
13	K	48	MG	CASPR2	NA	Normal	-	-	-	Oral steroid	-
14	E	72	MG	Anti-titin	NA	Normal	-	-	-	PF+oral steroid	-
15	K	54	SPS	Anti-amfifizin	NA	NA	NA	-	-	Pulse steroid+oral steroid	-
16	E	69	SPS	NMDA,LGI-1	NMDA,LGI-1	Yüksek	-	-	-	Pulse steroid+oral steroid	-
17	K	84	MNH	Anti-tr,amfifizin	Negatif	Normal	-	-	GIS	-	-
18	E	89	MNH	Anti-tr	Anti-tr	Yüksek	-	-	-	Pulse steroid+IVIg	-
19	K	67	Myelit	Anti-CV2	NA	Yüksek	+	-	-	Pulse steroid+IVIg+ PF	-
20	K	82	Nöropati	Anti-Yo	NA	Yüksek	-	-	HCC	IVIg	-
21	E	75	Myoklonus	Anti-amfifizin	NA	Normal	-	KHAK	-	Pulse steroid+IVIg	

K: Kadın, E: Erkek, PNS: Paraneoplastik nörolojik sendrom, LE: Limbik ensefalit, HPSS: Hızlı progresif serebellar sendrom, MG: Myastenia Gravis, MNH : Motor nöron hastalığı, SPS: Stiff man sendromu, NA:Non-applicable, HL : Hodgkin Lenfoma, KHAK: Küçük hücreli akciğer kanseri, GIS: Gastrointestinal sistem, HCC: Hepatosellüler karsinom, IVIg: intravenöz immunglobin, PF: Plazmaferez

izlendi. BOS' ta 6 hastada (%28,6) serum ile aynı antikor pozitifliği saptandı.

Başvuru sırasında 7 hastada (%33,3) bilinen malignite mevcuttu. Bunların dağılımı Tablo 2.' de gösterilmiştir. PNS tanısı takibinde yapılan malignite taramalarında 7 hastada yeni malignite saptandı. Bu hastalardan 6 hastada bilinen malignite tanısı bulunmamaktaydı ve PNS tanısı sonrası araştırmalarda malignite tanısı almışlardı, 1 hasta ise PNS döneminde bilinen mesane kanserine sahipti ve araştırmalarda yeni tanı küçük hücreli akciğer kansri (KHAK) tanısı almıştı. Toplam 8 hastada (%38,1) başvuru, tedavi ve takip süresince malignite izlenmedi. Hastaların malignite tanılarının dağılımları Tablo 2.'de gösterilmiştir.

Tanı sonrası 3 hastaya takip yada kontrole gelmemeleri nedeniyle tedavi uygulanamamıştı. Akut tedavi yöntemlerinde en sık birbirini izleyen 5 gün 1000 mg intravenöz pulse steroid tedavisi ve takibinde 5 gün 0,4g/kg intravenöz immunglobin (IVIg) uygulandı (n=4, %19,0). Taburculukta 3 hastada (%14,3) tedavi ile klinik bulgularda tam yanıt izlenirken 15 hastada (%71,4) kısmi yanıt izlendi.

Limbik ensefalit ile izlenen 6 hastanın tümü erkek cinsiyetindeydi. Bu hastaların 2'sinde bilinen KHAK, 1'inde meme kanseri tanısı bulunurken, 1 hastada tetkikler sırasında KHAK tanısı konulmuştur. 2 hastada malignite tetkiklerde saptanmadı. Başvuruda bu hastaların 3'ü ileri yaşta yeni gelişen nöbet diğer 3 hasta ise hızlı ilerleyen kognitif etkilenim nedeniyle değerlendirilmişti ve hastaların çoğunda semptomlar subakut seyirliydi. Hastaların yapılan beyin MR görüntülemelerinde 2 hastada sol insular korteks ve temporal lobda intensite artışı izlenirken diğer hastaların beyin MR görüntülemelerinde kronik iskemik gliotik değişiklikler ve yaş ile uyumlu serebral atrofi dışında patolojik bulgular izlenmedi. EEG incelemelerinde 3 hastada paroksismal/epileptiform aktivite gözlendi. 6 hastadan 4'üne BOS incelemesi yapılmış olup 3 hastada protein artışı, 1 hastada ise pleositoz saptandı. Limbik ensefalit ile izlenen 6 hastadan 5'inde takipte

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ölüm izlendi.

Hızlı progresif serebellar sendrom tanısı ile takip edilen hastaların % 66,7'si kadın cinsiyetindeydi. Bütün hastalar yürüme güçlüğü ve dengesizlik şikayeti ile acil servis yada polikliniklere başvurmuştu. Nörolojik muayenelerinde 6 hastanın tümünde yürüyüş ataksisi bulunmaktaydı. Hastaların tümünde malignite mevcut olup, yarısında bilinen yada yeni tanı KHAK, 2 hastada yeni tanı over kanseri ve 1 hastada Hodgkin lenfoma bulunmaktaydı. KHAK olan 2 hastada anti-sox ve zic antikor birlikteliği izlenirken, over kanseri olan hastalarda anti-Yo ve Hodgkin lenfoma olan hastada anti-tr pozitifliği mevcuttu (Tablo 2.).

Stiff person sendromu (SPS) 2 hastada saptandı. Hastalarda takip süreleri içinde malignite saptanmadı. Her iki hastada da ekstremitelerde şiddetli kasılma, ağrı şikayeti mevcuttu. İki hastamızda da 5gün süreyle 1000 mg iv metilprednizolon tedavisini takiben oral idame metilprednizolon, baklofen ve diazepam tedavileri uygulanmıştı.

Motor nöron hastalığı (MNH) 2 hastada saptanmış olup, 2 hastada da anti-tr pozitifliği mevcuttu. Hastalardan birinin akciğer biyopsisinde gastrointestinal adenokarsinom infiltasyonu saptandı. Diğer hastada tetkiklerde malignite saptanmadı. Yapılan EMG incelemelerinde 2 hastada da spinal gangion proksimalinde yaygın motor ünit kaybına yol açan nörojenik değişiklikler mevcuttu. 1 hastaya 5 gün 1000 mg iv metiprednizolon + 5 gün 0,4 gr/kg IVIg uygulanırken diğer hasta kontrollerine gelmemesi nedeniyle tedavi alamamıştı.

İki hasta nöromusküler kavşak hastalığı tanısı ile takip edilmişti. Bir hasta bulber semptomlar, diğer hasta çift görme şikayeti ile başvurmuştu. Bir hastada anti-titin pozitifliği izlenirken diğer hastada anti-CASPR 2 antikoru bulunmaktaydıı. İki hastanın izleminde de malignite saptanmadı ve yapılan toraks bilgisayarlı tomografide timoma bulunmadı.

Hastaların takip süresi 10-720 gün arasında değişmekte olup, 14 hastanın (%66,7) farklı nedenlerle süreç içinde takibi sonlanmıştır. Takip süreci içinde toplam 5 hastada (%23,8) ölüm izlenmiş olup hastaların hepsi limbik ensefalit ile takip edilen hastalardır. Bu hastalardan 1 hasta pulmoner emboli nedeni ile kaybedilmiş olup, diğer hastalarda hastane dışı ölüm izlenmiş olması nedeniyle ölüm sebeplerine ulaşılamamıştır.

TARTIŞMA

Hastalarda PNS tanısı zor olabilir ve hastalarda beyin metastazı veya karsinomatöz menenjit gibi kanserin doğrudan tutulumu ile koagülopatinin, tedaviye bağlı nörotoksisitenin, metabolik problemlerin veya enfeksiyonların neden olduğu dolaylı tutulumların dikkatli bir şekilde dışlanması gerektirir (8).

Belirtilen insidans milyon kişi yılı başına 1,6 ila 8,9 arasında değişmektedir; bu da yetersiz teşhis ve eksik raporlamanın hala önemli sorunlar olduğunu göstermektedir (8). Altta yatan bir malignite ve/veya klinik sendrom için yüksek özgüllüğe sahip serolojik biyobelirteçlerin keşfi, bu sendromların daha fazla tanınmasına ve daha erken teşhis edilmesine yol açmıştır (1).

Antikorlar, nörolojik sendromların paraneoplastik kökeninin ve bazı durumlarda spesifik tümör türü varlığının belirteçleri olarak görev yapar (9). Ancak çok sayıda paraneoplastik antikor türü tanımlanmış olsa da, PNS'li hastaların %50'sinden azında paraneoplastik antikorlar tespit edilebilir (2). Bu nedenle paraneoplastik antikorların negatif saptanması PNS tanısını ekarte edemez (2).

PNS' ler yaklaşık 300 kanser hastasının 1'inde gelişir ve PNS' li hastalarda malignite insidansı sendroma bağlı olarak %5 ila %60 arasında değişir (2, 8). Hastalarda nörolojik bozukluk, kanser klinik olarak belirginleşmeden önce gelişebilir ve hastalar sendrom sonrası malignite tanısı alabilir (2, 10). Literatürde yapılan bir çalışmada hastaların %65' inde PNS tümör tespitinden önce ortaya çıkmıştır (11). Çalışmamızda 5 hasta (%33,3) PNS tanısı nedeniyle araştırılırken yeni kanser tanısı almış 1 hasta ise bilinen malignite türünden ayrı ikinci bir kanser tanısı almıştır.

PNS hastalarında her türlü kanser gelişebilir (12). PNS'ler çoğunlukla KHAK olmak üzere, meme, jinekolojik kanserler, endokrin tümörler ve Hodgkin, Non- Hodgkin lenfoma gibi birçok kanser türü ile ilişkili bulunmuştur (9, 12, 13). Literatür verileri ile benzer olarak bizim hasta grubumuzda da KHAK hastaları çoğunlukta saptanmıştı.

Hastalarda PNS ilişkili belirli bir nörolojik bulgu yoktur (8). Santral sinir sistemi yada periferik sinir sistemi hastalarda etkilenebilir (11). Daha önce "klasik PNS" olarak bilinen ve artık "yüksek riskli fenotipler" olarak tanımlanan spesifik klinik tabloların sıklıkla

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paraneoplastik bir etyolojisi vardır. Yüksek riskli bu fenotipler hastalarda ensefalomyelit, LE, HPSS, opsoklonus- myoklonus, sensoriyel nöronopati, gastrointestinal psödoobstrüksiyon ve Lambert-Eaton miyastenik sendromundan oluşmaktadır (8). LE dışı ensefalitler, SPS, Morvan Sendromu, izole myelopati, Myastenia Gravis (MG) ve paraneoplastik poliradikülonöropatiler ise hastalarda orta riskli fenotip grubunu oluşturmaktadır (10). HPSS ve sensoriyel nöropatiler hastalarda daha sık görülen sendromları oluşturmakta ve bunu sıklık olarak LE ve paraneoplastik ensefalomyelitler izlemektedir (11). Bizim çalışmamızda da literatür verilerine benzer olarak hastalarda en sık HPSS ve LE izlenmiştir.

Çalışmamızda hastaların yaklaşık yarısında BOS protein artışı saptanırken, %19' unda pleositoz izlenmiştir. Hastaların BOS tetkik sonuçları normal olabileceği gibi hastaların incelemelerinde hafif inflamatuvar özellikler, ılımlı hücre ve protein artışı yada oligoklonal bant pozitifliği saptanabilir (2, 10). BOS glukozu hastalarda genellikle normal düzeydedir (10). Otoantikorlar sıklıkla BOS'ta pozitif izlenir (10). Bizim hastalarımızda da BOS'ta antikor incelemesi yapılan 7 hastadan 6' sında serum antikoru BOS' ta da pozitif izlenmişti.

PNS'de farklı nörolojik sendromlar ile ilişkili çeşitli antikorlar rapor edilmiştir (2). Oliviera ve ark.' nın 17 hastalık serisinde en sık anti-Yo saptanırken, onu anti-Hu, Ma2 ve titin takip etmektedir (13). Bizim çalışmamızda ise en sık anti-amfifizin, anti-Yo ve anti-CASPR2 antikorları izlendi. CASPR2 antikorları literatürde daha çok erkek hastalarda ve en sık otoimmun ensefalit ve limbik ensefalit ilişkili bildirilmiştir (14). Benzer olarak bizde de 3 hastanın 2'si erkek cinsiyetinde olup, limbik ensefalit ile takip edilmişti. Anti-amfifizin ilk olarak SPS olan meme kanserli bir kadın hastada bildirilirken, ilerleyen dönemde limbik ensefalit, serebellar dejenerasyon ve polinöropati gibi birçok farklı nörolojik tablo ile ilişkisi olabildiği rapor edilmiştir (15). Çoğunlukla ileri yaşta ve her iki cinsiyette de benzer oranlarda görülmektedir (15). Hastalarımızda da daha önce bildirilen vakalara benzer olarak anti-amfifizin cinsiyet farkı gözetmeksizin farklı sendromlar (HPSS, SPS, MNH ve myoklonus) nedeniyle değerlendirilen hastalarda pozitif izlenmişti.

PNS'nin tedavisinde altta yatan kanserin tedavisi ve immünoterapiler olmak üzere iki önemli basamak bulunmaktadır (1). Hastalarda immünoterapiye yanıt hastalarda semptom sonrası tedaviye başlanma zamanı yada mevcut antikor tipine ve klinik sendroma göre farklılık gösterebilmektedir (1). Hücre içi antijene karşı otoantikor positifliği olan hastalar nöral hücre yüzey antijenine karşı pozitifliği bulunanlara göre daha dirençli bir seyre sahiptir (1). Hastalarda IVIg, plazmaferez ve intravenöz pulse metilprednizolon tedavileri başlıca akut tedavi seçeneklerini oluşturmakta ve hastalarda tek yada kombine biçimde tercih edilebilmektedir (1). İdame tedavisi için sıklıkla kullanılmasına rağmen, rituximab ve siklofosfamid gibi ikinci basamak ajanlar, özellikle kesin PNS tanı kriterlerini karşılayan hastalarda, hastalık seyrinin erken döneminde kullanılabilir (1).

PNS çoğunlukla subakut progresif seyirli olup hastalarda haftalar ile aylar içerisinde morbiditeye neden olabilir (2). Ancak relaps, yavaş progresyon yada benign seyir izlenmesi de PNS tanısını dışlamaz (2). PNS bireylerde ciddi sakatlık ve ölüme dahi neden olabilir (11). Prognoz ve ortalama hayatta kalma malignite türü ve PNS kliniğine göre değişkenlik gösterir (10, 13). Bununla birlikte, PNS hastaları ile ilgili veriler küçük ve oldukça seçilmiş gruplar, az sayıda randomize çalışma, spontan iyileşme raporları ve tedavinin yararlarına ilişkin yorumlar nedeniyle sınırlıdır (10). Oliviera ve ark.' nın PNS hastalarını inceledikleri çalışmalarında hastalarda %59 oranında ölüm saptanmıştır (13). Bizim çalışmamızda daha düşük oran mevcut olup, takiplerinde hastaların %23,8'inde ölüm izlenmiştir. Literatürde 20 farklı merkezden verilerin değerlendirildiği farklı bir çalışmada ise farklı antikorlara sahip 403 PNS hastasının ölüm nedenleri değerlendirilmesinde 109 hastanın PNS, 150 hastanın tümör progresyonu, 59 hastanın diğer nedenler ve 85 hastanın bilinmeyen sebeplerle öldüğü rapor edilmiştir (11). Ölüm oranlarının çalışmalar arası farklılık göstermesinin takip süreleri, takip dışı kalan hasta oranları ve retrospektif yada prospektif dizayn edilen çalışmalar nedeniyle olabileceğini düşünmekteyiz.

Limbik ensefalit tanımı ilk kez 1960'da yapılmış olup, 1980 ve 1990' larda nörogörüntüleme çalışmalarındaki gelişmeler ve yeni antikorların keşfi ile tanı sıklığı ve kolaylığı artmış ve aslında sıklığının hafife alındığı gösterilmiştir (16). Paraneoplastik LE tanısı semptomların kanser ilişkili birçok diğer durum ile (ilaç yan etkisi, enfeksiyon, toksik ensefalopati) ilişkisi

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olabilmesi nedeniyle zordur (7). KHAK, LE hastalarında en sık rastlanan kanser türüdür (7, 12). Gültekin ve ark. 50 hastayı değerlendirdikleri çalışmalarında hastalarda en sık %40 oranında KHAK tespit etmiştir (7). Bizim incelediğimiz LE hastalarımızında ise %50'si bilinen yada yeni tanı KHAK tanısına sahipti. Anti-Hu, anti-Ma2, CV2/CRMP 5 ve anti-amfifizin LE ilişkili başlıca hücre içi otoantijene karşı gelişen antikorlardır (16). Klasik LE hastalarında çoğunlukla 3 aydan kısa sürede gelişen irritabilite, depresyon, nöbetler, halüsinasyonlar ve kısa dönem bellek kayıpları izlenir (8, 16). Giometto ve ark. çalışmasında LE hastalarının %55,5'inde psikiyatrik semptomlar ve %48,0'ında nöbet saptamıştır (11). Gültekin ve ark.' nın çalışmasında ise hastaların çoğunluğunda bellek sorunları ve 50 hastanın 25'inde nöbet izlenmiştir (7). Bizim hastalarımızın da literatür verilerine benzer olarak yarısı nöbet, yarısı kognitif etkilenim nedeniyle başvurmuştu. Hastaların yaklaşık %80' inde BOS incelemelerinde hafif pleositoz ve artmış protein düzeyleri izlenirken, voltaj bağımlı potasyum kanalına (VGKC) karşı antikor pozitifliği olan hastalarda BOS protein düzeyleri normal saptanabilir (16). Bizim çalışmamızda LE tanısı ile takip edilen hastalarda 4 hastaya BOS incelemesi yapılmış olup %75' inde protein artışı, %25' inde ise pleositoz izlenmişti. BOS incelemelerinde inflamatuvar değişiklikler olsun yada olmasın hastaların çoğunda tek taraflı asimetrik medial temporal lobda FLAIR ve T2 ağırlıklı MR görüntüleme sekanslarda intensite artışı izlenir ve kontrast tutulumu sık izlenen bir bulgu değildir (16). Çok merkezli bir çalışmada hastaların %57,1' inde yapılan MR görüntülemelerinde limbik bölge etkilenimi saptanmış (11), Gültekin ve ark.' nın çalışmasında ise LE hastalarının %56' sında MR görüntüleme anormallikleri izlenmiştir (7). Ancak bizim çalışmamızda oran daha düşük olup, hastaların % 33,3' ünde MR görüntülemelerinde intensite değişikliği saptanmıştır. EEG değerlendirilmelerinde paroksismal/epileptiform aktivite değişiklikleri LE hastalarının yarısında izlenmekteydi. Bizim verilerimize benzer olarak yapılan bir çalışmada paraneoplastik LE hastalarının %54' ünde EEG değişiklikleri saptanmıştır (7).

Hızlı progresif serebellar sendrom önceleri subakut serebellar dejenerasyon olarak adlandırılmakta olup, hastalarda çoğunlukla 3 aydan kısa sürede hızlı ilerleyen ve hastayı önemli oranda etkileyen serebellar bulgular ile karakterizedir (8). Yürüyüş ataksisi ilk ve en temel bulgu olup hastalığın ilerleyen dönemlerinde gövde ve ekstremite etkilenimleri ile nistagmus eklenir (8, 10). Erken dönemde bulgular asimetrik olsa da hastalığın ilerleyen dönemlerinde simetrik bilateral etkilenim izlenir (9). Çalışmamızda da HPSS ile değerlendirdiğimiz hastaların hepsi yürüme güçlüğü ve dengesizlik ile başvurmuştu ve hepsinin başvuru anında nörolojik muayenelerinde ataksisi mevcuttu. Anti-Yo, serebellar bulgular ile ilişkişi olan en tipik antikordur ve sıklıkla jinekolojik yada meme kanseri olan kadın hastalarda saptanır (8). Anti-Yo dışında anti-tr, anti-Hu, anti-amfifizin ve zic 4 ilişkili HPSS vakaları mevcuttur (10, 17). Ülkemizden bildirilen iki HPSS olgusunun birinde anti-Yo ilişkili meme kanseri izlenirken, diğer hastada anti-Hu ilişkili KHAK mevcuttur (18). HPSS saptadığımız 6 olguda literatür ile benzer antikorlar izlendi. Bizim hastalarımızda da HPSS ve anti-Yo pozitifliği saptanan 2 kadın hastada araştırmalarında over kanseri saptandı. Anti-tr pozitifliği olan erkek hastada ise literatür ile uyumlu olarak tanı anında Hodgkin Lenfoma bulunmaktaydı.

Stiff person sendromu hasta grubumuzda oran olarak daha önce bildirilenlerden daha yüksek izlenmiş olup, SPS 2 hastada (%9,5) saptanmıştır. Klinik bulgular çoğunlukla aylar içerisinde gelişir (12). Sıklıkla kalça ve bacak kasları etkilenir ve hastalarda ağrılı kas krampları görülür (12). Hastalarımızda da benzer olarak bacaklarda kasılma şikayeti mevcuttu ve nörolojik muayene bulgularında ekstremitelerinde spastisite izlenmekteydi. Sendrom çoğunlukla anti-amfifizin ilişkili meme kanser hastalarında görülür. Bir hastamızda anti-amfifizin antikoru izlenmiş ancak araştırmalarında malignite saptanmamıştı. Farklı olarak Erkoyun ve ark. ise bildirdikleri 3 SPS tanılı hastanın 2 sinde anti-GAD antikorunu pozitif saptamışlardır (18).

Erişkinlerde paraneoplastik opsoklonus-myoklonus sendromu çoğunlukla KHAK, jinekolojik veya meme kanserleri ile ilişkilidir (8, 12). Hastalarda beyin MR görüntülemeleri normal saptanır (12). Erişkin hastalarda sıklıkla meme veya jinekolojik kanser ilişkili anti-Ri antikor pozitifliği saptanıken, pediatrik vakalarda antikor pozitifliği bulunmayabilir (12). Bizim hasta grubumuzda bir hastada izole myoklonus saptanmıştı. Opsoklonus gözlenmemişti ve anti-amfifizin antikoru

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pozitif bulunmuştu.

Paraneoplastik MNH daha nadir olup, çok merkezli bir çalışmada PNS hastaların %2' sinde MNH saptanmıştır (11, 17). Subakut sıklıkla alt motor nöron etkilenimi ile birlikte BOS' ta ılımlı inflamatuvar değişiklikler temel özelliklerini oluşturur (17). Hastaların azında antikor pozitifliği izlenir (12). Ancak bizim 2 hastamızda da anti-tr pozitifliği izlenmişti. 1 hastada araştırmalarda akciğerde gastrointestinal adenokarsinom metastazı bulunumştu. Ülkemizden de KHAK hastasında anti-Hu ve over kanseri hastasında anti-Yo ilişkili vakalar bildirilmiştir (12).

Oliviera ve ark., hasta serisinde 17 hastada 3'ünde MG saptamış ve bu hastaların hepsinde anti-titin ve timoma varlığı gözlemiştir (13). Anti-CASPR2 ilişkili nörolojik sendromlardan birisi de MG'dir ve yapılan bir sistematik derlemede 38 vaka bildirilmiştir (14). CASPR-2 antikor pozitifliği olan vakalarda mutlaka timoma varlığı da araştırılmalıdır. Bizim çalışmamızda MG saptanan hastalardan 1'inde CASPR2, diğer hastada anti- titin pozitifliği mevcuttu ve ancak 2 vakamızda da yapılan tetkiklerde timoma saptanmamıştı.

Çalışmamızın bazı kısıtlılıkları bulunmaktadır. İlk olarak çalışma retrospektif dizayn edilmiştir. İkincisi panellerde yer alan otoantikorlar merkezler arasında değişken olduğundan, daha önce bildirilen serilerle doğrudan karşılaştırma yapmak zordur. Takipte kaybolan hastalar nedeniyle uzun dönem hasta verilerinin değerlendirilmesi de kısıtlı olmaktadır.

SONUÇ

Sonuç olarak, PNS hastalarda tümör tanısı konulmadan önce ortaya çıkabilir. Anti-nöronal antikorlar hastalığın tanısında öneme sahiptir. PNS nadir olduğundan tanı zordur ve sıklıkla hastaya yanlış tanı konulur yada tanı atlanabilir. Hastalarda erken tanı ve tedavi semptomların iyileştirilmesi ve stabilizasyonu hastalarda disabilite ve ölüm gelişimi açısından önemlidir. Bu nedenle hekimlerin PNS semptom ve bulgularını iyi tanıması ve uygun tanı ve tedavi planını zamanında belirlemesi açısından büyük hasta sayılı prospektif çok merkezli çalışmalara ihtiyaç vardır.

Tasdik ve Teşekkür

Yazarlar arasında herhangi bir çıkar çatışması yoktur.

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EVALUATION OF THYROID DISORDERS IN EFFECTIVELY TREATED ACROMEGALIC PATIENTS

Etkili Tedavi Edilmiş Akromegali Hastalarında Tiroid Bozuklarının Değerlendirilmesi

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ABSTRACT

Objective: Acromegaly patients often develop goiter and thyroid nodules due to continuous stimulation of the thyroid follicle by growth hormon (GH) and insulin-like growth factor-1 (IGF-1). Recent studies suggest a decrease in thyroid disease rates in patients who have been successfully treated. This study aimed to investigate thyroid disorders in patients who had cured or controlled the disease.

Material and Methods: The patients who were surgically cured or were controlled with at least six months of somatostatin treatment were included in the study. The patients' GH levels were less than 1 ng/mL, and IGF-1 levels within the age sex adjusted normal range were categorized into controlled patients. Sonographic and biochemical findings of the thyroid gland were recorded.

Results: The study included 33 patients with acromegaly (14 males and 19 females) and 50 volunteers (14 males and 36 females). The prevalence of goiter was higher in patients with acromegaly compared to control group (21.2% vs. 6%, respectively; p<0.001). Acromegaly patients had a higher frequency of thyroid nodules, but nodules larger than 1 cm were similar between the two groups.

Conclusion: Acromegaly patients still have a high multinodular goiter incidence. Well control of disease may reduce the prevelance of thyroid cancer and risky nodules.

Keywords: *Acromegaly; Thyroid Disease; Thyroid Nodule*

ÖZET

Amaç: Tiroid foliküllerinin growth hormon (GH) ve insülin-like growth faktör-1 (IGF-1) aracılığıyla sürekli uyarılması akromegali hastalarında guatr ve tiroid nodüllerinin gelişmesine neden olur. Güncel çalışmalar, başarılı şekilde tedavi edilen hastalarda tiroid hastalığı sıklığının azaldığını ileri sürmektedir. Bu çalışma, kür veya kontrol altına alınmış hastalardaki tiroid bozukluklarını araştırmak için yapılmıştır.

Gereç ve Yöntemler: Cerrahi olarak kür sağlanan veya en az 6 ay somotostatin tedavisi verilerek kontrol altına alınmış hastalar çalışmaya dahil edildi. GH düzeyleri 1ng/mL'den düşük ve IGF-1 seviyeleri yaşa ve cinsiyete göre normal aralıkta olan hastalar kontrol altına alınmış hastalar olarak kategorize edildi. Tiroid bezinin sonografik ve biyokimyasal bulguları kaydedildi.

Bulgular: Çalışmada 33 akromegali hastası (14 erkek ve 19 kadın) ve 50 gönüllü yer aldı. (14 erkekve 36 kadın). Akromegali hastalarındaki guatr sıklığı kontrol grubuna kıyasla daha fazla idi (sırasıyla, %21,2 ve %6, p<0,001). Akromegali hastalarında tiroid nodülü daha sık görülmekle beraber 1 cm'den büyük nodül sıklığı iki grup arasında benzerdi.

Sonuç: Akromegali hastalarında multinodüler guatr sıklığı halen yüksektir. Hastalığın tam kontrol altına alınması tiroid kanseri ve riskli nodül sıklığını azaltabilir.

Anahtar Kelimeler: *Akromegali; Tiroid Hastalıkları; Tiroid Nodülü*

INTRODUCTION

Acromegaly is a rare disease caused by excessive secretion of growth hormone (GH), typically caused by a pituitary adenoma (1). The prevalence of acromegaly is approximately 2.8–3.7/100000 (2). A high GH level induces the liver to produce excess insulin-like growth factor-1 (IGF-1), leading to characteristic clinical manifestations. The slow progression of symp-toms and signs often causes diagnostic delays. Long-term exposure to high IGF-1 levels may result in hypertension, cardiomyopathy, diabetes, and obstructive sleep apnea (3).

The thyroid gland is the most affected organ in patients with acromegaly. Although the majo-rity of patients have normal thyroid function, goiters and thyroid nodules frequently develop as a result of GH and IGF-1 stimulation of the thyroid follicle (2). In some studies, the positi-ve correlation between IGF-1 levels, thyroid volume (TV), and thyroid nodules has been de-monstrated (4,5).

Thyroid cancer is the most common malignancy in acromegalic patients, but it is controversial whether acromegaly is an independent risk factor for thyroid cancer. In contrast to earlier research, recent studies suggest that the rate of thyroid cancer in controlled acromegaly pati-ents has not risen in comparison to the general population. This is still a matter of debate (6). There is insufficient data on changes in the thyroid gland in patients who were successfully treated. We conducted this study to examine the condition of thyroid disease in patients with cured or controlled disease.

MATERIAL AND METHODS

We conducted a cross-sectional study on following-up acromegaly patients at Saglik Bakanligi Istanbul Medeniyet University Goztepe Training and Research Hospital. The local ethics committee accepted the study protocol (no:20150127, date:10.12.2015). The study included 33 patients who were surgically cured or were controlled with at least six months of somatostatin treatment. Four active acromegaly patients were excluded. Fifty healthy volunteers were included as a control group. The criteria for surgical cure are defined as having an age-adjusted IGF-1 level within the normal range and a random GH level below 1 ng/mL, or a nadir GH level below 0.4 ng/mL on an oral glucose tolerance test. The controlled patient was defined as having GH levels less than 1 ng/mL and IGF-1 levels were not within the age-sex adjusted normal range. Patients with abnormal GH and IGF-1 levels were accepted as having an active disease (3).

The thyroid was examined using high-resolution B-mode ultrasound images obtained with a 7.5 Hz linear array transducer (EUB 7000 HV; Hitachi, Tokyo, Japan) in all individuals. The ellipsoid model formula (length × thickness × width × 0.52) was used to compute the volume of each tyhroid lobe (7). A goiter was defined as having a total TV greater than 18 mL in ma-les and greater than 13 mL in females. The levels of serum GH, IGF-1, free T4 (fT4), T4, free T3 (fT3), thyroid stimulating hormone (TSH) , anti-thyroid peroxidase (anti-TPO), and anti-thyroglobuline (anti-TG) were measured using chemiluminescent immunometric assays. (Siemens Healthcare, UK). All the nodules detected were measured, and their ultrasound characteristics were registered; cervical lymph nodes were also evaluated. Fine-needle aspiration (FNA) cytology was done on all nodules bigger than 1 cm in diameter and on those between 0.5 and 1 cm in diameter if they had ultrasound features that raised concerns, according to the American Society of Ultrasonography, such as microcalcifications, irregular borders, increased central flow on doppler examination, being taller than wide diameter, hypoechogenicity, and no halo (8). The patients' age at the time of diagnosis and follow-up periods were recorded in the hospital registry system. All the individuals included in the study were briefed about the study, and their informed written consent was obtained.

Statistical Analysis

Categorical variables are presented as a number (percentage). Quantitative data are presented as the mean (± standard deviation). For comparison of categorical variables, use the Chi-squared Test or the Fisher’s Exact Test. The data were tested for normality us¬ing the Shapiro-Wilk and Kolmogorov-Smirnov tests. Student’s t-test was used for normally distributed nu-meric variables, and the Mann-Whitney U-Test was used for non-normally distributed data. Correlation analysis was studied using Spearman's rho test. The

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p<0.05 value was considered statistically significant.

RESULTS

The study included 33 patients with acromegaly (14 males and 19 females, mean age 53 ± 10 years) and 50 volunteers (14 males and 36 females, mean age 50 ± 15 years). The acromegaly patients were diagnosed at 48.4 ± 9.2 years of age. All of them had transsphenoidal surgery for macroadenoma. Seventeen patients were cured by surgery. Twelve patients were control-led with long acting somatostatin analogues, and their treatment was completed. Four patients are still under somatostatin treatment. The duration of treatment was 4.6 ± 1.8 years. The characteristics of patients and volunteers are given in Table 1.

In the acromegaly group, two patients had a history of hypothyroidism. One patient was undergoing iodine restriction treatment for subclinical hyperthyroidism. In the control group, three patients had subclinical hypothyroidism. There was no difference in TSH and fT4 levels between the two groups. Anti-TPO positivity was found in 33% of acromegaly patients and 26% of the control group (p = 0.47). The sonographic and biochemical features of the thyroid gland are presented in Table 2.

Acromegaly patients had a higher TV than the control group (14.73±7.41 mL vs. 11.13±4.33 mL, P = 0.039). Males with acromegaly had a slightly larger TV than females (P = 0.136). The prevalence of goiter was increased in patients compared to controls (21.2% vs. 6%, respectively; p<0.001). Thyroid nodule incidence was 42.4% in patients with acromegaly com-pared to 24.0% in the control group (p<0.001). Multinodular goiter was significantly more frequent in acromegalic patients (p<0.001) (Figure 1). Nodules larger than 1 cm were found in five volunteers and four acromegaly patients. All of them underwent a fine needle aspiration biopsy. One of the patients with acromegaly had a undermined nodule (Bethesta category 3). She underwent another fine needle aspiration biopsy.

Table 1. Characteristics of patients and volunteers

	Acromegaly (n=33)	Control (n=50)	P value
Age (years)	53±10	50±15	0.325
Gender, (male/female)	14/19	14/36	0.178
Age at diagnosis (years)	48.4±9.2	-	-
Treatment duration (years)	4.6±1.8	-	-
BMI (kg/m²)	28.6	25.9	0.156
Random GH level (ng/mL)	0.85 ± 1.3	-	-
Random IGF-1 level (ng/mL)	256.8 ± 127.9	-	-

Data were presented mean±SD
BMI: Body mass index, GH: Growth hormone, IGF-1: Insuline like growth factor-1, kg:kilogram, m²: square meter, ng: nanogram, mL: mililiter

Table 2. Sonographic and biochemical findings of thyroid gland

	Acromegaly (n=33)	Control (n=50)	P value
Thyroid volume (mL) (mean±SD)	14.73±7.41	11.13±4.33	0.039**
Thyroid nodules % (male/female)	42.4% (18.2%/24.2%)	24.0% (6.0%/18.0%)	<0.001***
Single	12.1%	16.0%	0.156
Multiple	27.2%	8.0%	<0.001
Nodule diameter >1cm	12.1%	10.0%	0.189**
TSH (IU/mL)	1.47±2.6	2.9±3.2	0.061**
Free T4 (pg/mL)	1.29±0.6	1.54±1.62	0.072**
Anti-TPO IU/mL	41.3±15.7	36.7±7.2	0.128**
Anti-TG IU/mL	32.3±9.5	29.3±15.7	0.223**

**Fisher's exact test. ***Mann Whitney U test. TSH: Thyroid stimulating hormone, Free T4: Free thyroxine, Anti-TPO: Anti-thyroid peroxidase, Anti-TG: Anti thyroglobuline, mL: mililiter, SD: standard deviation, IU: international unit, mL: mililiter, pg: picogram

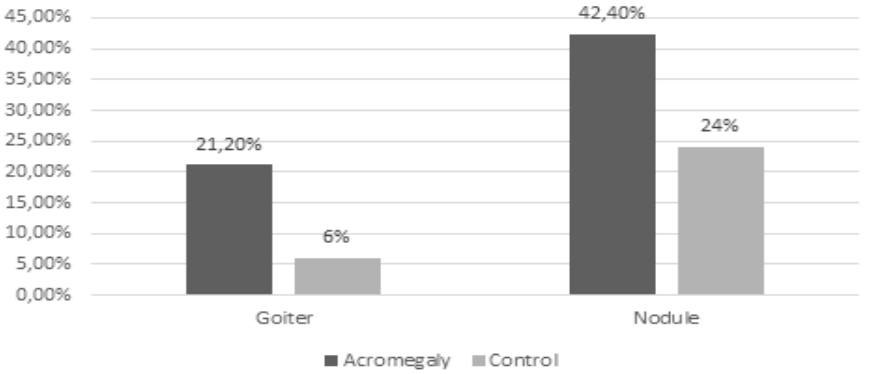

Figure 1. Prevalence of goiter and nodules in patients with acromegaly and controls.

The second biopsy result was Bethesta category 3. The patient was taken under clinical follow-up after obtaining her approval. The other nodules were benign. None of the nodules smaller than 1 cm showed ultrasonic proper-ties that raise suspicion of malignancy.

DISCUSSION

In this study, we assessed 33 controlled acromegaly patients to evaluate thyroid disorders. We found that thyroid dysfunction was present at the same frequency as in volunteers. TV in ac-romegaly was higher than in volunteers. Acromegaly patients had more thyroid nodules, while the number of nodules greater than 1 cm was similar.

Acromegaly can directly and indirectly disrupt the hypothalamic-pituitary-thyroid axis. Thy-roid hormones are usually normal in acromegaly patients, while hypothyroidism and hy-perthyroidism might be present in a small percentage (9). Manavela et al. found that 2.3% of the patients had hypothyroidism and 3.5% had hyperthyroidism. The prevalence of thyroid autoimmunity was 25% in acromegalic patients, whereas in the control group it was 10%. They proposed that thyroid autoimmunity may be a factor in thyroid dysfunction in addition to elevated IGF-1 levels (10). In our study, hypothyroidism was present in 6% and hypertyro-idism in 3% of acromegaly patients. There were no differences between patients and controls in terms of thyroid autoimmunity.

TSH is an essential hormone for thyroid gland growth. Thyrocyte sensitivity to TSH may be increased by growth hormone and IGF-1. Animal studies have revealed that the thyroid follu-cules contain IGF-1 receptors, and IGF-1 stimulation promotes thyroid growth (11). It has been shown in many studies that prolonged exposure of thyroid follicles to high GH and IGF-1 levels can cause goiter and thyroid nodules. Expansion of the thyroid gland can manifest as either diffuse or multinodular (4,12,13).

In a multicenter Italian study involving 258 active acromegaly patients, TV was higher than the control group (23.5±16.9 ml vs. 13.9±12.8 ml, $p<0.001$) (14). Cankurtaran et al. found multinodular goiter (47.3%) and diffuse goiter (14.7%) in 123 acromegalic patients (15). In our study, 9 patients (27.4%) had multinodular goiter, and 2 patients (2%) had diffuse goiter. A study of 34 newly diagnosed patients with active acromegaly followed for 7.3 ± 4.1 years showed a reduction of 19.5 ± 8.1% in thyroid volume with somatostatine treatment. The reason we found a lower prevalence of goiter may be the inclusion of patients with cure or controlled acromegaly.

According to a meta-analysis, the incidence of thyroid nodular disease is higher in acromegaly patients (mixed prevalence = 59.2%, odds ratio [OR] = 6.9, risk ratio = 2.1) than in controls (16). In studies conducted in our country, thyroid nodules were found in approximately 70% of cases. (17,18). We found that the frequency of thyroid nodules was 42.4% in controlled acromegalic patients.

Control of the disease can reduce the number or size of thyroid nodules. In a study, nodule growth increased 1.01 folds for every unit rise in IGF-1 levels, and active acromegaly disease raised nodule growth ninefold (19). Xu et al. found that patients with acromegaly had more

thyroid nodules than patients with a nonfunctioning pituitary adenoma. Furthermore, they demonstrated that the number of vascular and heterogeneous nodules was reduced in patients with post-treatment cure (20). After 12 years of following 92 acromegalies, Doğan et al. observed that the thyroid nodular rate reduced from 69.5 % to 47.8 % with therapy. Patients with nodules had a longer disease duration (14.2 ± 6.6 years) compared to those wit-hout nodules (9.4 ± 3.4 years, p = 0.043) (20). Kan et al. indicated that TV and total thyroid nodule volume are significantly reduced in well-controlled patients. In our study, we found that the frequency of nodules and the number of nodules greater than 1 cm are similar compared to controlled acromegaly patients and volunteers (21).

Cardiovascular and respiratory complications increase mortality and morbidity. Additionally, cancer may raise mortality rates. Prior studies demonstrated that acromegaly increases the risk of colon and thyroid cancer. Gullu et al. identified malignant disease in 15% of 105 patients with acromegaly in a study designed to screen for malignancy. They discovered that thyroid cancer is the most frequently encountered malignancy (22). A meta-analysis of 22 studies published in 2014 revealed that acromegalic patients have a higher incidence of thyroid can-cer, with an odds ratio (OR) of 7.5 and a relative risk (RR) of 7.2. The prevalence of thyroid cancer in this population was found to be 4.3% (23).

Numerous studies have revealed that thyroid cancer prevalence in patients with acromegaly is not significantly different or only slightly increased compared with that observed in the gene-ral population. Some studies have shown that people with acromegaly have a slightly greater risk of thyroid cancer compared to the general population. It's unclear whether there is a hig-her risk of thyroid cancer (6). In another study involving 313 patients conducted in our co-untry, the incidence of thyroid cancer was reported at 6% (24). On the other hand, a retrospective cohort study conducted in Turkey with 129 patients and 247 controls found no statistically significant disparity in the occurrence of thyroid cancer between the two groups (15).

A study conducted on the German Acromegaly Registry revealed that there was no significant increase in the occurrence of thyroid cancer among individuals with acromegaly compared to the general population (25). A Brazil study of 106 patients with acromegaly demonstrated that thyroid cancer occurred in only four patients (3.8%) (26). It may be thought that there is no significant difference in the frequency of thyroid cancer in acromegaly patients due to geographical or racial reasons. In previous studies, the relatively high frequency of TC in acromegaly patients may be due to the fact that the active and controlled patients were not evaluated separately.

In our study, there was no patient with thyroid cancer. Three patients are under follow-up due to an atypia of undetermined significance in a thyroid nodule. In controlled patients, goiter and thyroid nodules are still higher than in the control group. The decrease in thyroid volume and nodule diameter suggests that the thyroid disorders in acromegalic patients may be similar to those in normal populations in the long term. Prospective cohort studies with a large patient population are needed to reveal long-term changes in the thyroid gland and possible risk re-ductions.

CONCLUSION

The effective treatment of patients with acromegaly may reduce thyroid volume, nodule size and volume, and the risk of thyroid cancer. Thyroid volume and nodules can differ dramati-cally with regard to the activity of the disease. Thyroid disorders in acromegalic patients have reached levels that may not matter when the disease is well controlled.

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The authors declare that there is no conflict of interest between the authors.

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OSTEOPOROSIS IN CHRONIC KIDNEY DISEASE

Kronik Böbrek Hastalığında Osteoporoz

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ABSTRACT

Objective: When determining the treatment modality for bone mineral disorder in hemodialysis patients, the aim is to create an appropriate treatment approach by considering vascular complications.

Material and Methods: Thirty-three individuals (mean age 72.36±6.55 years; 20 females, 13 males) on hemodialysis for chronic kidney disease were included in the study. Body mass index, calcium, phosphorus, parathormone, bone densitometry results were recorded. In addition, the presence of intravascular calcification in the aorta on radiographs taken within the last 6 months was recorded. The relationships between these parameters were analyzed. Data were analyzed in SPSS. $p< 0.05$ was considered statistically significant.

Results: When the Dual-X-ray Absorptiometry (DEXA) scores of 33 individuals with stage 5 Chronic Kidney Disease (CKD) on hemodialysis were analyzed, the difference between T scores and Parathyroid hormone (PTH) values was found to be significant (p=0.020). As PTH increases, the risk of osteoporosis also increases. Osteopenia and osteoporosis were observed less in individuals with high calcium-phosphorus product. However, the difference between intravascular calcification and calcium-phosphorus product was significant (p=0.004). The calcium-phosphorus product was significantly higher in the group with extensive aortic calcification compared to the other groups. Calcium-containing agents given with osteoporosis treatment increase cardiovascular mortality in stage-5 chronic kidney disease.

Conclusion: Bone mineral density disorders should be treated in hemodialysis patients without increasing vascular calcification. In hemodialysis patients with high risk of cardiovascular disease, osteopenic follow-up can be performed by considering the benefit-harm relationship.

Keywords: *Bone Mineral Density Disorder; Osteoporosis; Hemodialysis; Cardiovascular Mortality*

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ÖZET

Amaç: Hemodiyaliz hastalarında kemik mineral yoğunluğunun azalması nedeniyle tedavi modalitesini belirlerken, vasküler komplikasyonları da göz önünde bulundurarak uygun tedavi yaklaşımını oluşturmak amaçlanmaktadır.

Gereç ve Yöntemler: Çalışmaya kronik böbrek hastalığına bağlı hemodiyaliz ile takipli 33 birey (ortalama yaş 72,36±6,55 olup; 20 kadın, 13 erkek) dahil edilmiştir. Hastaların beden kitle indeksleri, kalsiyum, fosfor, parathormon, kemik dansitometri sonuçları kaydedildi. Ayrıca bireylerin son 6 ay içerisinde çekilmiş grafilerinde aortada damar içi kalsifikasyon varlığı kaydedildi. Bu parametreler arasındaki ilişkiler incelendi. Veriler SPSS de analiz edildi. $p< 0,05$ istatistiksel açıdan anlamlı kabul edildi.

Bulgular: Evre 5 Kronik Böbrek Hastalığı (KBH) hemodiyalize giren 33 bireyin kemik dansitometri (DEXA) skorları incelendiğinde T skorları ile Parathormon (PTH) değerleri arasındaki farklılık önemli bulundu (p=0,020). PTH arttıkça osteoporoz riski de artmaktadır. Kalsiyum-fosfor çarpımı yüksek olan bireylerde osteopeni ve osteoporoz daha az gözlendi. Ancak damar içi kalsifikasyon ile kalsiyum-fosfor çarpımı karşılaştırıldığında aralarındaki fark anlamlı bulundu (p=0,004). Aortada kalsifikasyonun yaygın olduğu grupta kalsiyum-fosfor çarpımının diğer gruplarla karşılaştırıldığında daha anlamlı olarak daha yüksek olduğu gözlendi. Osteoporoz tedavisi ile verilen kalsiyum içerikli ajanlar Evre-5 kronik böbrek hastalığında kardiyovasküler mortaliteyi artırmaktadır.

Sonuç: Hemodiyaliz hastalarında vasküler kalsifikasyonu artırmadan kemik mineral dansite bozuklukları tedavi edilmelidir. Kardiyovasküler hastalık riski yüksek olan hemodiyaliz hastalarında fayda zarar ilişkisi gözetilerek osteopenik takip yapılabilir.

Anahtar Kelimeler: *Kemik Minerak Dansite Bozukluğu; Osteoporoz; Hemodiyaliz; Kardiyovasküler Mortalite*

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INTRODUCTION

Chronic kidney disease refers to functional and structural abnormalities that may cause impairment in renal function for more than 3 months. According to the Kidney Disease: Improving Global Outcomes (KDIGO) classification, end-stage renal failure is defined as a glomerular filtration rate below 15 ml/min/1.73 m2. In addition to medical treatment, renal replacement therapies such as hemodialysis and peritoneal dialysis are applied (1,2).

In chronic kidney disease, damage to the skeletal system occurs due to bone mineral disorder. Factors that cause this can be listed as insufficient vitamin D, bone loss secondary to uremia, electrolyte disorders, acid-base imbalances, excessive use of phosphate binders, hyperparathyroidism, hypoparathyroidism, dialysis-related amyloidosis, heparin use during dialysis, anemia, inflammation (3).

Osteoporosis is one of the bone mineral disorders encountered in chronic kidney disease. Direct radiography, computer tomography, bone densitometry and bone biopsy can be used in the diagnosis of osteoporosis. Bone densitometry is the most commonly used in clinical practice (4). Bone mineral density screening is recommended in patients with Chronic Kidney Disease (CKD) at risk for osteoporosis. (5,6). Lumbar and vertebral bone density is assessed by T and Z scores. The T score compares expected bone mineral density values in young and healthy individuals of the same sex, whereas the Z score compares bone mineral density values in individuals of the same age and sex. The T score is preferred in postmenopausal women and older men (7).

In treatment, the patient should be informed about increasing physical activity. Vitamin D should be replaced so that it is above 30 ng/dl. However, vitamin D should be avoided in the presence of hyperphosphatemia and hypercalcemia with PTH below 150 pg/ml. Hypocalcemia should be prevented, phosphorus should be restricted in the diet and phosphate binders should be used if necessary. Parathyroid hormone (PTH) should be kept in the range of 150-300 pg/ml. Calcimimetics and parathyroidectomy should also be considered in treatment. If there is no bone fracture in stage 5 patients, bisphosphanate should not be used. In patients in whom bisphosphonate is indicated, the maximum duration of treatment at half dose should be planned not to exceed 3 years (8-10).

Impaired mineralization caused by chronic kidney disease can lead to calcium and phosphorus deposits in the blood vessels. This can lead to atherosclerosis. It is very difficult to demonstrate atherosclerosis in patients with chronic kidney disease. Because in most of the methods used, we are faced with nephrotoxicity due to radiopaque material. For this reason, various methods have been developed to demonstrate atherosclerosis in this patient group, and one of them is calcification of the calcification level in the abdominal center on direct radiography. Thus, it is possible to make predictions about cardiovascular risk (11,12).

MATERIALS AND METHODS

Our study was approved by the Yozgat Bozok University Clinical Research Ethics Committee on 24.11.2022 with the protocol code 2017-KAEK-189_2022.11.24_02. Consent was obtained from the individuals participating in the study.

Based on KDIGO chronic kidney disease staging, 75 patients who were grouped as Stage 5 with a Glomerular filtration rate (GFR) below 15 and had been on hemodialysis for at least 3 months and three times a week for renal replacement therapies were included in our study. However, 42 of the 75 patients included in the study did not have bone densitometry since the women were under 65 years of age and the men were under 70 years of age, and were therefore excluded from the study.

Personal information such as age, gender, race as well as medical history and medications were recorded. Height and weight values were measured. Body mass index was calculated as weight/height^2. Calcium (Ca), phosphorus (P), PTH, vitamin D levels were recorded from the dialysis input blood of the individuals. Bone mineral density was measured according to the standards and measurements from lumbar and vertebral bones were recorded as T and Z scores. The presence of intravascular calcification in the aorta on radiographs taken within the last 6 months was graded on the basis of deposition indices as absent, minimal, or extensive (if it covered more than half of the aorta in the long axis). Comparisons were made with available computed tomography (CT) images of the individuals

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to confirm that the observational examination matched. Calcification conditions in the aorta on previously taken thoracic-abdominal tomographies were recorded from the radiology reports.

Individuals with acute renal failure, those who have been on hemodialysis for less than 3 months, individuals receiving treatment for bone mineral density disorders, individuals receiving lipid-lowering therapy, individuals receiving anticoagulant or antiaggregant therapy other than standard heparin used during hemodialysis, individuals with a body mass index of 35 kg/m² and above, and pregnant women were not included in the study.

Data were analyzed in statistical pacage for social sciences (SPSS version 20.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY: IBM Corp.)). Categorical measurements were summarized as number and percentage, continuous measurements were summarized as mean and standard deviation (median and min-max where necessary). Kruskal Wallis test was used to evaluate the significance of the difference between the group average in groups that did not show normal distribution. Analysis of variance and Tukey test were used to analyze the data. Statistically, $p<0.05$ was considered significant

RESULT

The study included 33 individuals who were followed up with hemodialysis due to chronic kidney disease. Of these individuals, 13 (39.4%) were male and 20 (60.6%) were female. Minimum age was 64 years and maximum age was 91 years, mean age was 72.36±6.55 years and median age was 71 years. Bone densitometry values performed within the indication were recorded (Table 1).

According to the recorded bone densitometry results, individuals were divided into three groups: a group with healthy bone densitometry results without osteoporosis, osteopenia, or both. When dexa scores of 33 individuals were analyzed, the difference between T scores and PTH values was found to be significant ($p<0.05$). The average parathormone level in individuals with osteoporosis was found to be more than 2 times higher than in individuals with osteoporosis. As the parathormone value increased, the risk of osteoporosis increased ($p = 0.02$). As a result, the relationship between parathormone level and bone mineral density is clearly observed. Osteoporosis was observed more in individuals with low vitamin D levels. The results show that the protective effect of vitamin D on bone is also important in this patient group. Osteopenia and osteoporosis were observed less in individuals with high calcium-phosphorus product. Data show the effect of calcium and phosphorus levels on bone and the necessity of CaxP monitoring for bone health. Body mass index (BMI) was calculated based on dry weight. No correlation was found between BMI and bone mineral density disorders in hemodialyzed individuals (Table 2).

Individuals were divided into 3 groups according to their calcification status in the aorta: non-existent, minimal and obvious. While the number of individuals without calcification was 14, minimal calcification was detected in 8 patients and overt calcification was detected in 11 patients. The product of the patients' serum calcium and phosphorus values taken before hemodialysis was calculated. It was observed that the calcium-phosphorus product was significantly higher in the group with extensive calcification in the aorta compared to the other groups ($p<0.05$). When the values were compared pairwise, the difference between non-calcification and diffuse, minimal and diffuse was found to be significant, while the difference between non-calcification and minimal group was found to be insignificant (Table 3).

Table 1. General data and mean values of the patients

Age (years)	72.36 ± 6.55 (64-91)
Gender (male/female)	20 (%60.6) / 13 (%39.4)
Weight –kilogram (kg)	75.71 ± 14.48
Length—metre (m)	1.64 ± 0.94
Body mass index - kg/m2	28.07 ± 4.89
T score (lumbar/femur)	-0.29 / -2.15

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Table 2. The Relationship of Bone Densitometry Results with Biochemical Markers and Body Mass Indexes in Hemodialysis Patients

	Non osteoporotic and Non osteoporosis	Osteopenia	Osteoporosis	Result
N (number of individuals)	3	21	9	33
Parathormon	209.00± 93.95	355.97± 31.72	713.86± 40.84	F=4.47 p=0,020
Vitamin D	17.46±7.16	14.95±10.33	10.07±3.84	F=1.29 p=0.307
Calcium-phosphorus product	20.95±3.49	17.43±5.66	18.05±4.89	F=0.57 p=0.569
Body mass index-kg/m²	27.41±3.31	27.71±4.55	29.14±6.28	F=0.28 p=0.755

*p <0.05 significant, (Bone mineral density measurement sites are lumbar vertebrae (1-4) and femur total and femoral neck. The T score was based on comparison with the younger population, while the Z score was based on comparison with the same age group. T score is more appropriate for postmenopausal women and both sexes over 65 years of age. T score > -1 is normal; T score -1 to -2.5 osteopenia; T score < -2.5 is considered osteoporosis)

Table 3. The relationship between intravascular calcification levels and serum Ca X P product in hemodialysis patients

Calcification in the aorta	N	Calcium-phosphorus product (mg/dl)	Result
Non-	14	15.31 ± 5.00	F=6.70 p =0.004*
Minimal	8	16.49 ±1.63	
Widespread	11	21.47 ± 4.58	
Total	33	17.65 ± 5.00	

(p<0.05 significant), mg: milligram, dl: deciliter

DISCUSSION

Bone mineral disorders are a common condition that increases with age and cause serious deterioration in quality of life when left untreated. Some chronic diseases have a higher risk of developing bone mineral disorders. Chronic kidney disease is one of them. Compared to the normal population, the risk of fracture, which is both itself and one of the complications of bone mineral density disorders, was found to be quite high in stage 5 chronic kidney disease patients (13). In our study, there were 33 individuals who underwent bone densitometry in hemodialysis patients with end-stage renal failure, especially within the indication due to age. In our study, bone mineral disorder was found in 90% of hemodialysis patients. This result shows that chronic kidney disease, especially hemodialysis, should be considered as a major risk factor for bone mineral disorders and screening criteria can be established for individuals undergoing hemodialysis at an early age.

The incidence of osteoporosis may vary in renal replacement therapy methods. In a study by Aslan et al. comparing the risk of osteoporosis in hemodialysis and peritoneal dialysis patients, peritoneal dialysis was found to be less risky. When deciding on renal replacement therapy in individuals with additional risk factors for osteoporosis, peritoneal dialysis may be considered as an alternative to hemodialysis (14). Although the risk of osteoporosis increases in the first period after renal transplantation, transplantation has been shown to be protective for bone mineral disease in the long term. In appropriate patients, early transplantation may be recommended in all aspects (15,16).

Obesity is known to be protective in osteoporosis (17). In our study, the mean body mass index of 33 individuals undergoing hemodialysis was found to be 28.07 ± 4.89 kg/m². Although the mean body mass index was within the range considered overweight; bone mineral density disorder was found in 90% of our patients. Our study shows that the ideal weight in these individuals is not the same as in individuals with normal renal function; the protective effect of obesity on osteoporosis is not

valid in hemodialysis patients.

Limited methods are used to demonstrate coronary artery calcification in individuals with renal failure. Because nephrotoxicity develops with the use of radiopaque material in standard examinations (such as interventional angiography, CT angiography) and progression of existing renal impairment is facilitated (18). For this reason, new noninvasive methods that would be the least nephrotoxic have been tried to be developed in patients for many years. In similar studies by Nallamothu et al. and Raggi et al. the correlation of angiography results with electron-beam computed tomography to demonstrate vascular calcification was examined. They found a statistically significant correlation between imaging and angiography results (19,20). In the study conducted by Wilson et al. on 2515 individuals, direct radiography was shown to be a method that can be used to show vascular calcification in almost most centers. In the study by Toussaint et al. it was concluded that abdominal aorta could be evaluated with lumbar radiography to show calcification. Calcific deposits in the aorta were classified and graded on abdominal radiographs (21,22). In our study, the presence of calcification was graded from the available radiographs of the patients and its accuracy was confirmed with the available computed tomography of the individuals.

Combating hyperphosphatemia in renal failure is very important. In cases where phosphorus levels exceed 6.5 mg/dl, mortality has been reported to increase with an increase in calcium. When the calcium phosphorus product exceeded 70 mg/dl, the risk of death increased by 34%. The reason for this increase in mortality is that when the calcium phosphorus product is 55 mg/dl, calcium phosphorus accumulation in tissues and vascular structures increases and causes intravascular calcifications (23,24). Agents used to prevent hyperphosphatemia may cause hypercalcemia and increase intravascular calcifications. Similarly, the aim of treatments used for osteoporosis is to increase bone mineralization. While osteoporosis is treated as a result of increased blood calcium with the treatment given, calcium and phosphorus levels should be closely monitored in patients with chronic kidney disease in order not to cause intravascular calcification. Especially in stage 5 hemodialysis patients, the use of high calcium-containing treatments should be avoided unless necessary (25). In the study by Okuno et al. it was aimed to evaluate whether abdominal aortic calcification is a reliable method in hemodialysis patients as well as being reported as a marker of cardiovascular mortality in the community. A total of 515 hemodialysis patients with stage 5 renal disease were included in the study. Abdominal lateral radiography has been found to have prognostic significance as a cardiovascular indicator in hemodialysis patients (26).

Similarly, in our study, as the calcium phosphorus product increased, the presence of intravascular calcification increased correlatively. The patients with chronic kidney disease included in the study were in the risk group who had never received osteoporosis treatment. Although the majority of the patients were in the osteopenic group, no correlation was found between intravascular calcification and bone mineral density in individuals with osteoporosis. The reason was thought to be that the deficient mineralization in the bones was obtained from the blood and was not present at the level to accumulate in the vein for a long time. When the bones reach sufficient saturation with minerals, accumulation occurs in the vessels. Therefore, it is necessary to compare the intravascular calcifications of these patients after osteoporosis treatment with those before.

There are some limitations in our study. The first of these is that calcifications cannot be shown more clearly with angiographic CT or interventional CT, the second is that the patients in our study are not available for comparison before and after osteoporosis treatment and the calcifications cannot be followed, and the third is that individuals do not have bone densitometric measurements before the development of osteoporosis.

CONCLUSION

It is very difficult and important to diagnose osteoporosis and manage the treatment process in chronic kidney disease, especially in hemodialysis patients. Bone mineral density disorders should be identified before the development of complications that will affect the comfort of life of the individual. Establishing a protocol that takes into account cardiovascular mortality both during the selection of renal replacement therapy,

when choosing a more appropriate treatment than hemodialysis, and when providing post-diagnostic treatment is a very demanding process. The need for appropriate treatment protocols for these individuals is obvious. Bone mineral density disorders should be treated without affecting cardiovascular mortality in hemodialysis patients. In order not to increase cardiovascular mortality, hemodialysis can be followed by osteopenic patients, taking into account the profit-loss relationship.

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ÇOCUKLARDA ÜROLİTİAZİS TEDAVİSİ: EKSTRAKORPOREAL ŞOK DALGA LİTOTRİPSİ İLE RETROGRAD İNTRARENAL CERRAHİ NE ZAMAN KOMBİNE EDİLMELİ?

Treatment of Urolithiasis in Children: When to Combine Extracorporeal Shock Wave Lithotripsy with Retrograde Intrarenal Surgery?

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ÖZET

Amaç: Bu çalışmanın amacı, çocuk hastalarda böbrek taşı tedavisinde yaygın olarak kullanılan ekstrakorporeal şok dalga litotripsi (ESWL) yönteminin, retrograd intrarenal cerrahi (RIRC) ile kombine edilmesinin gerekli olduğu durumları değerlendirmektir.

Gereç ve Yöntemler: Ocak 2013 ve Ekim 2020 tarihleri arasında kliniğimize üriner sistem taş hastalığı ile başvuran olgular retrospektif olarak değerlendirildi. ESWL ve RIRC ile kombine ESWL uygulanan 0-18 yaş arası toplam 118 pediatrik hasta ve hastaların taş bulunduran 165 böbreği çalışmaya dahil edildi. Olgular demografik verileri, taş boyutu, tarafı, yerleşimi, ESWL seans sayısı, taşsızlık sağlanması ve hidronefrozun takibi açısından değerlendirildi.

Bulgular: ESWL uygulanan çocukların yaş ortalaması 6,51±5,31 yıl, RIRC kombine ESWL uygulanan çocukların yaş ortalaması 6,21±3,17 yıldı. Taş boyutu ESWL grubunda ortalama 10,51(±3,32) mm ve RIRC kombine ESWL grubunda 10,16(±3,23) mm idi. Taş sayısı açısından iki grup arasında istatistiksel fark saptandı (p=0,023). Sadece ESWL uygulanan çocuklarda taşsızlık oranı %83.33, RIRC kombine ESWL uygulanan çocuklarda %86.96 olarak saptandı.

Sonuç: ESWL'nin tek ve renal pelvis yerleşimli taşlarda ilk seansta taşsızlık sağlama oranları daha yüksektir. RIRC kombine ESWL yöntemi, alt kaliks ve multipl taşlar gibi daha zorlu taş gruplarında etkinlik göstermiş ancak bu durum hastaya daha fazla seans yapılmasını gerektirmektedir. Çocuk olgularda üriner sistem taş tedavisinde ESWL planlanırken, özellikle taşın yerleşimi, boyutu ve sayısına göre RIRC ile kombine edilmesi gerebileceği unutulmamalıdır.

Anahtar Kelimeler: *Çocuk, Üriner Sistem Taşları; Ekstrakorporeal Şok Dalga Litotripsi; Retrograd İntrarenal Cerrahi; Taşsızlık Oranı*

ABSTRACT

Objective: The objective of this study was to evaluate the indications for extracorporeal shock wave lithotripsy (ESWL) in combination with retrograde intrarenal surgery (RIRC) in the treatment of kidney stones in paediatric patients.

Material and Methods: A retrospective evaluation was conducted on patients admitted to the clinic with urinary tract stone disease between January 2013 and October 2020. A total of 118 paediatric patients, aged between 0 and 18 years, who underwent ESWL in combination with ESWL and RIRS, and 165 kidneys of patients with stones, were included in the study. The patients were evaluated in terms of demographic data, stone size, side, location, number of ESWL sessions and stone-free status.

Results: The mean age of the children who underwent ESWL was 6.51±5.31 years, while the mean age of those who underwent RIRS combined with ESWL was 6.21±3.17 years. The mean stone size was 10.51 (±3.32) mm in the ESWL group and 10.16 (±3.23) mm in the RIRS combined ESWL group. A statistically significant difference was observed between the two groups in terms of the number of stones (p=0.023). The stone-free rate was 83.33% in children who underwent ESWL alone and 86.96% in children who underwent RIRC combined ESWL.

Conclusion: It can be concluded that ESWL has a higher success rate in achieving stone-free status in the first session for single stones and stones located in the renal pelvis. The RIRS combined ESWL method has demonstrated efficacy in more challenging stone groups, such as those located in the lower calyx and in multiple stones, although this requires a greater number of sessions. In planning ESWL as a treatment for urinary tract stones in paediatric patients, it is important to consider that it may need to be combined with RIRC, particularly in cases where the location, size and number of stones are significant.

Keywords: *Pediatric; Urinary Tract Stones; Extracorporeal Shock Wave Lithotripsy; Retrograde İntrarenal Surgery; Stone-Free Rate*

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GİRİŞ

Üst üriner sistem taşları pediatrik olgularda nadir görülür. Ancak son yıllarda prevalansı giderek artmaktadır (1,2). Pediatrik hastalarda üriner sistem taşları yaklaşık %2 prevalansa sahiptir (3). Bununla birlikte, pediatrik olgularda insidans özellikle gelişmekte olan ve gelişmiş ülkelerde sırasıyla %5-15 ve %1-5'tir (4). Nefrolitiazisin cerrahi tedavisinde birçok yöntem tercih edilebilir. Bu yöntemler ekstrakorporeal şok dalga litotripsi (ESWL), retrograd intrarenal cerrahi (RIRC), perkütan nefrolitotomi (PNL), açık veya laparoskopik taş cerrahisidir. Günümüzde minimal invaziv yöntemlerin gelişmesi ile ESWL, RIRC, PNL öncelikli olarak tercih edilir hale gelmiştir. Bu yöntemler arasında ESWL cerrahi yöntemlere göre daha az invazivdir (5,6). Kılavuzlar da pediatrik olgularda, uygun taşlara ESWL uygulanmasını endoskopik prosedürlerle birlikte tedavide ilk seçenek olarak önermektedir (7,8). Ancak ESWL'nin bazı dezavantajları da vardır. İlk seansta başarı oranı düşük olması ve çocukların yarısından fazlasının ek seanslara ihtiyaç duyması bu dezavantajların en önemlileridir (9,10). Bu nedenle ESWL diğer yöntemlerle kombine edilebilir. Bu çalışmanın amacı, Bu çalışmanın amacı, çocuk hastalarda böbrek taşı tedavisinde ESWL ve RIRC tekniklerinin kombine edilme endikasyonlarını değerlendirmektir.

MATERYAL VE METOD

Hastanemiz Girişimsel Olmayan Klinik Araştırmalar Etik Kurulunun No:2021-43 sayılı onayı sonrasında, Ocak 2013 ile Ekim 2020 tarihleri arasında böbrek ve proksimal üreter taşı tanısı alıp ESWL veya RIRC kombine ESWL yapılan 118 çocuk hasta (165 böbrek) retrospektif olarak değerlendirildi. Düşük fonksiyonlu böbrekler en uzun çapı >2,0 cm olan taşlar, kanama diyatezi bulunan olgular, ek üreteral patolojileri ve kompleks taşları olan çocuklar ile ESWL ve RIRC teknikleri dışında taş kırma tekniği uygulanmış olgular çalışma dışında bırakıldı. Tüm çocukların ameliyat öncesi idrar tahlili, idrar kültürü, serum biyokimyası, koagülasyon testleri yapıldı. Görüntüleme yöntemi olarak tüm çocuklarda direk karın grafisi çekildi. Renal ultrasonografi (USG) ve/veya gerektiğinde kontrastsız bilgisayarlı tomografide (BT) görüntüleme yöntemi olarak kullanıldı. Taş uzunluğu için USG ölçümü veya düz karın grafisi veya BT'de taşın ölçülen en uzun çapı kullanıldı. USG ve BT'de taş çapının yanı sıra taşın tarafı, yerleşim yeri ve rezidü taş varlığı değerlendirildi. Olgular kullanılan tekniklere göre 2 gruba ayrıldı. Sadece ESWL uygulanan olgular Grup 1 (n = 72 (%61); 92 renal ünite (%55,75)) ve RIRC kombine ESWL uygulanan olgular Grup 2 (n = 46 (%39); 73 renal ünite(%44,25)) olarak değerlendirildi. Perkütan nefrolitotomi, açık veya laparoskopik taş cerrahisi uygulanan hastalar çalışma dışında bırakıldı.

Düz karın grafisinde floroskopide görülebilecek opasiteye sahip, görüntüleme yöntemlerinde 2cm ve daha küçük taş izlenen, USG ve/veya BT'de taşa bağlı akut obstrüksiyon bulguları izlenmeyen ve 18 ay üstündeki hastalarda ESWL ile başlanmasına karar verildi. Hastalara genel anestezi uygulandıktan sonra elektrohidrolik şok dalgalı litotriptör (PCK,Ankara,Türkiye) ile litotripsi uygulandı. Taşın yerini belirlemek ve fragmantasyonu izlemek için floroskopi kullanıldı. Verilen şok dalgası 13-14 kV'ta başladı ve maksimum güç seviyesi olan 20 kV'a kadar artırıldı. Seans başına verilen maksimum şok sayısı 5000-5500 atımdı. ESWL seansı, görünür taş tespit edilmediğinde veya görünür taş kalıntıları küçük parçalar olduğunda veya istenen sayıda şok verildiğinde durduruldu.

Hastalar ESWL seansından 2 hafta sonra taşsızlık durumunu değerlendirmek için üriner USG ile değerlendirildi. >4 mm fragman varlığında veya ilk seansta başarısızlık durumunda diğer ESWL seansları uygulandı. Her ESWL seansı en az 2 hafta aralıklarda uygulandı. Üç seanstan sonra, ESWL başarısızlığı durumunda hastalara diğer taş tedavi yöntemleri önerildi. ESWL, yardımcı bir prosedüre gerek kalmadan en fazla üç seans sonrasında taşsızlık durumuna ulaştığında veya klinik olarak önemsiz <4 mm rezidüel fragmanlarla sonuçlandığında başarılı kabul edildi.

RIRC ile kombine ESWL tekniği uygulanan hasta grubunda, genel anestezi altında litotomi pozisyonunda semirijit 4,5 Fr üreterorenoskop (URS)(Richard Wolf, Germany) ile pelvikalisiyel sisteme ilerlendi. Öncelikle 0,038 hidrofilik kılavuz tel yerleştirildi. URS ile üst üriner sisteme ulaşılamadığında, proksimal üreterde yerleşimli taşa ulaşılamadığında, proksimal üreter veya ulaşılabilen pelvikalisiyel sistem taşı lazer litotripsi esnasında alt pole yer değiştirdiği için ulaşılamadığında olgulara JJ stent yerleştirildi. JJ stent takıldıktan 2 hafta sonra olgulara ESWL uygulandı. ESWL seansından 2 hafta

sonra USG ile taş boyutu değerlendirildi. Taşın boyunda yeterli küçülme sağlanmadıysa ESWL tekrar uygulandı. 2 hafta sonra USG ile tekrar değerlendirilen olgulara, taş boyutunda yeterli küçülme olmaması halinde ve fragmante taş parçalarının >4 mm olması halinde JJ stent çekilmesi ve RIRC planlandı. Takılan JJ stentler renal pelviste en fazla 2 ay süre ile bırakıldı. Tüm olgularda genel anestezi altında semirijit veya fleksibl URS ile pelvikalisiyel sisteme ilerlendi. Taş tamamen kırılana veya drene olabilecek boyuta kadar küçültülene kadar, uygun güç ve frekansta, 365 µ lazer probu (Accu Max, Boston, ABD) kullanılarak Holmiyum lazer litotripsi (30 W, Sphinx) ile litotripsi yapıldı. Ödem, enklave taşa bağlı hasar şüphesi ve olası fragmante taşın oluşturabileceği obstrüksiyon açısından işlem sonrası JJ stent yerleştirildi. Stent bir ay içerisinde çıkarıldı.

Her iki gruptaki çocuklar en az bir yıl boyunca düzenli aralıklarla değerlendirildi. Takip, USG veya düz karın grafisi ile yapıldı. Düz karın grafisi veya USG'de <4 mm taş görülen çocuklar taşsız kabul edildi. Çocukların takip aralıkları klinik durumları ve görüntüleme bulgularına göre belirlendi. Düz karın grafisinde ve/veya USG'de taş görülmeyen ve <4 mm taş saptanan çocuklar üç aylık aralıklarla 1 yıl takip edildi. Kliniği olmayan olguların takip aralıkları açılarak takibine devam edildi. Bu çalışmada, >4 mm rezidüel fragmanlar tedavi başarısızlığı olarak kabul edildi.

Yaş, cinsiyet, taş yerleşimi, taş boyutu, gerekli seans sayısı ve taşsızlık oranları 2 grup arasında karşılaştırıldı. Sürekli veriler ortalama ± standart sapma olarak verildi. Kategorik veriler yüzde (%) olarak verildi.Verilerin normal dağılıma uygunluğunu araştırmak için Shapiro Wilk's testi kullanıldı. Normal dağılıma sahip grupların karşılaştırılmasında, üç veya daha fazla grup bulunan vakalar için tek yönlü varyans analizi (one-way ANOVA) kullanıldı. Oluşturulan çapraz tabloların analizinde Pearson Ki-Kare ve Fischer kesin Ki-Kare analizleri kullanıldı. IBM SPSS Statistics 21.0 (IBM Corp. 2012 yılında yayınlandı. Windows için IBM SPSS Statistics, Sürüm 21.0. Armonk, NY: IBM Corp.). İstatistiksel anlamlılık için p<0,05 değeri kriter olarak kabul edildi.

BULGULAR

Sadece ESWL yapılan çocukların yaş ortalaması 6,51±5,31 yıldı. RIRC ile kombine ESWL uygulanan çocukların yaş ortalaması 6,21±3,17 yıldı. Gruplar arasında yaş açısından istatistiksel fark saptanmadı (p=0,791). Çocukların 58'i erkek 60'ı kızdı. ESWL ile tedavi edilen ürolitiyazis hastalarının 1,12:1 oranla ağırlıklı olarak erkek olarak bulundu. Ancak, RIRC kombine ESWL ile tedavi edilen ürolitiyazis hastaları 1,3:1 oranıyla ağırlıklı olarak kadındı. Her iki grupta baskın cinsiyet farklı olsa bile, iki grup arasında istatistiksel olarak anlamlı bir fark yoktu (p = 0,426). Taşla ilgili parametreler Tablo 1'de listelendi. Taş boyutu ve tarafı değerlendirildiğinde iki grup arasında istatiksel fark saptanmadı. Taş yerleşimi ve taş sayısı açısından istatiksel anlamlı olmasa da bazı farklılıklar görülmektedir (Tablo 1). RIRC ile kombine ESWL olgularında seans sayısı anlamlı ölçüde yüksek saptandı. Sadece ESWL uygulanan çocuklarda, seanslardan sonra taş izlenmeyen hasta oranı %58,33'tür (42/72). Rezidüel fragmanları <4 mm olan çocuklar dahil edildiğinde, taşsızlık oranı %83,33 (60/72)'tür. RIRC kombine ESWL uygulanan çocuklarda seanslar sonrasında taş izlenmeyen hasta oranı %56,52 (26/46)'dir. Rezidüel fragmanları <4 mm olan çocuklar dahil edildiğinde, taşsızlık oranı %86,96 (40/46)'dır. Hem ESWL hem de RIRC kombine ESWL gruplarında seanslar sonrasında elde edilen taşsızlık oranları Tablo 2'de verildi. ESWL'nin ilk seanslarda taşsızlık sağlama oranı daha yüksek saptanırken, ek seans gerektiren olgularda RIRC ile kombine tedavinin taşsızlık başarısının daha yüksek yüksek olduğu saptandı.

Çalışmamızda, taş boyutu ile ESWL seans sayısı arasında anlamlı bir ilişki saptandı. Tek seans ESWL <15 mm taşlarda %95,52 başarı göstermektedir. 10 mm'den büyük taşlarda daha fazla ESWL seansı gerektiği saptandı (Tablo 3). Gruplar arasında taş boyutu açısından istatiksel olarak anlamlı fark bulunmadı (p=0,336). Her iki yöntemin de taşsızlığı sağlamak için başarılı yöntemler olduğu saptandı (p<0,001).

TARTIŞMA

Çocuk yaş grubunda taş hastalığının tedavisinde, teknolojideki gelişmelerle birlikte minimal invaziv prosedürler olan ESWL, PNL ve RIRC öncelikle tercih edilmektedir (11,12). Tedavide kullanılacak yöntemin belirlenmesinde etkili birçok faktör bulunmaktadır. Bu faktörlerden başlıcaları taş sayısı, boyutu, yerleşim yeri, taş bileşimi ve idrar yollarının anatomisidir (13-15).

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Tablo 1. Taş parametreleri

	ESWL n (%)	RIRC kombine ESWL n (%)	p değeri
Taş tarafı			0,710*
Sağ	43 (46,73)	32 (43,83)	
Sol	49 (53,26)	41 (56,16)	
Taş yerleşimi			0,060*
Üst kaliks	3 (3,26)	4 (5,47)	
Orta kaliks	21 (22,82)	14 (19,17)	
Alt kaliks	27 (29,34)	28 (38,35)	
Renal pelvis	33 (35,87)	16 (21,91)	
Proksimal üreter	8 (8,69)	11 (15,06)	
Taş sayısı			0,023*
Bir	54 (75)	26 (56,52)	
İki	16 (22,22)	13 (28,26)	
Multipl	2 (2,78)	7 (15,21)	
	ESWL Ortalama ±SD Medyan(Q1-Q3)	RIRS kombine ESWL Ortalama ±SD Medyan (Q1-Q3)	p değeri
Taş ölçümü (mm)	10,51 ± 3,32 10,67(8,19–12,96)	10,16 ± 3,23 10,83 (8,02 – 13,21)	0,498**
Seans sayısı	1,25 ± 0,52 1,28 (0,89 – 1,63)	1,56 ± 0,77 1,72 (1,05 – 2,29)	<0,001***

ESWL: Ekstrakorporeal şok dalga litotripsi, RIRC: Retrograd intrarenal cerrahi, p: *Pearson Chi-Square Test, **Independent Samples t Test, mm: milimetre, SD: standart deviasyon ***Mann Whitney U TestD testleri uygulandı.

Tablo 2. Yerleşim yerine göre taşsızlık sağlanma oranları

Renal pelvis yerleşimli taşlar	ESWL(n=46) n (%)	RIRC kombine ESWL (n=20) n (%)	p değeri
			0,482*
Taşsızlık sağlanan			
1. Seans	29(63,05)	10(50,00)	
2. Seans	8(17,40)	6(30,00)	
3. Seans	2(4,34)	2(10,00)	
Taşsızlık sağlanmayan	7(15,21)	2(10,00)	
Alt kaliks taşları	ESWL(n=19)	RIRS kombine ESWL (n=19)	p değeri
	n (%)	n (%)	0,891*
Taşsızlık sağlanan			
1. Seans	15(78,94)	10(52,63)	
2. Seans	0(0)	3(15,79)	
3. Seans	0(0)	3(15,79)	
Taşsızlık sağlanmayan	4(21,06)	3(15,79)	
Tüm taşlar	ESWL(n=72)	RIRS kombine ESWL(n=46)	p değeri
	n (%)	n (%)	0,116*
Taşsızlık sağlanan			
1. Seans	49(68,05)	24(52,18)	
2. Seans	8(11,11)	11(23,92)	
3. Seans	3(4,17)	5(10,86)	
Taşsızlık sağlanmayan	12(16,67)	6(13,04)	

ESWL: Ekstrakorporeal şok dalga litotripsi, RIRC: Retrograd intrarenal cerrahi, p:* Pearson Exact Chi-Square testi uygulandı.

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Tablo 3. Taş boyutu ölçümüne göre ESWL seans sayısı dağılımı

	Seanslar				p değeri
Taş ölçümü (mm)	1. seans n (%)	2. seans n (%)	3. seans n (%)	Total n (%)	
5- 9,99	24 (35,82)	5 (27,78)	0 (0,0)	29 (31,52)	
10-14,99	40 (59,70)	12 (66,67)	4 (57,14)	56 (60,87)	0,004*
15-20	3 (4,48)	1 (5,55)	3 (42,86)	7 (7,61)	
Total	67 (100,0)	18 (100,0)	7 (100,0)	92 (100,0)	

n: taş sayısı, p: * Pearson Exact Chi-Square testi uygulandı, mm: milimetre

Ancak bazı durumlarda bu teknikler tek başına yeterli olmayabilir ve diğer tekniklerle desteklenmeleri gerekebilir. ESWL dirençli taşlarda, RIRC başarı oranı yüksek, komplikasyon oranı düşük güvenli bir tekniktir (16). Bu çalışmada da minimal invazif tekniklerden ESWL tekniğinin RIRC ile kombine edilmesini gerektiren faktörleri değerlendirdik.

Literatürde, pediatrik hastalarda ESWL'nin başarısını etkileyen en önemli faktör taş boyutu yaş olarak değerlendirilmektedir (17). Özellikle 10 mm'den küçük taşlarda ESWL en başarılı ve ilk önerilen tekniktir (18). Elsobky ve arkadaşları <10 mm taşlar için %91 taşsızlık oranına karşılık ≥10 mm taşlar için %75 taşsızlık oranı bildirmiştir (19). Bu çalışmada yaş taşsızlık başarısında iki grup arasında karıştırıcı bir faktör değildi. Bununla birlikte 10 mm'den büyük taşlarda ya daha fazla ESWL seansı gerektiği ya da RIRC ile kombine edilerek istenen taşsızlığa ulaşılabildiğini saptadık. Bu nedenle taş boyutu taş tedavisinde yöntemi belirleyen önemli kriterlerden biridir. ESWL ile 20 mm'nin altında tüm taşlara müdahale edilebilir ancak taş boyutu 10 mm'nin üzerine çıktıkça RIRC ile desteklenebileceği akılda bulundurulmalıdır.

Taş sayısı işlem başarısını etkileyen bir diğer faktördür. Taş yükünü yalnız en büyük taşın büyüklüğü değil böbrekte bulunan bütün taşlar oluşturmaktadır (20). Abdel-Khalek M ve ark. tek taşı olan hastalarda taşsızlık durumunun ESWL'de multipl taşlara göre 1,9 kat daha fazla olduğunu bildirmiştir (21). Azili ve ark. RIRC'de benzer şekilde taş sayısı arttıkça komplikasyon riskinin arttığını ve taşsızlık başarısının düştüğünü bildirmiştir (22). Bu çalışmada, taş yükü arttıkça ESWL'de uygulanan seans sayısının arttığı, hatta başarıya ulaşmak için hastalarda RIRC'ın birlikte kullanılması gerektiği görüldü. Bu da bize multipl taşlarda, tedavide tek yöntem yerine gerekli hastalarda taş durumunun yeniden değerlendirilip tekniklerin kombine edilmesi gerektiğini gösterdi.

Üriner sistem taşlarının böbrek ve üreterdeki yerleşimi taş tedavisinde başarıyı etkileyen bir diğer faktördür. Literatürde bir çalışmada 3 aylık ESWL sonrası böbrek taşlarındaki başarı oranları: Pelvis %89 ve alt kaliks %71,1 olarak bildirilmiştir. (23). ESWL'de alt pol taşları tedavi başarısı açısından en düşük başarıya sahip yerleşimdir (21). Lingeman ve ark. yaptığı 2927 alt kaliks taşını değerlendirdikleri bir meta-analiz çalışmasında <10mm, 10-20mm, >20 mm çaplarındaki taşların ESWL başarı oranları sırasıyla %74, %56 ve %33 olarak bildirilmiştir (24). Singh ve ark. orta büyüklükteki alt pol taşlarında RIRC'ın ESWL'ye göre daha başarılı olduğu göstermiştir (25). Bizim çalışmamızda da ESWL grubunda alt kaliks taşlarında başarı oranında belirgin düşük başarı oranı saptandı. Ancak RIRC ile kombine edilen grupta da alt pol taşlarında başarı şansı diğer lokalizasyonlara göre düşüktü. Bu da kullanılan teknikten bağımsız olarak alt pol taşlarının zorlu olduğunu göstermektedir. Ancak gruplar karşılaştırıldığında alt pol taşlarında ESWL ile kombine RIRC yapılan grupta taş başarısının arttığı görüldü. Özellikle fleksibl enstrümanların alt pol taşlarının tedavi başarısında büyük rolü olduğu söylenebilir.

Taş kırma yöntemlerinin başarı oranları değerlendirilirken kullanılan 'taşsızlık' kavramı çalışmalara göre farklılık gösterebilmektedir. Klinik bulgu olmaksızın 4 mm'ye kadar taş varlığı ile hiç taş yokluğu arasında taşsızlık olarak kabul edilen çalışmalar mevcuttur (26-28). ESWL, taş boyutu <20 mm olan pediatrik ürolitiyazis hastaları için tercih edilen bir tedavi yöntemidir ve ESWL sonrası taşsızlık oranı %57-92 arasında değişmektedir (29). Literatür ile uyumlu olarak bizim çalışmamızda da taşsızlık başarıları tüm gruplarda %80'in üzerinde saptandı. Bu başarıyı sağlamak için özellikle ESWL dirençli, 10 mm'den büyük, multipl ve alt kaliks taşlarında RIRC'ın

tedaviye dahil edilmesi önerilebilir.

Bu çalışmanın hasta sayısı ve retrospektif bir çalışma olmasından dolayı kısıtlılıkları bulunmaktadır. Teknoloji bağımlı yöntemler olmasından dolayı ESWL ve RIRC'ın başarılarının daha sağlıklı değerlendirilebilmesi için geniş serilerle yapılmış çalışmalara ihtiyaç vardır.

SONUÇ

Üriner sistem taşlarının tedavisinde nihai amacın taşı temizlemekten önce böbreği korumak olduğu unutulmamalıdır. Bu nedenle uygun olan hastalarda daha az invaziv olması nedeniyle ESWL öncelikli olarak düşünülebilir. Ancak ESWL planlanırken, özellikle taşın yerleşimi, boyutu ve taş sayısına göre RIRC ile kombine edilmesi gerebileceği unutulmamalıdır.

Tasdik ve Teşekkür

Yazarlar arasında herhangi bir çıkar çatışması bulunmamaktadır.

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CLINICAL OUTCOMES OF 100% GLISTENING FREE INTRAOCULAR LENS IMPLANTATION

%100 Glistening Free Göz İçi Lens İmplantasyonu Sonuçlarımız

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ABSTRACT

Objective: The purpose of this study is to investigate the outcomes of ENOVA GF3 intraocular lens (IOL) implantation.

Material and Methods: In this retrospective study, we evaluated the clinical results of patients who underwent phacoemulsification surgery with implantation of ENOVA GF3, a hydrophobic acrylic IOL, in Yozgat Bozok University Health Practice and Research Center ophthalmology clinic. A total of 320 eyes of 292 patients were included in the study with all procedures performed by the same surgeon. The postoperative follow-up examinations were conducted on the 1st and 7th postoperative days and at the 1st , 3 rd , 6 th and 12 th months. In these visits, we examined uncorrected and corrected distance visual acuity, as well as visual acuity. Photographs of the anterior segment were taken after pupil dilation, glistening, and posterior capsule opacification (PCO) formations were noted and postoperative auto-refractometer values were used for determining deviations from the target refraction. The patients underwent contrast sensitivity tests in the post-operative 6th month. All patients' quality of life was determined with the National Eye Institute-Visual Function Questionnaire after surgery (NEI VFQ 25).

Results: In the 282 eyes (88%) the mean incision size was 2.20 mm and in 38 eyes (12%) it was 2.80 mm. In terms of intraoperative complications, intraoperative floppy iris (IFIS) occurred in 3 patients (0.01%) and posterior capsule rupture (PCR) occurred in 1 patient (0.003%). Evaluations conducted at 6 and 12 months showed no glistening, PCO, or any other complications. The deviation from the target refraction was 0.06 ± 0.71 and the mean corrected visual acuity was 0.98 ± 20 at the 12-month evaluation after IOL implantation.

Conclusion: The ENOVA GF3 IOL exhibited a safe profile in terms of intraoperative complications, postoperative fibrin reaction, deviation from target refraction, posterior capsule opacification (PCO), and glistening. Considering both short- and long-term outcomes, ENOVA GF3 appears to be a reliable option for clinical application.

Keywords: *ENOVA GF3; Glistening; Hydrophobic Lens; Cataract*

ÖZET

Amaç: Bu çalışmanın amacı ENOVA GF3 göz içi lens implantasyonunun klinik sonuçlarını araştırmaktır.

Gereç ve Yöntemler: Bu retrospektif çalışmada, Yozgat Bozok Üniversitesi Sağlık Uygulama ve Araştırma Merkezi göz kliniğinde fakoemülsifikasyon uygulanan ve hidrofobik akrilik bir göz içi lens (GİL) olan ENOVA GF3 implante edilen hastaların sonuçları değerlendirildi. Çalışmaya tamamı aynı cerrah tarafından opere edilen, 292 hastanın 320 gözü dahil edildi. Ameliyat sonrası takip muayeneleri ameliyat sonrası 1. ve 7. günlerde ve 1., 3., 6. ve 12. aylarda yapıldı. Bu muayenelerde düzeltilmemiş uzak görme keskinliği, düzeltilmiş uzak görme keskinliği, düzeltilmemiş ve düzeltilmiş yakın görme keskinliği incelendi. Pupil dilatasyonundan sonra ön segmentin fotoğrafları çekildi, glistening ve arka kapsül kesafeti (AKK) oluşumları not edildi. Hedef refraksiyondan sapmalar hastaların postoperatif otorefraktometre değerlerine bakılarak belirlendi. Hastalara kontrast duyarlılık testleri uygulandı. Hastaların cerrahi sonrası yaşam kaliteleri Ulusal Göz Enstitüsü Görme Fonksiyonları Ölçeği (NEI VFQ 25) anketi ile belirlendi.

Bulgular: Çalışmaya dahil edilen 282 gözün (%88) ortalama kesi boyutu 2,20 mm, 38 gözün (%12) ortalama kesi boyutu ise 2,80 mm idi. İntraoperatif komplikasyonlar, 3 hastada (%0,01), gevşek iris (IFIS) ve 1 hastada (%0,003) arka kapsül rüptürü idi. 6. ve 12. aydaki değerlendirmelerde glistening, AKK veya başka herhangi bir komplikasyon görülmedi. ENOVA GF3 implantasyonundan sonraki 12 aylık değerlendirmede hedef refraksiyon sapma değerleri 0,06 ± 0,71 ve ortalama düzeltilmiş görme keskinliği 0,98 ± 20 idi.

Sonuç: ENOVA GF3 GİL, intraoperatif komplikasyonlar ve postoperatif fibrin reaksiyonu, hedef refraksiyondan sapma, AKK ve glistening açısından güvenilir bir lenstir. ENOVA GF3'ün kısa ve uzun dönem sonuçları incelendiğinde, klinik pratikte tercih edilebileceğini düşünmekteyiz.

Anahtar Kelimeler: *ENOVA GF3; Glistening; Hidrofobik Lens; Katarakt*

INTRODUCTION

Phacoemulsification cataract surgery is the most widely used treatment modality in the cataract surgery. While phacoemulsification allows the emulsification of the patient's lens through small incisions with ultrasonic power, it also allows the implantation of foldable intraocular lenses (IOLs) via this small incision. Currently, with advanced lens technologies, phacoemulsification surgeries can also be applied as refractive surgery (1).

A wide variety of materials are used in the production of intraocular lenses. Some of these materials are polymethylmethacrylate (PMMA), silicone, hydrophilic and hydrophobic acrylics. PMMA, the first artificial IOL material, is resistant to environmental changes and the aging process. Silicone IOLs, with their elastic structure, allow for smaller incisions, and their hydrophobic nature enhances capsular biocompatibility, reducing the risk of posterior capsular opacification (PCO). However, because silicone reacts with oils, certain complications may occur after vitreoretinal surgery (2). Acrylic IOLs, which have a high refractive index, are the thinnest IOL material, offering high biocompatibility, reduced capsular fibrosis, and good centralization. They can be either hydrophilic or hydrophobic. Hydrophilic IOLs do not damage the endothelium and are easy to fold and unfold due to their water content (3). On the contrary, because hydrophobic IOLs have less water content and are more rigid, they are resistant to folding and allow slower and more controlled openings. As the hydrophilic surface allows the proliferation and migration of lens epithelial cells, posterior capsule opacification rates are high. To prevent PCO, hydrophobic IOLs were produced but they are vulnerable to surface microtrauma. The biggest disadvantages of hydrophobic IOLs are dysphotopsia and glistening formations (2-5).

Glistening are small water-filled vacuoles forming in the IOL material. It is believed that they are formed as a result of water getting into the microchannels in the IOL material and forming small inclusions. Their dimensions may vary between 1-30 µm. They are visible as bright spots on slit biomicroscope examination (6-8). IOLs composed of different materials have different water contents. Hydrophobic acrylic, silicone, and PMMA IOLs have lower water content, whereas hydrophilic acrylic IOLs have higher water content (6,7). Even though glistening is most frequently detected in hydrophobic acrylic IOL materials, PMMA, silicone, and hydrophilic acrylic materials may also produce glistening (8-10). The exact mechanism of glistening development has not been fully elucidated. Two different theories have been proposed (11). The first theory is based on the changing water absorption rates of the polymers in the IOL material resulting from temperature changes. According to this theory, glistening is caused by the water absorption of the IOL material due to environmental temperature changes. The second theory suggests that the changes in the osmolarity of the environment inside the eye cause water flow into the IOL material under isothermal conditions (6,12). AcrySof IOL is one of the most commonly used IOLs with a hydrophobic acrylic structure. It has been reported to produce approximately 55% glistening despite such frequent use (12). These glistening have been reported to have little effect on image quality but can create difficulties, especially in driving (13).

This study evaluates the results obtained with ENOVA GF3, a 100% glistening-free new-generation hydrophobic monofocal IOL.

MATERIALS AND METHODS

In this retrospective study, we examined the outcomes of patients who underwent phacoemulsification and implantation an ENOVA GF3 (VSY Biotechnology GmbH, Germany) hydrophobic acrylic intraocular lens (IOL) at the ophthalmology clinic of Yozgat Bozok University Research Hospital.

The study was conducted in accordance with the Declaration of Helsinki ethical principles and was conducted with the approval of the local ethics committee. Ethical approval was taken from Yozgat Bozok University Clinical Research Ethics Committee with number 2017-KAEK-189_2023.04.28_3. Patients were informed about the study and signed a consent form.

Exclusion criteria included patients with prior eye surgeries in the eye undergoing phacoemulsification, those with ocular conditions other than cataracts, and those with systemic diseases that could affect vision. Preoperative evaluations included assessments

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of uncorrected and corrected visual acuity, detailed fundus examinations, and biometry with an optical device (Lenstar LS 900, Haag-Streit AG, Köniz, Switzerland). IOL power was calculated using the SRK/T and Barrett's universal formulas.

All surgeries were done by the same surgeon. In all patients, the pupils were dilated with 1% cyclopentolate hydrochloride (Cycloplegin 1%), phenylephrine HCl (Mydfrin 2.5%) and tropicamide (Tropamide 1%). Anesthesia of the cornea and conjunctiva was achieved with a drop of proparacaine (Alcaine 0.5%).

The surgeries were carried out with the standard phacoemulsification method. The clear corneal incision was performed with 2.2 mm at 90 degrees. Afterwards, side accesses were made. After the anterior chamber was created first with dispersive viscoelastic (Protectalon 3.0%) and then with cohesive viscoelastic (Protectalon 1.4%), capsulorhexis was applied. Following hydrodissection, phacoemulsification of the nucleus was performed with the "stop and chop" method by Centurion (Alcon Laboratories, Fort Worth, TX, USA) and cortex was cleaned using bimanual irrigation aspiration. After cohesive viscoelastic (Protectalon 1.4%) was injected into the capsular sac, the IOL was implanted through the available incision with an injector system. Again, the viscoelastic materials were cleaned by irrigation aspiration. The wound sites were inflated with stromal hydration. Surgery was finalized with intracameral cefuroxime in the anterior chamber.

Technically, ENOVA GF3 is a one-piece hydrophobic acrylic foldable lens with C haptic, haptic angle 0 degrees, optical diameter 6.00 mm, total diameter 13 mm and A constant 118.0. ENOVA GF3 is the first intraocular lens with hydrophobic acrylic structure that does not require prior hydration and is the first non-glistening lens to be stored dry. With a Tg of -2.0 degrees, ENOVA GF3 offers controlled and soft opening at room temperature. It requires no prior heating or other special conditions.

Intraoperative complications that occurred during cataract surgery such as disruption of continuity of the capsulorhexis, posterior capsule rupture, zonular dialysis, corneal scleral suturing were recorded and removed from the study.

Postoperative follow-up assessments were conducted on days 1 and 7, and at 1, 3, 6, and 12 months. During these visits, uncorrected and corrected distance visual acuity were measured according to Snellen's chart, and near visual acuity was evaluated. Anterior segment photographs were taken (TOPCON IMAGEnet i-base), and the presence of glistening and PCO were recorded. Glistening was assessed by slit-lamp biomicroscopy; light scattering and/or microvacuole presence indicated glistening formation. Anterior segment photographs were taken for further analyze (14). Patients' target refractions were determined according to SRK-T and Barrett Universal II formula and deviations from the target refraction were identified by looking at autorefractometer values in postoperative follow-up. The contrast sensitivity tests were performed at 4 different frequencies with and without glare (VECTOR VISION CSV-1000HGT, Ohio, USA).

All patients' vision defects and quality of lifes were measured with the The National Institute of Ophthalmology Visual Function Questionnaire (NEI VFQ 25) questionnaire after 6th months of cataract surgery (15). NEI VFQ 25 measures self-reported vision quality and symptoms and consists of 12 subscales score between 0-100. Higher scores are related to better visual functions (16).

Statistical Analysis

SPSS package program for Windows (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp) was used to analyze the data. Descriptive statistics were presented as mean ± standard deviations for numeric and frequencies and percentages for categorical variables. Normality was tested with Kolmogrov Smirnov and $p<0.05$ was selected for statistical significance level. The chi-square test was used to compare categorical variables, and one-way variance and repeated measures ANOVA tests were used in three-group comparisons and in the analysis of repeated measurements.

RESULTS

A total of 320 eyes of 292 patients were included in the study. The characteristics of the patients are shown in Table-1. Characteristics of the surgery are shown in Table-2. In 320 eyes, the mean incision size was 2.20 mm in 282 eyes (88%) and 2.80 mm in 38 eyes (12%).

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Regarding intraoperative complications, intraoperative floppy iris (IFIS) occurred in 3 (0.01%) and posterior capsule rupture (PCR) in 1 (0.003%) of 320 eyes. At the 12-month follow-up, there was no evidence of glistening formation, asymptomatic posterior capsular opacification (not requiring Nd:YAG laser treatment), or other complications. Glistening assessment conducted with anterior segment photography was shown in Figure 1. Results of the NEI VFQ-25 questionnaire applied to the patients are shown in Table 3.

No complications occurred intraoperatively during lens opening or implantation. There were no postoperative complications such as intraocular pressure elevation or fibrin reaction in the anterior chamber in the early postoperative period. Additionally, no capsular fibrosis was observed at any follow-up visit.

Table 4 showed the visual acuities, spherical equivalent values, deviation from target refraction, glistening, and PCO formation and contrast sensitivity of the individuals. There was a statistically significant difference between the corrected and uncorrected visual acuities recorded preoperatively and postoperatively at 6 and 12 months ($p<0.01$).

DISCUSSION

The purpose of this retrospective study is to analyze the relationship between ENOVA GF3 hydrophobic monofocal intraocular lens (IOL) and glistening, and PCO formation following phacoemulsification surgery and to analyze the reliability of ENOVA GF3 IOL. In the literature, although there are studies that examine the relationship between various hydrophobic IOLs and glistening, there is no study that examines the relationship between ENOVA GF3 intraocular lens and glistening and PCO (9).

Changes in temperature, disturbances in osmotic and

Table 1. Characteristics of the Individuals

PARAMETER	VALUE
Patient/Eye (n)	292/320
Age (years) (X ± SD)	66.86 ± 9.33
Gender	
Female n (%)	141 (44%)
Male n (%)	179 (56%)
Eye, n (%)	
Right	165 (51.5%)
Left	155 (48.5%)
Mean CDVA (X ± SD)	
Decimal	0.19±0.15
Mean UDVA (X ± SD)	
Decimal	0.26±0.16
Mean LT (µm) (X ± SD)	4.33±0.39
Mean AL (µm) (X ± SD)	23.43±0.81
Intraocular lens power, D	21.63±1.87
Corneal Astigmatism, D	0.82±0.60

SD: standard deviation, CDVA: Corrected distance visual acuity, UDVA: Uncorrected distance visual acuity, LT: Lens thickness, AL: Axial length.

Table 2. Surgery Parameters

PARAMETER	X ± SD
Effective PHACO Time (sec)	4.29±2.98
Total Surgery Time (min)	11.43 ±3.55
Volume of Liquid Used (mL)	75.91±26.52
Final Incision Size (mm)	2.27±0.19

SD: standard deviation, sec: second, min: minute, mL: mililiter, mm: milimeter.

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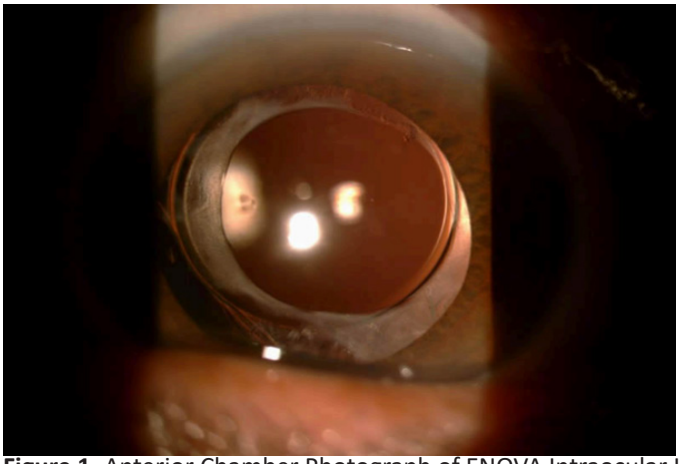

Figure 1. Anterior Chamber Photograph of ENOVA Intraocular Lens
Anterior chamber photograph of ENOVA IOL at post-operative 6th months

Table 3. Visual Function Questionnaire (VFQ-25) survey results

Subscale	Average ± SD	Range
NEI-VFQ-25		
GH: General health	55.84±11.30	18-83
GV: General eyesight	65.15±14.81	5-85
EP: Eye pain	60.40±20.65	25-100
NA: Near activities	78.41±21.20	4-100
DA: Distance activities	82.35±25.31	8-100
Eyesight-related		
ESF: Social function	87.12±19.54	17-100
EMH: Mental health	65.35±23.54	0-100
ERR: Role restrictions	70.12±22.85	0-100
ED: Dependency	78.06±26.49	6-100
D: Driving	89.55±17.23	42-100
RV: Color vision	94.14±15.21	0-100
PV: Peripheral vision	82.32±22.1	25-100
TS: Total score	77.53±17.42	13.42-97.73

SD: standard deviation, NEI-VFQ: National Eye Institute-Visual Function Questionnaire

water balance changes in environmental factors some main causes of glistening formations (17-19). And also, production of IOLs by casting molding, control of the polymerization process may contribute to glistening formation (11).

The polymers used in the production of intraocular lenses (IOLs) contain various components, including different monomers, chromophores, and cross-linking agents. Within the polymer network, microvacuoles may be present depending on the structure of the materials. Under experimental conditions, in the same IOL, glistening reappears in identical positions when microvacuoles proliferate in the voids within the polymer, representing their original locations. Thus, material design plays a key role in determining glistening formation with phenyl groups are predominantly favored in IOL formulations due to their high refractive index. However, these groups are generally bulky, providing suitable cavities within the microvacuoles for water accumulation and subsequent glistening formation. For instance, the high glistening in AcrySof IOLs can be attributed to the significant

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Table 4. Postoperative values of visual acuity, refraction and contrast parameters

Parameters	1st Week X ± SD	1st Month X ± SD	3rd Month X ± SD	6th Month X ± SD	12th Month X ± SD
UDVA Decimal	0.44±0.29	0.73±0.42	0.87±0.29	0.89±0.34	0.92±0.54
CDVA Decimal	0.73±0.30	0.89±0.21	0.89±0.27	0.91±0.31	0.98±0.20
UNVA Decimal	3.02±2.14	3.13±2.1	3.19±1.88	3.22±1.73	2.98±1.09
DCNVA Decimal	4.70±1.77	4.92±1.51	4.98±1.66	5.02±1.44	5.05±1.88
CNVA Decimal	1.09±0.35	1.07±0.42	1.06±0.21	1.08±0.16	1.09±0.44
Required near add power* (D)	2.33±0.82	2.40±0.77	2.41±0.88	2.42±0.72	2.45±0.92
SE Refraction (D)	-0.28±0.70	-0.22±0.80	-0.17±0.73	-0.18±0.66	-0.15±0.55
Deviation from Target Refraction	0.14±0.64	0.5±0.6	0.06±0.59	0.07±0.62	0,06± 0,71
Contrast Sensitivity (Log Units)					
With Glare					
3 cpd			1.54±0.18	1.55±0.17	1.52±0.22
6 cpd			1.94±0.21	1.97±0.23	1.95±0.44
12 cpd			1.76±0.27	1.75±0.22	1.74±0.33
18 cpd			1.21±0.29	1.23±0.27	1.21±0.45
Without Glare					
3 cpd			1.61±0.18	1.62±0.19	1.62±0.26
6 cpd			1.86±0.16	1.88±0.21	1.87±0.33
12 cpd			1.54±0.28	1.55±0.19	1.55±0.48
18 cpd			1.12±0.23	1.10±0.29	1.11±0.30

SD: standard deviation, UDVA: Uncorrected distance visual acuity, CDVA: Corrected distance visual acuity, UNVA: Uncorrected near visual acuity, DCNVA: Distance-corrected near visual acuity, CNVA: Corrected near visual acuity.

amount of phenyl groups present in PEA and PEMA. In contrast, the Enova GF3 formulation has reduced phenyl group content, replacing it with a hydrophilic monomer, HEA, and optimizing cross-linker concentration. If the polymer is placed in warm water and then the temperature is reduced, the water within the polymer becomes supersaturated. Excess water accumulates in the voids within the polymer network, leading to glistening formation. However, if the polymer is placed in water below its glass transition temperature (Tg), no glistening is observed. Thus, it is likely that in-vivo glistening may occur when the lens experiences minor temperature fluctuations in the aqueous environment. With a Tg of -2°C, ENOVA GF3 is considered a soft copolymer

It has been shown that disruption of the blood-aqueous barrier and intraocular inflammatory factors are some reasons of glistening formation (21). It was demonstrated in the literature that diabetic patients have more glistening formation than non-diabetic ones (11). It was reported that the common occurrence of disruption of the blood-aqueous barrier in patients with diabetes mellitus might lead to an increased incidence of glistening formation (21). Furthermore, there is an association between glaucoma and glistening, and this association is likely to be due to the impairment of the blood-aqueous barrier by topical antiglaucomatous drops (12). Additionally, both uveitis and inflammation in post-operative period cause glistening by disrupting the blood-aqueous barrier (18, 22). In the literature, a positive correlation between high IOL power and glistening formation has been suggested. This may be

because the optical component of the high diopter IOL is thicker and its content is denser (23).

There are some studies evaluated the association between glistening and visual performance. Despite the various results presented in these studies, it was found that glistening had no significant impact on visual performance in the majority of these studies (12, 23-26). Additionally, reduced contrast sensitivity and color sensitivity are the most common findings in patients with impaired visual performance. The number, size, and distribution of glistenings are important factors influencing vision. Studies have indicated a higher quantity of glistenings in eyes with reduced visual performance; however, it should be noted that there is no objective classification for glistening staging (27-29). The literature includes studies examining glistening formation in IOLs. In a study by Colin et al., which analyzed glistening formation following hydrophobic Acrysof implantation in 111 eyes, glistenings were observed in 86.5% of the individuals (30). In another study by Auffarth et al., which evaluated glistening formation in Alcon and HOYA IOLs, a follow-up period of 2 years showed an 88% incidence of glistening in Alcon IOLs and a 25% incidence in HOYA IOLs (31). In our study, however, no glistening formation was observed during the 6-month follow-up period after ENOVA GF3 IOL implantation.

Satisfaction rates following cataract surgery are closely related to the outcomes associated with the implanted intraocular lens (IOL) (32). One of the primary cause of dissatisfaction post-surgery is deviation from the expected refractive outcome. In IOL implantation, the goal is to minimize refractive deviation by utilizing optical biometry devices and formulas suited to the patient. In our study, the deviation from the target refraction reached its lowest values at 3 and 6 months postoperatively, recorded as 0.06 D and 0.07 D, respectively, with a deviation of 0.14 D observed on the first postoperative day. In a study by Simon et al., which analyzed 1,275 phacoemulsification surgeries, it was similarly reported that deviation from the target refraction was influenced by the type of lens used, with an average deviation of 0.1 D (33).

For individuals implanted with the ENOVA IOL, contrast sensitivity under photopic conditions ranged from 1.21 to 1.97, while contrast sensitivity under mesopic conditions varied between 1.10 and 1.88. These findings closely align with those reported by Pomerance et al. for average contrast values among individuals aged 50-75 (34). Given the similarities between our results and findings in the literature, the ENOVA GF3 IOL can be considered a reliable choice in terms of refractive target deviation and contrast sensitivity, making it a recommendable option for clinical practice. The most important condition that reduces visual acuity after uncomplicated cataract surgery is PCO. Another cause of decreased visual acuity and quality is IOL opacification, which is more common in hydrophilic lenses. Especially, it is seen after pars plana vitrectomy and after gas injection (35). PCO is caused by the proliferation of epithelial cells in the capsule that grow into the space between the IOL and the posterior capsule (36). The material and design of the lens should be intended to prevent the formation of PCO. Hydrophobic lenses have a lower rate of PCO formation than hydrophilic lenses (37). According to our study, only 0.003% of individuals who were implanted with hydrophobic IOLs developed PCO. In a 2017 meta-analysis conducted by Zhao et al. in which the risks of PCO formation were evaluated between hydrophilic and hydrophobic lenses, it was stated that hydrophobic lenses had a lower Nd:YAG laser capsulotomy rate and subjective PCO rates were also lower (36). In the study conducted by Aufarth et al. in which two different hydrophobic acrylic lenses were compared with respect to PCO and glistening, it was observed that 31% PCO developed in Alcon IOL and 25% PCO developed in HOYA IOL in the 3-year follow-up of the lenses (31). When these results are taken into consideration, it can be concluded that although our duration of follow-up was short, the development of PCO was much lower and ENOVA GF3 IOL may be as safe as the current lenses in terms of PCO development.

NEI-VFQ-25 is a scale consisting of 25 questions that evaluates the difficulties in daily life due to visual symptoms and quality of life. In a study, Lin et al compared aspherical and spherical Alcon IOLs' clinical outcomes after 3 months of implantation. Our NEI VFQ 25 results after cataract surgery showed similarity to Alcon aspherical (AcrySof IQ SN60WF) and better than spherical IOL (AcrySof SA60AT). Alcon aspherical IOL's

ocular pain and peripheral vision scores were higher and social function scores were lower than ENOVA. But we couldn't compare the baseline characteristics of patients because we couldn't assess NEI VFQ 25 before phacoemulsification surgery (16).

Our study has various strengths and limitations. Strengths of our study include the high number of patients and eyes and being the first study to evaluate the results of ENOVA GF3 IOL implantation. Nevertheless, the limitations of our study are the short follow-up period due to the occurrence of PCO and glistening formation in some cases more than 6 months and the fact that the visual function, which we assessed with a questionnaire, was not evaluated in the preoperative period. We recommend using longer follow-up durations in further studies to analyze glistening and posterior capsule opacification (PCO) formation.

Taking all this information into consideration, the ENOVA GF3 IOL demonstrates a similar efficacy as other commercially available IOLs with proven efficacy regarding the development of common phacoemulsification surgery complications such as glare and PCO, postoperative visual function, and deviation from target refraction. PCO development is less common in hydrophobic IOLs, whereas glistening development is more common in hydrophilic IOLs. Although ENOVA GF3 IOL has the advantages of hydrophobic lenses, it has been emphasized that the development of glistening is minimized and the results of our study confirm this. Thanks to its low deviation from the target refraction, low risk of postoperative complications and minimal glistening, ENOVA GF3 IOL is safe and can be used in surgical practice.

CONCLUSION

ENOVA GF3 IOL was tested in terms of visual acuity, refraction, glistening and postoperative complications in this study and showed low deviation from the target refraction, minimal postoperative complications and glistening. According to our results, ENOVA GF3 IOL hydrophobic IOL demonstrates a similar or higher level of efficacy than other commercially available IOLs.

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The authors declare that they have no conflict of interest to disclose.

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MEME KANSERİ CERRAHİSİNDE EREKTÖR SPİNA PLAN BLOĞUNUN AKUT VE KRONİK AĞRIYA ETKİSİ: RETROSPEKTİF ÇALIŞMA

The Effect of Erector Spina Plan Block on Acute and Chronic Pain in Breast Cancer Surgery: A Retrospective Study

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ÖZET

Amaç: Bu çalışmada meme kanseri cerrahisinde erektör spina plan bloğunun post-operatif analjezik tüketimi, ağrı skorları, hasta memnuniyeti ve cerrahi sonrası persistan ağrı üzerine olan etkisini araştırmaktır.
Gereç ve Yöntemler: Etik kurul onayı alındıktan sonra Eylül 2018-Aralık 2019 tarihleri arasında elektif meme kanseri geçiren hastalar retrospektif olarak incelendi. Dışlanma kriterleri uygulandıktan sonra kalan 40 hasta çalışmaya alındı. Hastalar Erektör Spina Plan Bloğu (ESPB) grubu (n=20) ve kontrol grubu (n=20) olarak ikiye ayrıldı. Hastaların postoperatif morfin tüketim miktarı kaydedildi. Vizüel Analog Skala (VAS) kullanılarak değerlendirilen ağrı skorları değerlendirildi. Taburculuk sonrası 3. ve 6. aydaki kronik nöropatik ağrı insidansı kaydedildi.
Bulgular: Postoperatif ilk 24 saatteki morfin tüketimi tüm ölçüm zamanlarında ESPB grubunda kontrol grubundan daha düşüktü (p<0,05). VASstatik skorları 24. saat hariç tüm ölçüm zamanlarında ESPB grubunda kontrol grubundan daha düşüktü (p<0,05). VASdinamik skorları 12. ve 18. Saat hariç gruplar arasında benzerdi (p>0,05). Ek analjezik tüketimi EPSB grubunda kontrol grubundan daha düşüktü (p<0,05). Hasta memnuniyeti ESPB grubunda istatistiksel olarak daha yüksekti (p<0,05). Bulantı-kusma insidansı arasında gruplar arasında farklılık yoktu (p>0,05). Meme kanseri sonrası persistan ağrı (MKCPA), 3. ve 6. ayda sırasıyla %23 ve %8 bulundu ve iki grup arasında anlamı bir fark yoktu (p>0,05). Ağrısı olan tüm hastalarda nöropatik komponent ön planda düşünülmedi (LANSS≤12).
Sonuç: ESPB ile daha düşük sistemik opioid tüketimi ve VAS skorlarının gözlemlenmesi, postoperatif multimodal analjezinin bir parçası olarak ESBP'nin etkin bir şekilde kullanılabileceğini göstermektedir. MKCPA insidansının benzer olması, uzun vadeli dönemde ESBP'nin etkisiz olabileceğini düşündürmektedir.

Anahtar Kelimeler: *Akut Postoperatif Ağrı; Sinir Bloğu; Meme Cerrahisi; Opioid Analjezikler; Kronik Postoperatif Ağrı*

ABSTRACT

Objective: In this study, it was aimed to evaluate effects of erector spinae plane block on postoperative analgesic consumption, pain scores, patient satisfaction and chronic pain after breast cancer surgery.
Material and Methods: After ethic approval, we retrospectively reviewed patients who underwent elective breast cancer surgery between September 2018-December 2019. 40 patients were included to the study after exclusion criterias. Patients were divided into Erector Spina Bifida Block (ESPB) group (n=20) and control group (n=20). We recorded postoperative morphine consumption . The pain assessed by Visual Analog Scale (VAS) score. Chronic and neuropathic pain incidence were assessed at 3 and 6 months.
Results: The morphine consumption within postoperative 24 hours was significantly higher in ESPB group than controls (p<0.05). VASstatic scores were lower in ESPB group than control except 24. hour (p<0.05). VASdynamic scores were comparable between groups except 12. and 18. hours (p>0.05). The additional analgesic consumption was significantly lower in ESPB group than controls (p<0.05). The patient satisfaction was higher in ESPB group when compared to controls (p<0.05). There was no significant difference incidence of nausea-vomiting (p>0.05). The persistent pain after breast cancer surgery (PPBCS) was found to be 23% and 8% on months 3 and 6, respectively, indicating no significant difference between groups (p>0.05). Neuropathic component was not considered in patients with pain (LANSS≤12).
Conclusion: Lower systemic opioid consumption and VAS scores with ESPB suggests that ESBP can be effectively used as part of postoperative multimodal analgesia However, similar incidence of PPBCS suggests that ESPB may be ineffective in long term.

Keywords: *Acute Postoperative Pain; Nerve Block; Breast Surgery; Opioid Analgesics; Chronic Postoperative Pain*

GİRİŞ

Kadınlarda en sık görülen kanser tipi olan meme kanserinin temel tedavisi cerrahidir (1). Memenin yoğun ve karmaşık innervasyonu nedeniyle orta veya yüksek şiddette postoperatif ağrı meydana gelmektedir (2,3). Ağrının yetersiz yönetimi, hasta memnuniyetinin azalmasına ve kronik ağrıya yol açabilir (4). Bu nedenle postoperatif ağrının tedavisi ciddiyetle ele alınmalıdır.

Meme kanseri cerrahisinde multimodal analjezinin bir parçası olarak rejyonel tekniklerin kullanılması, etkin analjezi sağlamanın yanı sıra opioid tüketimini ve dolayısıyla opioid yan etkilerini azaltmaya yardımcı olabilir (5,6). Torakal paravertebral blok (TPVB) analjezik etkinliği iyi bilinen en etkili tekniklerden birisidir. Ancak, derin bir blok olması ve uygulanmasının deneyim gerektirmesi, ayrıca plevra, nöraksiyel ve vasküler yapılara yakınlığı nedeniyle pnömotoraks, kanama ve total spinal anestezi gibi ciddi komplikasyonlara yol açabilmesi, kullanımını kısıtlayan en önemli faktörlerdendir (7,8). Ultrasonun rejyonel anestezi pratiğinde kendine yer bulmasıyla kolay uygulanabilir, komplikasyonlar açısından daha güvenli olan yeni teknikler literatüre girmiştir (9). Erektör spina plan bloğu (ESPB), ilk kez torasik nöropatik ve postoperatif ağrıda tanımlanmıştır. Torakal 4. vertebra (T4) ile erektör spina kasları arasına verilen lokal anesteziğin kraniokaudal yönde yayıldığı ve paravertebral alana geçtiği gösterilmiştir (10). Bu nedenle TVPB'ye göre uygulanması daha kolay ve güvenli bir alternatif olmuştur.

Bu çalışmanın amacı ESPB' nin meme kanseri cerrahisi sonrası postoperatif opioid tüketim miktarı ile akut ve kronik ağrı üzerine olan etkisinin araştırılmasıdır.

GEREÇ VE YÖNTEMLER

Bu çalışmada, Erciyes Üniversitesi Klinik Araştırmalar Etik Kurulu onayı (26.02.2020 tarih-2020/134 sayılı karar) alındıktan sonra, Eylül 2018 ile Aralık 2019 tarihleri arasında meme kanseri cerrahisi geçiren hastanın dosyaları retrospektif olarak incelendi. Hastalardan rutin preoperatif değerlendirmenin bir parçası olarak genel anestezi ve rejyonel tekniklere dair onam alınmıştır. ESPB dışında başka bir rejyonel teknik kullanılan, hasta kontrollü analjezi (HKA) uygulanmayan ve kayıtlarında eksiklik olan hastalar değerlendirmeye alınmamıştır.

Hastalarda akut ağrı Vizuel Analog Skala (VAS) ile değerlendirilmiştir. İstirahat halindeki (VASstatik) ve cerrahi tarafta kol abdüksiyonuyla (VASdinamik) ağrı skorları dosyalardan elde edilmiştir.

Grup Kontrol: Vaka sonunda tüm hastalara 0,05 mg/kg morfin, 1 gr parasetamol intravenöz (iv) uygulanmıştır. Serviste hastalar 1 mg morfin bolus ve 10 dk kilit süresi HKA ile takip edilmiştir. VASstatik>3 iken veya hastanın talebi olduğunda hastaya 50 mg deksketoprofen iv uygulanmıştır.

Grup ESPB: İndüksiyon öncesi tüm hastalarda ESPB, T4 vertebra seviyesinden 25 ml %0,25 bupivakain ile gerçekleştirilmiştir. Vaka sonunda tüm hastalara 0,05 mg/kg morfin, 1 gr parasetamol intravenöz uygulanmıştır. Serviste hastalar 1 mg morfin bolus ve 10 dk kilit süresi HKA ile takip edilmiştir. VASstatik>3 iken veya hastanın talebi olduğunda hastaya 50 mg deksketoprofen iv uygulanmıştır.

Hastaların dosyasından 3. ve 6. aya ait ağrı verileri değerlendirildi. Herhangi bir ağrısı olan hastalar kaydedildi. VAS≥3 olan hastalarda meme kanseri cerrahisi sonrası persistan ağrının (MKCPA) olduğu kabul edildi. hastaların ağrı vasfını değerlendirmek için Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) skorlaması kullanıldı. LANSS≥12 olan hastalarda nöropatik ağrı düşünüldü.

Veriler IBM SPSS v25 (IBM Corp., Armonk, New York, ABD) istatistik paket programında değerlendirildi. Tanımlayıcı istatistikler birim sayısı (n), yüzde (%), ortalama±standart sapma (x+-ss), ortanca (M), 25.yüzdelik (Q1), 75.yüzdelik (Q3) değerleri olarak verildi. Sayısal değişkenlere ait verilerin normal dağılımı Shapiro-Wilk normallik testi ve Q-Q grafikleri ile değerlendirildi. Varyansların homojenliği Levene testi ile değerlendirildi. Normal dağılıma uyan sayısal değişkenler için parametrik testlerden bağımsız değişkenlerde t testi, normal dağılıma uymayan sayısal değişkenlerde ise non-parametrik testlerden Mann Whitney U testi kullanıldı. Kategorik değişkenler Ki-kare veya Fisher exact yöntemi ile karşılaştırıldı. Grupların hemodinamik verileri ve morfin tüketiminin zamana göre karşılaştırılmasında genel doğrusal modellerden tekrarlı ölçümlerde iki yönlü varyans analizi kullanıldı. İki yönlü varyans analizi sonucu fark bulunması durumunda ana etki karşılaştırmaları Bonferroni düzeltmeli çoklu karşılaştırma testi ile değerlendirildi.

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P<0,05 değeri istatistiksel olarak önemli kabul edildi.

BULGULAR

Çalışma gruplarının yaş, vücut kitle indeksi (VKİ), American Society of Anesthesiologists (ASA) sınıfı, cerrahi tipi, ameliyat ve derlenme ünitesinde kalış süresi, intraoperatif fentanil tüketimi arasında istatistiksel olarak bir fark yoktur. Ek analjezik kullanımı ESPB grubunda istatistiksel olarak daha düşüktür (Tablo 1). ESPB yapılan hastalarda postoperatif morfin tüketim miktarları kontrol grubuna göre istatistiksel olarak anlamlı düşük bulunmuştur (Tablo 2).

VASStatik değerleri 24. saat hariç diğer ölçüm zamanlarında ESPB grubunda kontrol grubuna göre istatistiksel olarak daha düşüktür (Şekil 1A). Postoperatif 12. ve 18. saat VASdinamik değerleri istatistiksel olarak ESBP grubunda kontrol grubuna göre daha düşüktür. VASdinamik değerleri arasında diğer ölçüm zamanlarında istatistiksel olarak bir fark yoktur (Şekil 1B).

3. ve 6. ay sonunda herhangi bir ağrı tarifleyen ve meme kanseri cerrahisi sonrası persistan ağrısı (VAS≥3) olan hasta sayısı iki grup arasında istatistiksel olarak benzerdi (Tablo 3). Her iki grupta da ağrısı olan hastaların tamamının LANSS skoru 12 ve altında olup nöropatik ağrı gözlenmemiştir.

Hasta memnuniyeti gruplara göre istatistiksel olarak farklılık göstermektedir. Kötü, orta ve iyi memnuniyet

Tablo 1. Hastaların Perioperatif Tanımlayıcı Özelliklerinin Karşılaştırılması

	Gruplar		Test İstatistikleri	
Değişkenler	ESPB n=20	Kontrol n=20	Test Değeri	p değeri
Yaş (yıl),	47,9±11	50,2±8,6	t=0,730	0,470
VKİ (kg/m²),	26,88±2,67	25,57±1,89	t=1,769	0,085
ASA, n(%) ASA-I ASA-II	 13 (65) 7 (35)	 8(40) 12 (60)	χ^2=2,506	0,113
Cerrahi Tipi, n(%) MKC+SLNBx Mastektomi+SLNBx MR Mastektomi+ALND	 5 (25) 12 (60) 3 (15)	 4 (22,2) 12 (61,1) 4(16,7)	χ^2=0,254	0,881
Süre (dakika),	142,6±13,28	142,1±14,41	t=0,114	0,910
Derlenme Ünitesinde Kalış Süresi (dakika),	38,8±5,8	40,1±6,0	t=0,728	0,471
İntraoperatif Fentanil Tüketimi (μg) M (Q_1-Q_3)	50 (6,3-75)	63 (50-100)	z=1,113	0,289
Ek Analjezik kullanımı (Deksketoprofen-mg) M (Q_1-Q_3)	0 (0-50)	75 (0-100)	z=2,218	0,038

x: Aritmetik ortalama, ss: Standart sapma, t: Bağımsız iki örneklem t testi, χ2: Ki-kare testi, M: Medyan; Q1: Birinci çeyreklik değer; Q3: Üçüncü çeyreklik değer, z: Mann-Whitney U testi, VKİ: Vücut Kitle İndeksi, MKC: Meme koruyucu cerrahi, MR: Modifiye radikal, SLNBx: Sentinel lenf nodu örneklemesi, kg/m²: kilogram/metrekare, ASA: Amerikan Anestezi Uzmanları Derneği

Tablo 2. Postoperatif Morfin Tüketiminin Karşılaştırılması

Ölçüm Zamanı	Gruplar						Test İstatistikleri	
	ESPB (n=20) ±ss			Kontrol (n=20) ±ss			F	p
2.saat$_{morfin}$	4,26	±	3,21	12,43	±	5,22	35,456	<0,001
6.saat$_{morfin}$	7,01	±	3,66	16,56	±	4,78	50,300	<0,001
12.saat$_{morfin}$	9,03	±	4,36	19,77	±	4,91	53,442	<0,001
18.saat$_{morfin}$	10,18	±	4,87	21,67	±	4,81	56,178	<0,001
24.saat$_{morfin}$	11,32	±	5,29	23,81	±	4,71	61,944	<0,001

*Tekrarlı Ölçümlerde İki Yönlü Varyans Analizi, Model İstatistikleri: Grup Etkisi: F=57,732; p<0,001; Zaman Etkisi: F=176,157; p<0,001; GrupX-Zaman Etkisi: F=9,467; p=0,001, ESPB: Erektör Spina Plan Bloğu

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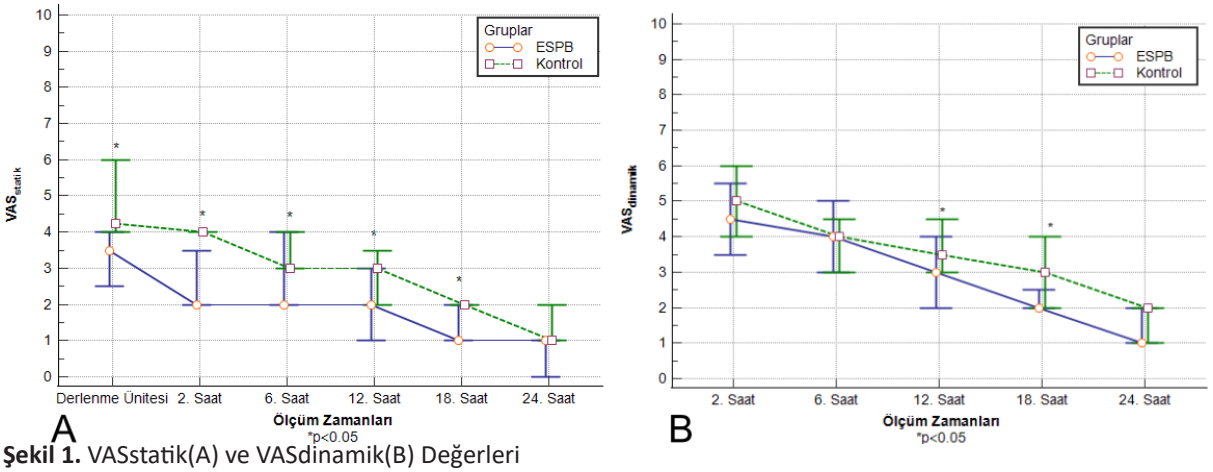

Şekil 1. VASstatik(A) ve VASdinamik(B) Değerleri

Tablo 3. Kronik Ağrıya İlişkin Verilerin Karşılaştırılması

		Gruplar		Test İstatistikleri	
Aylar	Değişkenler	ESPB n=20	Kontrol n=20	Test Değeri	p değeri
3. Ay	Herhangi bir ağrısı olan hasta, n(%)				
	Var (%33)	5 (25)	8 (40)	χ^2=1,026	0,311
	Yok (%67)	15 (75)	12 (60)		
	VAS≥3 ağrısı olan hasta, n(%)			χ^2=3,243	0,231
	Var (%8)	0 (0)	3 (15)		
	Yok (%92)	20 (100)	17 (85)		
6. Ay	Herhangi bir ağrısı olan hasta, n(%)			χ^2=0,902	0,342
	Var (%48)	8 (40)	11 (55)		
	Yok (%52)	12 (60)	9 (45)		
	VAS≥3 ağrısı olan hasta, n(%)			χ^2=1,290	0,451
	Var (%23)	3 (15)	6 (30)		
	Yok (%57)	17 (85)	14 (70)		

χ2: Ki-kare testi, ESPB: Erektör Spina Plan Bloğu, VAS: Vizuel Analog Skala

düzeyi gruplarda benzer dağılım göstermekte iken mükemmel memnuniyet düzeyine sahip hastaların sayısı ESPB grubunda istatistiksel olarak yüksektir. Bulantı ve kusma görülme sıklığında iki grup arasında istatistiksel bir fark yoktur (Tablo 4).

TARTIŞMA

Bu çalışmada meme kanseri cerrahisi geçiren hastalarda ESPB'nin ilk 24 saatteki morfin tüketimini azalttığı gösterilmiştir. Aynı zamanda akut ağrı skorları ve hasta memnuniyetinde iyileşme, non-opioid analjezik tüketiminde azalma gözlemlenmiştir. Ancak kronik ağrıya ilişkin bulgularda bir fark izlenmemiştir. Paravertebral blok, meme cerrahisinde uzun yıllar boyunca anestezi ve analjezi amacıyla kullanılmıştır. Ciddi komplikasyon riski ve uygulamasının deneyim gerektirmesi nedeniyle daha güvenli alternatif arayışı vardır. Ultrasonografi eşliğinde serratus anterior plan bloğu (SAPB) ve pektoral bloklar kullanılabilmekte fakat interkostal sinirlerin anterior kutanöz dallarını

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Tablo 4. Gruplar Arasında Hasta Memnuniyeti, Bulantı ve Kusmanın Karşılaştırılması

	Gruplar		Test İstatistikleri	
	ESPB (n=20) n(%)	Kontrol (n=20) n(%)	χ^2	p değeri
Hasta Memnuniyeti				
Kötü	0 (0,0)	5 (25)		
Orta	1 (5)	3 (15)	11,650	0,009
İyi	7 (35)	9 (45)		
Mükemmel	12 (60)[a]	3 (15)[b]		
Bulantı				
Var	5 (25)	8 (40)	1,026	0,510
Yok	15 (75)	12 (60)		
Kusma				
Var	3 (15)	5 (75)	0,625	0,695
Yok	17 (85)	15 (25)		

χ2: Ki-kare testi, a ve b üst simgeleri gruplar arası farklılığı göstermektedir, ESPB: Erektör Spina Plan Bloğu

etkilememektedir (3). Aynı zamanda pektoral blokların uygulama alanının cerrahi sahaya yakın olması doku ödemi ve elektrokoterin etkinliğinin azalmasına yol açabilmektedir (11).

Periparavertebral blok olarak tanımlanan ESPB, spinal sinirlerin tüm dallarını etkileyerek tüm hemitoraksta analjezi sağlayabilmesi ve transvers proçes üzerine uygulamanın plevra ve vasküler yapılara uzak olmasıyla paravertebral bloğa güvenli bir alternatif oluşturduğu bildirilmiştir. Erektör spina kas planı sadece spinal sinirlerin dorsal ramusunu içerdiğinden dolayı bloğun ön ve yan toraks duvarında nasıl analjezi sağladığı tartışma konusu oluşturmuştur. Bloğun tanımlandığı ilk olgu serisinde kadavraya uygulanan kontrast madde ve metilen mavisi içeren solüsyon kostotransvers foramenin boyanmasına yol açmıştır. Böylece dorsal ve ventral ramusun başlangıç noktalarında bloke edilmesi etki mekanizması olarak öne sürülmüştür (10). Kadavra ve canlı gönüllü enjeksiyonlarını içeren 29 çalışmanın incelendiği sistematik derlemede tüm enjeksiyonlar ortalama 9 spinal seviyede erektör spina kas planında dağılmıştır. Fakat tüm hemitoraksta analjezi sağlamak için gerekli olan interkostal, epidural veya paravertebral alana yayılım ise enjeksiyonların yaklaşık yarısında görülmüştür. Duyusal değerlendirmenin bildirdiği çalışmalarda da paravertebral alana yayılıma benzer oranlarda duyusal kayıp oranları bildirilmiştir (12). ESPB'nin analjezik etkisi ile etki mekanizması arasındaki bu farkın lokal anesteziğin sistemik emilimine bağlı olabileceği ileri sürülmüştür (13–15).

Erektör spina plan bloğunun meme cerrahisinde opioid tüketimi azaltmada ve ağrı skorlarını iyileştirmede sistemik analjeziye üstün olduğu bulunmuştur. Aynı zamanda paravertebral blokla eşdeğer bir analjezi sağlamaktadır (16). Bizim çalışmamızda da tüm ölçüm zamanlarında morfin tüketimi kontrol grubuna kıyasla daha düşük bulunmuştur. İstirahat ağrı skorları (VASstatik) kontrol grubuna göre klinik olarak anlamlı azalmasına rağmen, kol abdüksiyonu ile olan ağrıdaki azalma (VASdinamik) bazı zaman dilimlerinde istatiksel anlama ulaşsa bile tüm zamanlarda klinik anlama ulaşamamıştır. Bu sonuç hareketle meydana gelen fasyal gerilme nedeniyle oluşan ağrının brakial pleksusa ait sinirlerle taşınması ve ESPB'nin bu sinirleri etkilememesi nedeniyle olabilir (17).

Cerrahi ve analjezik tedavideki kaydedilen ilerlemelere rağmen, hastaların bir kısmında akut postoperatif ağrı, iyileşme süresinin ötesinde (≥3 ay) devam ederek

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kronik ağrıya dönüşmektedir. Cerrahi insizyonla başlayan, cerrahinin büyüklüğüne bağlı olarak değişen doku ve sinir hasarına bağlı olarak ortaya çıkan nosiseptif sinyaller periferik ve santral sensitizasyona yol açmaktadır. Aynı zamanda analjezi amaçlı kullanılan narkotik ajanlarda nöronal dokuda gen ekspresyonunda değişikliğe bağlı opioid ilişkili hiperaljeziye sebep olmaktadır. Bütün bunlar maladaptif bir nöroplastisiteyle sonuçlanmakta akut ağrının kronik ağrıya geçişini kolaylaştırmaktadır (18). Psikososyal destek, anestezik ve cerrahi tekniklerin modifiye edilmesi, preemptif analjezi, gabapentinoid, antidepresan ve lokal anestezik kullanımı, rejyonel anestezi ve analjezi kronik ağrı oluşumunu belli oranda azaltabilir. Rejyonel teknikler kronik ağrıyı, nosiseptif sinyalleri modüle ederek ve nöroplastisiteyi önleyerek azaltmaktadır (19).

Meme kanseri cerrahisi sonrası persistan ağrı (MKCPA) literatürdeki farklı tanımlamalar göz önüne alındığında hastaların %10-60'ını etkilemektedir (20). Yılda gerçekleşen meme kanseri cerrahisi sayısı göz önüne alındığında, kronik ağrı yaşam kalitesini ve fonksiyonel kapasiteyi etkileyen önemli bir sorundur (21,22). MKCPA gelişimi için depresyon, anksiyete, ağrı felaketleştirme, şiddetli akut postoperatif ağrı, genç yaş, aksiller lenf nodu diseksiyonu, interkostobrakial sinir hasarı, adjuvan terapiler gibi risk faktörleri vardır (23–25). Meme kanseri cerrahisinde akut postoperatif ağrı üzerinde etkinliği bilinen blokların kronik ağrıyı önlemedeki etkinliği de bu nedenle önem kazanmaktadır.

Cassai ve ark., mastektomi veya lumpektomi yapılan hastalarda Pektoral blok (PECS) II bloğunun akut ağrıda etkili olduğu kadar 3. aydaki kronik ağrı insidansında (%14,9'e karşın %31,8) etkili olduğunu buldular (26). 6, 9 ve 12. aylarda ise anlamlı bir fark gözlemlemediler. PECS II bloğunun postoperatif akut ağrıya etkilerini plaseboyla kıyaslayan Versyck ve ark., çalışma sonrası yayınladıkları raporda 2. yılda hastaların yaklaşık % 40'ında MKCPA tespit ettiler ve iki grup arasında bu insidans benzerdi (27,28). SAPB'nin modifiye radikal mastektomi (MRM) ve aksiller lenf nodu diseksiyonu (ALNDx) geçiren hastalarda akut ağrıda etkili olmasına rağmen 1. ve 6. ayda kronik ağrı ve yaşam kalitesi üzerinde etkili değildi (29). Lumpektomi ve sentinel lenf nodu diseksiyonu (SLNBx) geçiren hastalarda PECS II ve ESPB'nin 3. ayda kronik ağrı insidansını kontrol grubuna göre anlamlı azalttığı tespit edildi (30). Çalışmalar arasındaki farklı sonuçlar cerrahi rezeksiyonun genişliğine (lumpektomi, mastektomi, MRM), lenf nodu eksizyonunun kapsamına (SLNBx veya ALNDx), cerrahi tekniğe (interkostobrakial sinirin korunması vb.) bağlı olabilir. Aynı zamanda PECS ve SAPB'nin memenin medialini ilgilendiren cerrahilerde yetersiz kalabilmesi veya ESPB'nin paravertebral alana geçişteki değişkenliği, çalışmalarda dermatomal yayılımın değerlendirilmediği göz önüne alındığında kronik ağrıya ilişkin sonuçları etkileyebilir.

Bizim çalışmamızda kronik ağrı 3. ve 6. ayda değerlendirildi ve gruplar arasında kronik ağrı insidansında bir fark yoktu. Nöropatik ağrı LANSS ile değerlendirildi ve her iki grupta da nöropatik ağrı gözlemlenmedi. Çalışmamızda birden çok cerrahi tipinin olması, özellikle MRM ve ALNDx vakalarında ESPB'nin brakial pleksus dalları ve aksillayı yetersiz kapsaması gibi sebepler kronik ağrı insidansının benzer olmasına yol açmış olabilir (31).

Çalışmamızın bazı kısıtlılıkları mevcuttu. Retrospektif tek merkezli bir çalışma olması nedeniyle sonuçları genele uyarlamak zor olabilir. Aynı zamanda hastaların preoperatif ağrı ve duygudurum ve blok sonrası dermatomal tutulumun değerlendirilmemesi de bir kısıtlılıktır.

SONUÇ

ESPB meme kanseri cerrahisi sonrası multimodal analjezi protokolünün bir parçası olarak postoperatif opioid tüketimini ve ağrı skorlarını azaltmaktadır. Kronik ağrı üzerine anlamlı bir etkisi tespit edilememiştir. Daha geniş hasta grubuyla çalışmalara ihtiyaç vardır.

Tasdik ve Teşekkür

Yazarlar arasında herhangi bir çıkar çatışması bulunmamaktadır.

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INVESTIGATION OF ANTIBIOTIC RESISTANCE RATES OF BACTERIA CAUSING URINARY SYSTEM INFECTION

Üriner Sistem Enfeksiyon Etkeni Bakterilerin Antibiyotik Direnç Oranlarının Araştırılması

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ABSTRACT

Objective: Urinary tract infection (UTI) is a prevalent health concern globally. The objective of this study was to evaluate the frequencies of pathogens associated with UTI and their antimicrobial susceptibility patterns, as well as extended-spectrum beta-lactamase (ESBL) rates.

Material and Methods: Urine culture results between January 2023 and December 2023 were examined retrospectively. Additionally, variables such as age, sex, and medical department were documented. The study included patients aged 18 years or above with pathogenic bacterial growth in their urine cultures. The identification of bacteria and their antibiotic susceptibility was conducted using conventional methods or the VITEK2-Compact system.

Results: Of 3135 urine samples considered to be causative agents were evaluated. 2495 Escherichia coli, 404 Klebsiella spp., 117 Proteus mirabilis, 57 Pseudomonas spp., 19 Acinetobacter spp., and 43 other enterobacterales members were detected. ESBL positivity rates were found to be for E. coli 14.9% and for Klebsiella spp. 23.2%. Resistance rates of hospital-acquired infection agents were found to be significantly higher than community-acquired. More than 90% susceptibility to carbapenems and aminoglycosides has been detected.

Conclusion: It is beneficial to be aware of the evolution of antibiotic resistance over time, particularly when embarking on empirical therapy. The elevated level of quinolone resistance in hospital-acquired infections can be attributed to its utilisation for a multitude of indications, including pneumonia, gastroenteritis, and urinary tract infections. Our findings indicate that ciprofloxacin, trimethoprim-sulfamethoxazole, and ampicillin are unsuitable for the empirical treatment of UTIs, while nitrofurantoin and fosfomycin represent rational options. We believe that these data will shed light on empirical treatments in our hospital.

Keywords: *Antibiotics; Escherichia Coli; Urinary Tract İnfections; Esbl; Klebsiella Spp.*

ÖZET

Amaç: İdrar yolu enfeksiyonu (İYE) yaygın küresel bir sağlık sorunudur. Bu çalışmada amacımız, hastane kökenli ve toplum kökenli üropatojenlerin sıklıklarını ve antimikrobiyal duyarlılık paternlerinin yanı sıra genişlemiş spektrumlu beta-laktamaz (GSBL) oranlarını araştırmaktır.

Gereç ve Yöntemler: Ocak 2023 ve Aralık 2023 tarihleri arasındaki hastalara ait idrar kültür sonuçları retrospektif olarak incelenmiştir. Yaş, cinsiyet ve örneğin gönderildiği bölüm araştırılmıştır. Çalışmaya, idrar kültürlerinde üreyen ve etken olarak değerlendirilen 18 yaş ve üzeri hastalara ait kültür sonuçları dahil edilmiştir. Bakterilerin tanımlanması ve antibiyotik duyarlılıkları geleneksel yöntemler ve VITEK2-Compact sistemi kullanılarak gerçekleştirilmiştir.

Bulgular: Etken kabul edilen 3135 Gram negatif üropatojen irdelenmiştir. 2495 Escherichia coli, 404 Klebsiella spp., 117 Proteus mirabilis, 57 Pseudomonas spp., 19 Acinetobacter spp. ve 43 diğer enterobacterales üyeleri tespit edilmiştir. GSBL pozitiflik oranları E. coli için %14,9 ve Klebsiella spp. için %23,2 olarak bulunmuştur. Hastane kökenli enfeksiyon etkenlerinin direnç oranları toplum kökenlilere göre anlamlı derecede yüksek bulunmuştur. Karbapenemlere ve aminoglikozidlere karşı %90'dan fazla duyarlılık tespit edilmiştir.

Sonuç: Hastane kaynaklı enfeksiyonlarda yüksek kinolon direnci seviyesi, pnömoni, gastroenterit ve idrar yolu enfeksiyonları dahil olmak üzere çok sayıda endikasyonda kullanılmasına bağlanabilir. Bulgularımız, siprofloksasin, trimetoprim-sülfametoksazol ve ampisilinin İYE'lerin ampirik tedavisi için uygun olmadığını, nitrofurantoin ve fosfomisinin ise rasyonel seçenekler olduğunu göstermektedir. Bu verilerin hastanemizdeki İYE ampirik tedavilerine ışık tutacağına inanıyoruz.

Anahtar Kelimeler: *Antibiyotikler; Escherichia Coli; İdrar Yolu Enfeksiyonları; Gsbl; Klebsiella Spp.*

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INTRODUCTION

One of the most common bacterial infections is urinary tract infection (UTI). There are an estimated about 200 million cases documented globally each year (1). In over 95% of cases of urinary tract infection, a monobacterial infection is observed, with a higher prevalence in females except during the first three months of life (2). The presentation of UTI can range from a relatively mild form, such as cystitis, to a more severe and potentially life-threatening condition like urosepsis (3). Additionally, the spectrum of pathogens responsible for UTI can vary significantly, particularly depending on geographical location. It is of paramount importance to select an appropriate antibiotic that is efficacious against the causative organism to treat UTI (4).

Developing bacterial resistance mechanisms also presents a challenge to the treatment of these infections. One of the crucial benchmarks in the stewardship of antimicrobial resistance is the implementation of a treatment policy in accordance with the findings of antibiotic susceptibility tests (5). As a consequence, inadequate treatment is delivered, the requirement for empirical treatment modifications arises and hospitalisation periods are extended. Furthermore, the necessity for empirical treatments increases costs, while morbidity and mortality rates also rise (6).

While urinary tract infections (UTIs) are typically caused by a single bacterium, other common and isolated bacteria may also be involved. These include E. coli, Klebsiella spp., Pseudomonas spp., Proteus spp., Enterobacter spp., enterococci and staphylococci (7).

The inappropriate and/or improper utilisation of antibiotics renders the treatment of UTIs an increasingly challenging endeavour (8). Frequently, antibiotics are initiated empirically, yet this approach may not be as effective as previously thought. The primary challenge in achieving successful empiric UTI therapy is the emergence of antibiotic-resistant bacteria. This resistance can be intrinsic, acquired or clinical. The prevalence of antibiotic-resistant bacteria is likely to be exacerbated by factors such as poor patient compliance and the utilisation of an inappropriate diagnostic approach. In order to select an appropriate antibiotic regimen, it is essential to implement a resistance surveillance programme. The European urology guideline states that antibiotics with resistance above certain rates are not suitable for use in empirical treatment (9,10).

There are limited number of studies on antibiotic susceptibilities of urinary tract infectious agents in the region where our hospital is located. The aim of this study was to determine the distribution of Gram-negative microorganisms, causative bacteria and antibiotic resistance rates of community-acquired (CA) and hospital-acquired (HA) UTIs by retrospectively analysing urine culture results.

MATERIAL AND METHODS

The study was conducted in the Ankara province, which is a metropolitan city located in the capital of Turkey. The hospital is a tertiary-level training and research facility with a bed capacity of 625. It serves a population of approximately 1 million, with an annual average of 250,000 emergency admissions. Urine specimens sent to the microbiology laboratory of Sincan Training and Research Hospital between January 2023 and December 2023 from a range of wards, out patient clinics and intensive care units with evidence of pathogenic bacteria growth were included in the study. The culture results were analyse using the laboratory information system. The inclusion criteria were as follows: the subject must have been at least 18 years of age, the urine cultures must have been performed in the laboratory, and there must have been pathogenic growth in the culture results. Patients with culture requests but no growth, and those with growth but for whom typing could not be performed for example, due to the presence of fungal or other anaerobic bacterial growths (anaerobic culture is not conducted) or polymicrobial growths—were excluded from the study. In instances of recurrent growths, the result of the initial sample was taken into consideration. The antibiotic susceptibility results of the microorganisms were categorised according to gender, age, outpatient and inpatient status. The susceptibility rates of the antibiotics (amikacin, ampicillin, amoxicillin/clavulanicacid, ceftriaxone, ceftazidime, ciprofloxacin, fosfomycin, gentamicin, meropenem, ertapenem, nitrofurantoin, piperacillin/tazobactam, trimethoprim/sulfamethoxazole) (Bioanalyse, Turkey) were recorded.

Developing in the community or occur within the first 48 hours of hospitalization are defined as community-acquired UTIs (11). A quantitative analysis of the urine samples was conducted on both blood agar and eosin methylene blue (EMB) agar media, employing a sterile inoculation loop. The samples were then incubated in an aerobic environment at 37°C for a duration of 24 hours. Samples with bacterial growth of 10^4cfu/ml and above; Identification of lower numbers of microorganisms thought to be causative and antibiotic susceptibility tests were performed, taking into account characteristics such as the number of breeding colonies, the number of species, the presence of leukocytes in the urine sample, and the clinical condition of the patient (12). Isolated bacteria Gram staining, catalase test, oxidase test, carbohydrate and citrate use. Bacterial typing and susceptibility testing were conducted using conventional disc diffusion and an automated VITEK 2 Compact system (bioMerieux, Marcy-l'Étoile, France). The results of the antibiotic susceptibility tests were evaluated in accordance with the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The production of extended-spectrum beta-lactamases (ESBL) was determined through the utilisation of a double disk synergy test and the Vitek2 automated system (13). The study was approved by Ankara Bilkent City Hospital (Decision no. - TABED 1-24-574). The study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments or similar ethical standards.

Statistical Analysis

The data were analysed statistically using IBM SPSS Statistics 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The data were expressed as numbers and percentages in accordance with the Fisher exact test. In the analysis of the results, the Fisher exact test and the chi-square test were employed, and values with a p-value of less than 0.05 were considered to be statistically significant.

RESULTS

In our study, 3,135 urine samples, determined to be the causative agent and sent to our laboratory from various outpatient clinics and services, and for which antibiotic susceptibility tests were performed, were evaluated. Of the total number of samples studied, 77.9% (2,442) were from female patients and 22.1% (693) were from male patients. The median age was found to be 43.1 ± 16.3 (range: 0–95) years. A total of 2,869 (91.5%) of the urinary tract infections were determined to be CA, while 266 (8.5%) were determined to be HA. A single bacterium was isolated in all samples. The distribution of the factors according to clinics and at the bacterial level is shown in Table 1. It has been demonstrated that there is a statistically significant increase in resistance to all antibiotics except meropenem, ertapenem, amikacin and gentamicin in HAIs compared to CAIs. Antibiotic susceptibility rates of Enterobacterales species in CA and HAIs are shown in Table 2. ESBL positivity rates were found to be 14.9% and 23.2% for E.coli and Klebsiella spp, respectively.

DISCUSSION

UTIs are among the top infections that occur both in the hospital and in the community (14). The importance of these infections is increasing due to high recurrence rates and increasing antibiotic resistance in

Table 1. Distribution of bacteria causing urinary system infections according to clinics and distribution of bacteria caused by CA-HA

Clinics	N	Bacteria	CA-UTI (N=2869)	HA-UTI (N=266)
Urology	1040	E.coli	2381(%82.9)	114
Gynecological Diseases	703	Klebsiella spp.	308(%10.7)	96
Pediatry	490	Proteus spp.	99(%3.4)	18
Internal Medicines	478	Pseudomonas spp.	32(%1.1)	25
Urgent	105	Acinetobacter spp.	13(%0.4)	6
ICU	122	Others enterobacterales	36(%1.2)	7
Others	197			

ICU:Intensive care units CA:Community acquired HA:Hospital acquired UTI:Urinary tract infection

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Table 2. Antibiotic susceptibility rates of Enterobacterales species (%)

Antibiotics	CA Infection Susceptibility (%)	HA Infection Susceptibility (%)	Total Susceptibility (%)	p
Ampicillin	%34.1	%8.2	%31,5	<0.001
AMC	%57.1	%11.2	%52.5	<0.001
Ceftazidime	%74.2	%28.5	%69.6	<0.001
Ceftriaxone	%73.8	%25.8	%69	<0.001
Nitrofurantoin (for E.coli)	%98.4	%73.6	%95.9	<0.001
Fosfomycin (for E. coli)	%97.1	%14.3	%88.8	<0.001
Ciprofloxacin	%82	%36	%77.4	<0.001
Amikasin	%99.2	%74.3	%96.7	<0.001
Gentamicin	%94	%64.9	%91.8	<0.001
TMP-SXT	%74.1	%38.3	%70.5	<0.001
TZP	%61.9	%53.9	%61	<0.001
Meropenem	%99.4	%89.8	%98.4	<0.001
Ertapenem	%96.4	%86.4	%95.4	<0.001

AMC:Amoxicillin-clavulanate; TZP:Piperacillin-tazobactam; TMP-SXT:Trimethoprim-sulfamethoxazole

isolated bacteria (15). The gold standard method in the diagnosis of UTI is culture (16). Culture and antibiogram procedures complete at least two days, which leads to the application of empirical treatment. To ensure the appropriate selection of antibiotics for empirical treatment, it is essential that each region and each centre conducts regular monitoring of the agent distribution and antibiotic resistance status (17). The most common cause of CA and HA UTIs in all age groups is Gram-negative bacteria, and the most frequently isolated agent is E.coli (50-90%), followed by Klebsiella pneumoniae. In a study, four-year urinary system infection agents were analyzed and Enterobacterales species were detected in 73.7% of urine cultures with bacterial growth. The most frequently isolated agent was E. coli (55.6%), while the second most frequently isolated agent was identified as K. pneumoniae (14.2%) (18). Similarly, in our study, Enterobacterales species were isolated as the causative agent from the majority of the samples. Of these, 82.9% were E.coli and 10.7% were Klebsiella spp. While the rate of E. coli is decreasing in HAIs, the rate of Klebsiella spp. has increased.

In a study, CAIs were detected E. coli (58.2%), Klebsiella spp. (10.8%) and E. faecalis (6.7%); In HAI, E. coli (47%), E. faecalis (9.4%), P. aeruginosa (6.6%) were detected (19). When the distribution of bacteria causing UTIs was examined in other studies investigating the prevalence of HAIs, the first place was; E. coli and Enterococcus faecium (20,21).

In our study, the HAI agent ranking was made for Gram negatives, and results similar to the literature were found. This shows that although resistance rates may change over the years, there is no significant change in the bacterial species that cause HAIs.

In our study, general antibiotic resistance rates of Enterobacterales strains were found as ampicillin 31.5%, AMC 52.5%, ceftriaxone 69%, TMP-SXT 70.5%, ciprofloxacin 77.4%, aminoglycoside >90% and carbapenem >95%. E. coli, the most common causative agent of UTIs, was 3% for fosfomycin and 2% for nitrofrontain. In a study evaluating E. coli isolates grown in urine culture, these rates were found to be 4% for fosfomycin and 4% for nitrofurantoin, which is compatible with our study (22). In addition, in our study, it was found that antibiotic susceptibilities of Enterobacterales species were lower in HAIs compared to CAIs. The existence of susceptibility limit values for in uncomplicated urinary tract infections for fosfomycin should be taken into consideration when using it in

empirical treatment.

In a study conducted with enteric bacteria grown in urine cultures, resistance to amikacin, gentamicin, and imipenem was not reported. In a study revealing antibiotic resistance rates in ESBL-positive Enterobacterales isolates, the resistance rate was found to be 0.3% for imipenem and 3.5% for amikacin (12,23). In our study, the antibiotics with the lowest resistance rates in Enterobacterales species were ertapenem (5%), meropenem (2%), amikacin (3%) and gentamicin (8%).

The results of our study indicate that the prevalence of antibiotic resistance among the bacteria commonly associated with UTIs is relatively high. A review of the literature reveals that studies have reported results that are consistent with our findings in the context of E. coli bacteria (5,7,12). In conclusion, there is overwhelming evidence that the implementation of antimicrobial stewardship programmes in our country, which have been in place for approximately 20 years, is of significant benefit and should be expanded. However, individual reports have indicated discrepancies in regional antibiotic susceptibility rates. It is recommended that clinicians consider both international guidelines and local antibiotic resistance rates, particularly when making decisions regarding the empirical treatment of urinary tract infections. There sults of our study indicate that ciprofloxacin, co-trimoxazole, and ampicillin are not recommended for the empirical treatment of UTIs. Conversely, there is evidence that indicates that nitrofurantoin and fosfomycin are effective pharmaceutical agents that warrant further consideration.

It appears that, in addition to the elevated resistance rates observed in relation to frequently prescribed drugs in outpatient settings, increased resistance rates have also been documented in relation to antibiotics such as piperacillin-tazobactam, carbapenem and aminoglycoside group antibiotics employed in inpatient settings (24,25). This illustrates the significance of adapting the course of treatment in accordance with the results of the culture test. Quinolone resistance rates in HA infectious agents were found to be significantly higher than CA ones (24-26). This is due to the use of quinolones for many reasons such as pneumonia, gastroenteritis, and urinary tract infections.

The increasing prevalence of extended-spectrum beta-lactamases (ESBLs) represents a further challenge in the management of urinary tractinfections (UTIs). A study conducted in our country revealed that ESBL positivity was 50.5% in HA UTIs caused by E. coli and 38.2% in CA UTIs (27). A review of the literature reveals considerable variation in the rates of resistance observed in different regions of the world. One such study, conducted at multiple centres in China, reported a 37.2% ESBL positivity rate, which is comparable to our own findings (28). The rising prevalence of ESBLs represents a significant concern in the management of UTIs. The discrepancy in ESBL rates has been linked to numerous factors (28). For instance, the inappropriate utilisation of antibiotics and their accumulation in wastewater may be associated with anthropogenic influences, such as agricultural and livestock practices. Prolonged exposure to antibiotics among inpatients may also have contributed to the observed high resistance rates.

In our study, the resistance rate of cephalosporins was found to be approximately 30%. Our country is included in The Central Asian and European Surveillance of Antimicrobial Resistance network (CESAR) and provides regular data. Antimicrobial resistance surveillance in Europe 2023 according to 2021 data Third-generation cephalosporin (cefotaxime, ceftriaxone, ceftazidime) resistance rates about 50% (29). Another studied show that resistance was detected against the antibiotics cefixime (38.2%), ceftriaxone (34.2%), ceftazidime (32.3%), and cefepime (29.6%) (30).

The limitations of our study are as follows: 1. The study is retrospective in nature. 2. The study is single-centred. 3. The study does not include anaerobes in bacterial classes. 4. The study lack ssusceptibility results for fungal infections.

CONCLUSION

It is very important to reveal the change in antibiotic resistance over time, especially when starting empirical treatment. We believe that these results will shed light on empirical treatments.

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The authors declare that they have no conflict of interest to disclose.

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IDENTIFICATION OF PROGNOSTIC MARKERS IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE

Akut Dekompanse Kalp Yetersizliği Olan Hastalarda Prognostik Belirteçlerin Tanımlanması

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ABSTRACT

Objective: This study aims to evaluate the effectiveness of prognostic markers in predicting 90-day mortality in patients admitted to the hospital with a diagnosis of acute decompensated heart failure (ADHF).

Material and Methods: This retrospective study analyzed data from 559 ADHF patients admitted between 01.05.2023 and 01.09.2024. Age, sex, laboratory parameters, and 90-day mortality data were collected, and independent variables affecting mortality were evaluated via logistic regression and receiver operating characteristic (ROC) analysis.

Results: Age, blood urea nitrogen, albumin, and lactate levels were identified as independent predictors of 90-day mortality. The blood urea nitrogen level demonstrated the highest area under the curve (AUC = 0.673) for a cutoff value of 30.9 mg/dL. A significant increase in mortality risk was observed for patients with lactate levels >1.45 mmol/L.

Conclusion: Age, blood urea nitrogen, albumin, and lactate levels are strong prognostic markers for 90-day mortality in patients with ADHF. These findings may contribute to early risk stratification and the development of personalized treatment strategies.

Keywords: *Albumin; BUN; Heart Failure; Lactate; Mortality; Age*

ÖZET

Amaç: Bu çalışmada akut dekompanse kalp yetmezliği (ADKY) tanısıyla hastaneye yatırılan hastalarda 90 günlük mortaliteyi öngörmede prognostik belirteçlerin etkinliği değerlendirildi.

Gereç ve Yöntemler: Bu retrospektif çalışmada 01.05.2023 ile 01.09.2024 tarihleri arasında hastaneye yatırılan 559 ADHF hastasının verileri analiz edildi. Yaş, cinsiyet, laboratuvar parametreleri ve 90 günlük mortalite verileri toplandı ve mortaliteyi etkileyen bağımsız değişkenler lojistik regresyon ve alıcı işletim karakteristiği (ROC) analizi ile değerlendirildi.

Bulgular: Yaş, kan üre azotu, albümin ve laktat düzeyleri 90 günlük mortalitenin bağımsız belirleyicileri olarak tanımlandı. Kan üre nitrojen düzeyi, 30,9 mg/dL kesme değeri için en yüksek eğri altında kalan alanı (AUC = 0,673) göstermiştir. Laktat düzeyi >1,45 mmol/L olan hastalarda mortalite riskinde anlamlı bir artış gözlenmiştir.

Sonuç: Yaş, kan üre azotu, albümin ve laktat düzeyleri ADHF hastalarında 90 günlük mortalite için güçlü prognostik belirteçlerdir. Bu bulgular erken risk tabakalandırmasına ve kişiselleştirilmiş tedavi stratejilerinin geliştirilmesine katkıda bulunabilir.

Anahtar Kelimeler: *Albümin; BUN; Kalp Yetersizliği; Laktat; Mortalite; Yaş*

INTRODUCTION

Heart failure (HF) is a major public health issue worldwide associated with high mortality and morbidity rates. In the United States, it has been reported that 10–51% of patients hospitalized with HF require intensive care, and 10.6% of these patients die (1). Acute decompensated heart failure (ADHF) is characterized by the sudden onset or progressive worsening of HF symptoms and requires urgent medical intervention (2). ADHF accounts for approximately 70% of acute heart failure syndromes and is among the leading causes of hospitalization, healthcare costs, morbidity, and mortality. According to the literature, the annual mortality rate in patients with ADHF ranges between 20% and 30% (3,4).

Identifying appropriate treatment strategies for ADHF patients is crucial for improving care and reducing morbidity, mortality, and healthcare costs (5). Various biomarkers and risk stratification tools have been investigated to predict the prognosis of HF patients (6–9). Predicting mortality at the time of admission allows for the identification of high-risk patients, facilitates personalized treatment options, reduces costs, and improves patient prognosis (10). Therefore, this study aims to identify risk factors for 90-day mortality in hospitalized ADHF patients, enabling the early recognition of high-risk individuals and a more accurate prognosis estimation.

MATERIALS AND METHODS

This study was conducted retrospectively in a tertiary hospital and included patients aged 18 years and older admitted to the emergency department (ED) with a diagnosis of ADHF between 01.05.2023 and 01.09.2024. Approval was obtained from the local clinical research and ethics committee (Decision No: 2025/10). All procedures in this study were conducted in accordance with the ethical principles and guidelines outlined in the Declaration of Helsinki.

Patients presenting to Ordu University Research Hospital between 01.05.2023 and 01.09.2024 with a known diagnosis of HF and ADHF symptoms (dyspnea, orthopnea, or body swelling) who were evaluated by a cardiology specialist and subsequently admitted with an ADHF diagnosis were included in the study.

Patients under 18 years of age, pregnant women, those newly diagnosed with HF at the time of ED admission, those with a history of malignancy, those receiving renal replacement therapy, those with incomplete data in the data recording form, and those diagnosed with acute coronary syndrome, myocarditis, or pulmonary embolism in addition to ADHF were excluded from the study.

Demographic data, such as age and sex, as well as laboratory parameters, including white blood cell count (WBC), hemoglobin, red blood cell count (RBC), platelet count, neutrophil count, eosinophil count, glucose, blood urea nitrogen (BUN), creatinine, glomerular filtration rate (GFR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), sodium, potassium, chloride, albumin, and lactate, along with 90-day mortality status, were recorded in the data collection form. The data were obtained from the hospital's automated system. Inflammatory indices were calculated from the collected data:

Neutrophil-to-lymphocyte ratio (NLR) = neutrophil count/lymphocyte count

Platelet-to-lymphocyte ratio (PLR) = Platelet count/ lymphocyte count

Systemic immune-inflammation index (SII) = neutrophil count × platelet count/lymphocyte count

Statistical Analysis

Statistical analyses were performed via the IBM® SPSS® Statistics v.26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.) software package. Descriptive statistics are presented as the means ± standard deviations, medians (25th and 75th percentiles), frequencies, and percentages (%). The normality of the variable distributions was assessed via histograms, the Kolmogorov–Smirnov test, and skewness–kurtosis parameters. Quantitative variables were compared via the independent samples t test or Mann–Whitney U test, depending on the assumption of normality, whereas categorical variables were compared via the chi–square test.

To investigate the independent effects of variables on 90-day mortality, univariate and multivariate logistic regression analyses were performed, and odds ratios (ORs) were calculated. Variables that were found to be statistically significant ($p < 0.05$) in predicting 90-day

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mortality in the univariate logistic regression analysis were included in the multivariate logistic regression analysis to assess their independent effects. The diagnostic performance of variables identified as independent predictors of 90-day mortality via multivariate logistic regression analysis was evaluated via the receiver operating characteristic (ROC) curve and area under the curve (AUC) with a 95% confidence interval (CI). The cutoff values were determined via the Youden index. A p value <0.05 was considered to indicate statistical significance.

RESULTS

The mean age of the 559 patients included in the study was determined, with 45.08% (n=252) being male. 90-day mortality occurred in 40.43% (n=226) of the patients. No significant relationship was found between 90-day mortality and sex, while the mean age of deceased patients was significantly greater (p<0.001).

The mean WBC and neutrophil counts were greater in deceased patients than in survivors, but this difference was not statistically significant (p=0.299 and p=0.095). A statistically significant relationship was found between 90-day mortality and the NLR, RBC count, and platelet count (p=0.015, p=0.001, p=0.028, respectively). The median BUN, creatinine and lactate levels were significantly greater in the deceased patient group than in the survivor group (p<0.001), whereas the median lymphocyte, GFR, chloride, and albumin levels were significantly lower (p values: 0.014, <0.001, 0.018, and <0.001, respectively). The relationships among demographic characteristics, laboratory findings, and 90-day mortality are presented in Table 1.

To evaluate the independent effects of variables on 90-day mortality, univariate and multivariate logistic regression analyses were performed. Accordingly, age (OR: 1.036, p<0.001), BUN (OR: 1.023, p<0.001), albumin (OR: 0.573, p=0.001), and lactate (OR: 1.444, p<0.001) were identified as independent predictors of 90-day mortality in multivariate analysis. Details regarding the logistic regression analysis are provided in Table 2.

ROC analysis was performed on the independent predictors of 90-day mortality identified in the logistic regression analysis. Accordingly, BUN demonstrated the best predictive performance (AUC: 0.673, p<0.001), followed by age (AUC: 0.623, p<0.001). The highest sensitivity was observed with an age of 75.7%, whereas the highest specificity was observed with a BUN level of 71.8%. The ROC analysis graph is shown in Figure 1, and the performance characteristics of the variables in predicting 90-day mortality are provided in Table 3.

DISCUSSION

In the present study, age, BUN, albumin, and lactate levels measured at the time of ED admission were identified as independent predictors of 90-day mortality in ADHF patients. The BUN level had the highest AUC (0.673) for the prediction of 90-day mortality, with a cutoff value of 30.9 mg/dL. Age demonstrated the highest sensitivity (75.7%) at a cutoff value of 71.5 years.

A significant proportion of patients admitted with a diagnosis of ADHF are aged 75 years or older (11). Studies have shown that advanced age is associated with increased comorbid conditions, physical and cognitive impairment, and decreased self-care capacity. Owing to these risk factors, ADHF is associated with increased mortality rates in elderly patients (12,13). Lombardi et al. demonstrated that advanced age is an independent predictor of both in-hospital and long-term mortality in patients with acute HF (14). Similarly, Jacob et al. identified advanced age (≥75 years) as an independent predictor of short-term mortality (15). Consistent with these findings, the present study also revealed that advanced age independently predicts mortality in ADHF patients. In the ROC analysis, an age cutoff of >70.5 years was the second strongest predictor of 90-day mortality after BUN.

HF is frequently associated with impaired renal function. Studies have reported that impaired renal function can predict mortality in HF patients (6). BUN is a metabolic byproduct synthesized in the liver and serves as an indicator of the balance between urea production and renal excretion (16). Reduced renal perfusion leads to elevated BUN levels. In HF, decreased cardiac output results in renal hypoperfusion, activating neurohormonal mechanisms, including the renal sympathetic nervous system and the renin–angiotensin–aldosterone system, leading to increased

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Table 1. Relationships with 90-day mortality and patient demographic characteristics and clinical and laboratory findings.

	90-Day Mortality		
	Alive (n=333)	Deceased (n=226)	p values
Sex; n (%)			0.501
Male	154 (61.1%)	98 (38.9%)	
Female	179 (58.3%)	128 (41.7%)	
Age (year)	72(63-82)	78(72-85)	<0.001
WBC count (cells/mm^3)	7.93(6.3-10.12)	7.6(6.05-10.65)	0.676
RBC count	4.20 (3.78-4.74)	4.01(3.55-4.50)	0.015
Hemoglobin (mg/dL)	11.80 (10.20-13.40)	11.40(9.90-13.00)	0.177
Neutrophil count (cells/mm^3)	5.5(3.95-7.4)	5.47(4.1-7.85)	0.401
Lymphocyte count (cells/µl)	1.46(0.95-2.09)	1.3(0.86-1.8)	0.014
Platelet count (cells/mm^3)	235(184-309)	212(165-282)	0.003
NLR	3.67(2.28-6.31)	4.28(2.74-7.83)	0.004
PLR	153.89(107.45-258.22)	171.75(111.67-265.15)	0.376
SII	871.33(514.1-1550.74)	899.75(562.5-1789.91)	0.230
Glucose (mg/dl)	127(104-185)	135(107-171.5)	0.888
BUN (mg/dL)	22.4(16.4-32.6)	32.6(22-51.5)	<0.001
Creatinine (IU/L)	1.01(0.81-1.37)	1.28(0.9-1.7)	<0.001
GFR	64(46.94-87)	50(38-71.98)	<0.001
Sodium	139(136-141)	138(135-141)	0.141
Potassium	4.4(4.04-4.82)	4.41(4-4.9)	0.646
Chloride	101(98.9-104)	101(97-103)	0.018
ALT	18(12-26)	17(11-28)	0.310
AST	21(16-30)	22(14-31.5)	0.712
Albumin	3.7(3.3-4.1)	3.4(3.1-3.8)	<0.001
Lactate	1.6(1.2-2.1)	1.8(1.3-2.3)	<0.001

The values are presented as the means ± SDs, medians (25th and 75th quartiles), or n (%). ALT: alanine aminotransferase, AST: aspartate aminotransferase, BUN: blood urea nitrogen, GFR: glomerular filtration rate, NLR: neutrophil–lymphocyte ratio, PLR: platelet–lymphocyte ratio, SII:, RBC: red blood cell, WBC: white blood cell.

urea reabsorption and elevated BUN levels (17). Jujo et al. reported that high BUN levels were associated with increased cardiovascular mortality rates in acute HF patients. Furthermore, in their multivariate logistic regression analysis, high BUN levels were identified as independent predictors of mortality (18). Similarly, Cauthen et al. reported that elevated BUN levels were associated with increased long-term mortality in HF patients (17). Additionally, an analysis of Acute Decompensated Heart Failure National Registry (ADHERE) data identified BUN >37 mg/dL as one of the most important predictors of mortality (19). Consistent with the literature, the present study revealed that high BUN levels were independent predictors of 90-day mortality in ADHF patients, with the highest AUC (0.673) in the ROC analysis. Moreover, BUN is a stronger predictor of adverse outcomes than both the GFR and creatinine level are (16–18).

Tissue hypoperfusion due to decreased cardiac output in ADHF leads to impaired tissue oxygenation and subsequently elevated lactate levels. Additionally, activation of the neurohormonal system and increased oxygen demand further contribute to lactate elevation (3,20). Several studies have demonstrated an association between increased lactate levels and poor outcomes in patients with acute HF (21–23). Kawase et al. identified lactate as an independent predictor of short-term mortality in ADHF patients admitted to

Table 2. Logistic regression analysis for predicting 90-day mortality.

Parameters	Model 1		Model 2	
	OR (%95 CI)	p value	OR (%95 CI)	p value
Age	1.038(1.022-1.054)	<0.001	1.036(1.018-1.054)	<0.001
RBC	0.795(0.636-0.994)	0.044	1.038(0.8-1.346)	0.782
Lymhocyte	0.872(0.743-1.024)	0.094	*	*
Platelet	0.997(0.995-0.999)	0.002	0.998(0.996-1)	0.091
NLR	1.03(1.004-1.056)	0.026	1.017(0.995-1.039)	0.132
BUN	1.029(1.019-1.039)	<0.001	1.023(1.011-1.036)	<0.001
Creatinine	0.997(0.954-1.042)	0.883	*	*
GFR	0.984(0.978-0.991)	<0.001	1.001(0.992-1.011)	0.782
Chloride	0.957(0.926-0.99)	0.011	0.997(0.947-1.049)	0.910
Albumin	0.494(0.365-0.669)	<0.001	0.573(0.409-0.802)	0.001
Lactate	1.36(1.169-1.582)	<0.001	1.444(1.217-1.713)	<0.001

*Not applicable because these variables were not statistically significant in the univariate logistic regression analysis. Model 1: unadjusted model Model 2: Each marker was adjusted for other variables. BUN: blood urea nitrogen, CI: confidence interval, GFR: glomerular filtration rate, NLR: neutrophil–lymphocyte ratio, OR: odds ratio, PLR: platelet–lymphocyte ratio, RBC: red blood cell.

Table 3. Cutoff Points and Performance Characteristics of Variables in Predicting 90-Day Mortality

Parameters	AUC (95% CI)	Cutoff	Sensitivity	Specificity	+LR	-LR	p values
Age	0.623(0.576-0.669)	71.5	0.757	0.486	1.47	0.50	<0.001
BUN	0.673(0.628-0.719)	30.9	0.549	0.718	1.95	0.63	<0.001
Albumin	0.609(0.562-0.656)	3.45	0.509	0.667	1.53	0.74	<0.001
Lactate	0.587(0.539-0.635)	1.45	0.735	0.426	1.28	0.62	<0.001

AUC: Areas under the curve, BUN: Blood urea nitrogen, CI: Confidence interval, GFR: Glomeruler filtration rate, LR: Likehood ratio, NLR: Neutrophil-lymphocyt ratio, PLR: Platelet to lymphocyte ratio, RBC: Red blood cells.

the intensive care unit. They reported an AUC of 0.071 for a lactate cutoff of >3.2 mmol/L (24). Similarly, Zymlinski et al. reported that elevated blood lactate levels measured at hospital admission were predictive of all-cause mortality, even in the absence of peripheral hypoperfusion in acute HF patients (22). In the present study, a serum lactate cutoff of >1.45 mmol/L was used to predict 90-day mortality. Furthermore, consistent with the literature, lactate was an independent predictor of mortality according to the multivariate logistic regression analysis. Compared with that in the study by Kawase et al., the lactate cutoff value was lower (>3.2 vs. >1.45 mmol/L). This difference may be attributed to the fact that the study by Kawase et al. was conducted on a more severely ill patient population admitted to the intensive care unit, whereas the present study included hospitalized ADHF patients (24).

Hypoalbuminemia is commonly observed in HF patients. The underlying causes of hypoalbuminemia in HF patients include malnutrition, hemodilution, increased metabolic activity, proteinuria, and inflammatory mechanisms (1,25). Hypoalbuminemia has been associated with poor prognosis in ADHF patients (26). Uthamalingam et al. investigated the relationship between albumin levels and mortality in ADHF patients and reported that albumin levels <3.4 g/dL were associated with increased 1-year mortality (25). In another study, Karki et al. reported that hypoalbuminemia was associated with prolonged hospital stays and increased mortality in patients hospitalized for HF (27). A study conducted on patients admitted with acute HF revealed that those with albumin levels ≤3.4 g/dL had higher in-hospital mortality rates, and logistic regression analysis confirmed that hypoalbuminemia was an independent predictor of in-hospital mortality in acute HF patients (28). In the present study, the serum ALB

concentration was identified as an independent predictor of 90-day mortality in ADHF patients. According to the ROC analysis, the serum ALB concentration demonstrated good predictive performance for mortality, with an AUC of 0.609 at a cutoff value of <3.45 g/dL.

This study has several limitations. First, owing to its retrospective design, data collection may be subject to limitations in terms of accuracy and completeness. Second, as the study was conducted at a single center, the generalizability of the findings may be restricted. Therefore, multicenter studies with larger and more diverse patient populations are needed to validate these results and enhance their applicability to broader clinical settings. Finally, the study was conducted within a specific time frame and included a particular patient population; further studies with larger datasets are necessary.

CONCLUSION

This study highlights the prognostic significance of age and blood urea nitrogen, albumin, and lactate levels in predicting 90-day mortality in patients with acute decompensated heart failure and highlights the clinical relevance of these parameters. The findings contribute significantly to optimizing treatment strategies, improving patient outcomes, and reducing healthcare costs through the early identification of high-risk patients. However, to increase the clinical applicability of these parameters and validate them in broader patient populations, multicenter and prospective studies are needed.

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The authors declare that they have no conflict of interest to disclose.

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AI MODELS FOR ACCURATE BACTERIAL PNEUMONIA DIAGNOSIS IN CHEST X-RAY IMAGES

Akciğer Röntgeni Görüntülerinde Doğru Bakteriyel Pnömoni Teşhisi için Yapay Zeka Modelleri

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ABSTRACT

Objective: This study aims to contribute to this gap by evaluating the performance of various deep learning models, including a proposed Convolutional Neural Networks (CNN) model, ResNet50, and EfficientNetB0, for the detection of bacterial pneumonia from chest X-rays.

Material and Methods: This study investigates the use of artificial intelligence (AI) in detecting pneumonia from chest X-ray (CXR) images using deep learning techniques, specifically CNN, ResNet50, and EfficientNetB0.

Results: A created novel dataset consisting of 1228 images of bacterial pneumonia and 1228 images of non-pneumonia cases, is used for model training and evaluation. X-ray images obtained from Yozgat Bozok Medical Faculty are classified by a specialist physician and supplemented with additional images from a publicly available dataset to eliminate class imbalance. Three deep learning models are implemented and evaluated in terms of accuracy, precision, recall, and F1-score. All models achieved an accuracy of 97%, with high performance in detecting both pneumonia and non-pneumonia cases. The Proposed CNN model showed precision and recall values of 1.00 and 0.94 for non-pneumonia and 0.95 and 1.00 for pneumonia detection, respectively. EfficientNetB0 and ResNet50 demonstrated similar robust performance.

Conclusion: The results indicate that AI-based models can offer reliable and accurate pneumonia detection, supporting clinical decision-making processes and acting as a valuable second opinion for physicians. These findings highlight the potential of AI in enhancing diagnostic accuracy and efficiency, particularly in resource-limited healthcare settings. Further validation with larger datasets and clinical trials is necessary to confirm the generalizability of these models for widespread clinical use.

Keywords: *Deep Learning; Neural Networks; Pneumonia; Classification; Mass Chest X-Ray*

ÖZET

Amaç: Bu çalışma, akciğer röntgeninden bakteriyel pnömoninin saptanması için önerilen Evrişimsel Sinir Ağları (CNN) modeli ResNet50 ve EfficientNetB0 dahil olmak üzere çeşitli derin öğrenme modellerinin performansını değerlendirerek bu boşluğa katkıda bulunmayı amaçlamaktadır.

Gereç ve Yöntemler: Bu çalışma, özellikle CNN, ResNet50 ve EfficientNetB0 olmak üzere derin öğrenme tekniklerini kullanarak akciğer röntgeni görüntülerinden pnömoniyi tespit etmede yapay zekanın kullanımını araştırıyor.

Bulgular: Model eğitimi ve değerlendirmesi için 1228 bakteriyel pnömoni görüntüsü ve 1228 pnömoni olmayan vaka görüntüsünden oluşan oluşturulmuş yeni bir veri seti kullanıldı. Yozgat Bozok Tıp Fakültesi'nden alınan röntgen görüntüleri, uzman hekim tarafından sınıflandırılıp, sınıf dengesizliğini ortadan kaldırmak amacıyla kamuya açık bir veri setinden alınan ek görüntülerle desteklendi. Üç derin öğrenme modeli uygulandı ve doğruluk, kesinlik, geri çağırma ve F1 puanı açısından değerlendirildi. Tüm modeller hem pnömoni hem de pnömoni dışı vakaların tespitinde yüksek performansla %97'lik bir doğruluğa ulaştı. Önerilen CNN modeli, pnömoni dışı için sırasıyla 1,00 ve 0,94 ve pnömoni tespiti için 0,95 ve 1,00 hassasiyet ve geri çağırma değerleri gösterdi. EfficientNetB0 ve ResNet50 benzer güçlü performans sergiledi.

Sonuç: Sonuçlar, yapay zeka tabanlı modellerin güvenilir ve doğru pnömoni tespiti sunabileceğini, klinik karar verme süreçlerini destekleyebileceğini ve hekimler için değerli bir ikinci görüş olarak hareket edebileceğini gösteriyor. Bu bulgular, yapay zekanın özellikle kaynakların sınırlı olduğu sağlık hizmetlerinde teşhis doğruluğunu ve verimliliğini artırma potansiyelini vurgulamaktadır. Bu modellerin yaygın klinik kullanıma yönelik genelleştirilebilirliğini doğrulamak için daha büyük veri kümeleri ve klinik çalışmalarla daha fazla doğrulama yapılması gerekmektedir.

Anahtar Kelimeler: *Derin Öğrenme; Yapay Sinir Ağları; Pnömoni; Sınıflandırma; Akciğer Grafisi*

INTRODUCTION

Pneumonia is a fatal disease caused by the inflammation of the lung parenchyma (1). Bacteria, viruses, and less commonly fungi are the pathogenic microorganisms that cause lung inflammation. Pneumonia can cause fatal disease through a dysregulated inflammatory response and activated hypercoagulation (2). These pathological responses to infections have the potential to lead to multiple organ dysfunction syndrome (MODS) (3). As a result of these pathophysiological processes, pneumonia is a potentially fatal disease.

Globally, causes of death are categorized into communicable and non-communicable diseases (4). According to the World Health Organization (WHO), lower respiratory tract infections were the fifth leading cause of death in 2021. The same report also listed COVID-19 as the second leading cause of death. Fatal COVID-19 infections often lead to death due to severe sepsis, which is caused by lower respiratory tract infections (5). These findings underscore the importance of addressing lower respiratory tract infections as a leading cause of death, especially given that COVID-19, which is also a lower respiratory tract infection, was a major contributor to mortality during the pandemic. However, with the pandemic's decline, pneumonia and other lower respiratory tract infections remain critical causes of death worldwide.

Additionally, death in low-income countries presents crucial findings. Lower tract respiratory infections were reported to be 1st death cause (4). One more aspect to address is that lower tract respiratory infections are one of the communicable diseases. Preventing the transmission could have a key role in managing infections to reduce mortality.

The diagnosis of infection is the first and essential step in preventing transmission. Chest radiography plays a key role in diagnosing pneumonia, with the primary options being chest X-ray (CXR) and computed tomography (CT) scans (6). Although CT scans provide more detailed chest images, chest X-rays remain critical due to their accessibility and affordability. CXR is a widely used and common imaging modality for identifying pneumonia. It is important to note that lower respiratory tract infections are the leading cause of death in low-income countries, where access to CT scanning facilities is often limited. In these regions, CXR continues to be a crucial tool for early detection and diagnosis of pneumonia.

While many studies focus on the use of artificial intelligence (AI) for detecting COVID-19 pneumonia, fewer studies have explored AI-based approaches for detecting bacterial pneumonia (6–10). Khan et al propose a framework utilizing deep explainable artificial intelligence (XAI) techniques for the classification of COVID-19 from chest X-ray (CXR) images (7). The authors emphasize the importance of explainability in AI models for medical applications, aiming to make the decision-making process more transparent to clinicians. Kufel et al. submitted an overview of various AI techniques, particularly deep learning, that have been used to detect COVID-19-related changes in chest X-rays (8).

The authors discuss the performance, limitations, and potential of AI in the clinical setting, while also identifying the challenges such as data quality, model generalization, and the need for large, diverse datasets to train robust AI systems. Gupta et al. focused on using neural architecture search (NAS) to optimize deep learning models for pneumonia diagnosis from chest X-ray images (9). NAS is a technique for automating the design of neural network architectures, allowing for the discovery of more efficient and effective models for medical image classification.

This study aims to contribute to this gap by evaluating the performance of various deep learning models, including a proposed Convolutional Neural Network (CNN) model, ResNet50, and EfficientNetB0, for the detection of bacterial pneumonia from chest X-rays. We investigate the potential of AI to support clinicians in diagnosing pneumonia and enhancing the accuracy and efficiency of the diagnostic process. The findings from this study could provide valuable insights into improving AI-based diagnostic systems in clinical settings.

MATERIAL AND METHOD

This study was approved by the local ethics committee (Date:18.09.2024, approval number: 2024-GOKAEK-248_18.09.2024_147). This single-center retrospective study was conducted in a tertiary referral center. The chest X-ray (CXR) images of patients visiting internal medicine and pulmonology

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outpatient clinics were collected from the hospital's database. The CXR images were retrieved from the hospital system, ensuring that only anonymized data were used to maintain patient confidentiality.

The identification of pneumonia was performed by a physician, who provided manual annotations of the images based on clinical findings and radiological evaluation. In addition, AI-based software was used to assist in the detection of pneumonia. For the artificial intelligence technique, a deep learning approach was employed, using CNNs for image classification. The proposed CNN model was trained on the CXR dataset, with both pneumonia and non-pneumonia cases. The accuracy of the AI-based detection system in identifying pneumonia was evaluated by comparing the model's predictions against the physician's annotations. This approach aims to assess the potential of AI in supporting clinical decision-making processes, providing a second layer of diagnostic verification to ensure high detection accuracy in pneumonia diagnosis.

The original dataset consists of 106 images of Bacterial Pneumonia and 1,228 images of No_Pneumonia. To address class imbalance, additional Bacterial Pneumonia images from a publicly available dataset are incorporated into the original dataset (11). A specialist clinician carefully reviewed these images before inclusion to ensure data accuracy and quality.

Deep learning is a sophisticated subset of machine learning that leverages multiple layers of nonlinear computing to extract and transform intricate features from data. Unlike traditional machine learning models that rely on handcrafted feature engineering, deep learning algorithms autonomously learn hierarchical representations of data through an iterative process. Each successive layer in a deep learning architecture takes the output of the previous layer as input, allowing the model to progressively capture higher-level abstractions and gain a deeper understanding of complex patterns and relationships within the data (12).

Convolutional Neural Networks represent the most commonly used architecture in deep learning, particularly in the domain of image and video processing. CNNs consist of two main components and have gained widespread adoption due to their remarkable capabilities. In a CNN, the neurons in the initial layer are responsible for extracting features from the input data, while the subsequent layers combine these extracted features to form higher-level representations (13). The success of CNNs can be attributed to their hierarchical feature extraction capability, enabling them to effectively capture intricate patterns and structures in the data at various levels of abstraction.

EfficientNetB0 is a convolutional neural network model that balances accuracy and efficiency by employing a compound scaling approach, where depth, width, and resolution are systematically scaled. This architecture is part of the EfficientNet family, known for achieving state-of-the-art performance on various image classification benchmarks while maintaining computational efficiency. The foundation of EfficientNetB0 lies in its use of Mobile Inverted Bottleneck Convolution (MBConv) blocks and the Swish activation function, optimizing both speed and accuracy (14).

ResNet50, on the other hand, is a 50-layer deep convolutional neural network architecture that introduced the concept of residual learning. The residual blocks in ResNet50 address the problem of vanishing gradients, enabling the training of deeper networks by bypassing the direct mapping of inputs to outputs through shortcut connections. ResNet50 has been widely adopted in image processing tasks for its robustness and simplicity (15). Both architectures are frequently used in medical image analysis due to their pre-trained weights on large-scale datasets such as ImageNet, allowing for transfer learning to enhance performance in domain-specific tasks.

In this study, we propose a convolutional neural network architecture designed to effectively classify images into two categories. As outlined in Table 1, the model consists of several key layers that work together to extract hierarchical features from input images. The input image is first passed through a series of convolutional layers, each followed by batch normalization and spatial dropout, aimed at enhancing training stability and reducing overfitting.

Cross-validation techniques are commonly used in machine learning to evaluate and validate model performance (16). One frequently used method is 5-fold cross-validation, where the dataset is split into

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Table 1. Architecture details of the proposed Convolutional Neural Networks (CNN)

Layer No	Layer Type	Output Shape	Number of Parameters
1	Input	(224, 224, 3)	0
2	Conv2D	(224, 224, 32)	896
3	BatchNormalization	(224, 224, 32)	128
4	SpatialDropout2D	(224, 224, 32)	0
5	MaxPooling2D	(112, 112, 32)	0
6	Conv2D	(112, 112, 64)	18,496
7	BatchNormalization	(112, 112, 64)	256
8	SpatialDropout2D	(112, 112, 64)	0
9	MaxPooling2D	(56, 56, 64)	0
10	Conv2D	(56, 56, 128)	73,856
11	BatchNormalization	(56, 56, 128)	512
12	MaxPooling2D	(28, 28, 128)	0
13	Conv2D	(28, 28, 256)	295,168
14	BatchNormalization	(28, 28, 256)	1,024
15	GlobalAveragePooling2D	(256)	0
16	Dense	(512)	131,584
17	Dropout	(512)	0
18	Dense (Output Layer)	(2)	1,026
• Trainable Parameters: 522,946 • Non-trainable Parameters: 0 • Total: 522,946			

five approximately equal-sized subsets or folds. In this approach, the model is trained using four of the folds and validated on the remaining fold. This process is repeated five times, each time with a different fold serving as the validation set. The performance metrics from each fold are then averaged to estimate the model's overall performance. 5-fold cross-validation helps reduce the risk of overfitting and provides a more reliable assessment of the model's ability to generalize to unseen data.

Evaluation metrics are crucial for assessing the performance of machine learning algorithms, especially in deep learning models. These metrics help determine how well a model generalizes to new, unseen data. Various evaluation criteria are available, and using multiple metrics provides a more comprehensive view of model performance, as a model might excel in one metric but underperform in another. Classification estimates rely on four key values: True Positive (TP) when a model correctly predicts the positive class, False Positive (FP) for incorrect positive predictions, True Negative (TN) for correct negative predictions, and False Negative (FN) for incorrect negative predictions (17,18).

$$\text{Accuracy}=(TN+TP)/(TN+TP+FN+FP)$$

$$\text{Recall}=TP/(TP+FN)$$

$$\text{Precision}=TP/(TP+FP)$$

$$\text{F1-Score} =2x\ (\text{Precision} \times \text{Recall})/(\text{Precision}+\text{Recall})$$

RESULTS

This study analyzes three different models for pneumonia detection in chest X-ray images: a custom CNN, ResNet50, and EfficientNetB0. The models are trained and evaluated using a 5-fold cross-validation approach to ensure robust performance assessment. The dataset used includes images categorized into Bacterial Pneumonia and No Pneumonia, with the Bacterial Pneumonia class verified by expert clinicians before being added to the dataset. Various performance metrics are used to evaluate and compare the models, including accuracy, precision, recall, and F1 score. This section details the steps taken

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to prepare the dataset, train the models, and assess their effectiveness in classifying pneumonia from chest X-ray images. The experiments were conducted on a system with the following specifications: 32 GB of memory, Intel(R) Core i7 CPUs 12700F operating at 2.10 GHz, and an NVIDIA GeForce RTX 3090 TI graphics card. The system runs Windows 10 Pro, and the machine learning tasks are carried out using Python 3 in Jupyter Notebook. This configuration provided the necessary computational power for training and evaluating the deep learning models used in this study.

The classification reports and confusion matrix given in Table 2 for the 5-fold cross-validation of the three models—Proposed CNN, EfficientNetB0, and ResNet50—demonstrate the effectiveness of each model in detecting pneumonia from chest X-ray images. The accuracy for all three models is 0.97, indicating high performance across all folds.

• Proposed CNN: The model achieves an accuracy of 97%, with precision, recall, and F1-score of 0.97 for both classes (0: No Pneumonia, 1: Bacterial Pneumonia). The high recall and precision for class 1 (Bacterial Pneumonia) highlight its effectiveness in identifying pneumonia cases.

• EfficientNetB0: The performance is very similar to the Proposed CNN model, with an accuracy of 97%. Precision and recall are slightly lower for the "No Pneumonia" class (0) compared to the Proposed CNN model, but the overall F1-score remains consistent at 0.97 for both classes, indicating reliable classification performance.

• ResNet50: This model also shows an accuracy of 97%, with the precision, recall, and F1-scores all nearing 0.97. Precision and recall for both classes are slightly lower than the other two models but still exhibit a strong balance in performance across both classes.

The graph given in Figure 2 (a) illustrates the accuracy trends for each model over multiple epochs. All models show a steady increase in accuracy, stabilizing around 97% at the end of training, confirming the models' strong ability to generalize well to the test data.

Figure 2 (b) represents the models' loss over time during training. The loss values for all models decrease consistently, with EfficientNetB0 and ResNet50 showing slightly lower loss values toward the end, indicating efficient training. The CNN model demonstrated a strong performance during the training process, with a rapid decline in validation loss, particularly in the initial epochs. While the difference between validation loss and training loss is slightly more pronounced compared to the other models, this indicates that the model is effectively utilizing its learning capacity and adapting to the data across different epochs. The fluctuations observed in the validation loss suggest that the model is attempting to generalize over different features of the data during training. Additionally, the rapid decrease in validation loss at the beginning highlights the model's ability to quickly learn and adapt. Given

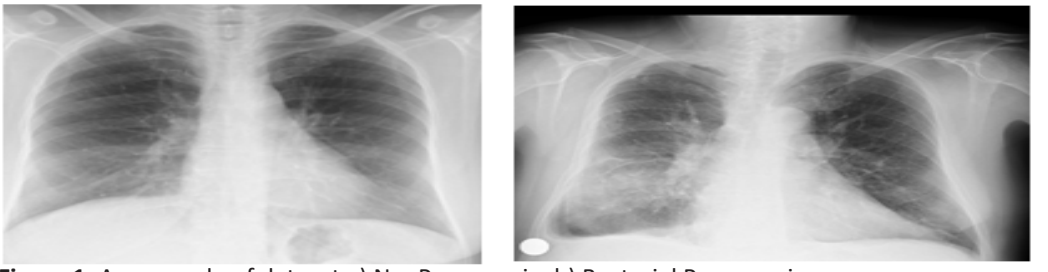

Figure 1. An example of dataset a) No_Pneumonia, b) Bacterial Pneumonia

Table 2. Classification reports and confusion matrix

Model	Accuracy	Precision (0)	Recall (0)	F1-score (0)	Precision (1)	Recall (1)	F1-score (1)	TN	FP	FN	TP
Proposed CNN	0.97	1.00	0.94	0.97	0.95	1.00	0.97	231	14	1	245
EfficientNetB0	0.97	1.00	0.94	0.97	0.94	1.00	0.97	237	8	5	241
ResNet50	0.97	0.98	0.97	0.97	0.97	0.98	0.97	230	15	1	245

CNN: convolutional neural networks

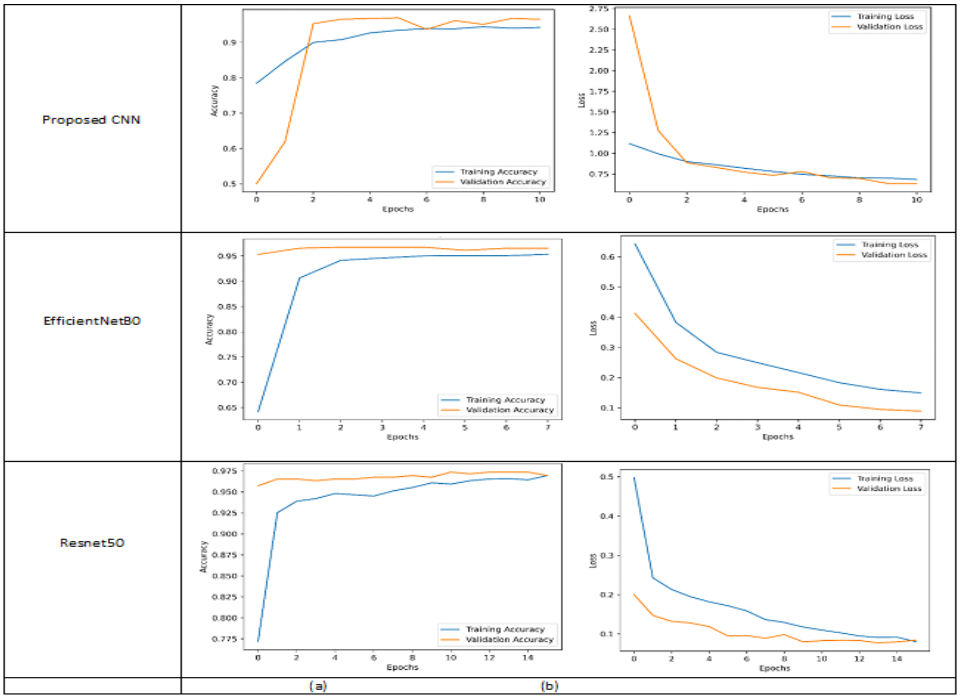

Figure 2. Accuracy and Loss graph of models

its simpler architecture compared to ResNet50 and EfficientNetB0, the CNN model stands out as a practical solution for scenarios where computational efficiency is critical. From an accuracy perspective, the CNN model also performs well, with validation accuracy quickly reaching around 95% and maintaining a trend similar to training accuracy. However, slight fluctuations in validation accuracy in later epochs indicate a moderate level of instability compared to the other models. On the other hand, ResNet50 and EfficientNetB0 achieve validation accuracies above 95%, offering both higher precision and stability. ResNet50, in particular, excels in both accuracy and loss reduction, while EfficientNetB0 closely follows with comparable performance. The CNN model delivers acceptable accuracy and loss performance with lower computational requirements, making it a viable option for applications where efficiency is a priority. However, for studies demanding the highest accuracy and stability, ResNet50 and EfficientNetB0 emerge as more robust choices.

The ROC curves given in Figure 3 demonstrate the trade-off between true positive rate and false positive rate. All models show a high area under the curve (AUC), suggesting excellent discriminative ability between the two classes.ResNet50 (AUC = 1.00): ResNet50 achieves a perfect AUC score of 1.00, indicating excellent classification capability with no compromise between sensitivity and specificity. This highlights ResNet50 as the most reliable model for this task. EfficientNetB0 (AUC = 0.98): With an AUC of 0.98, EfficientNetB0 also demonstrates high classification performance. While slightly below ResNet50, it remains an excellent choice with a strong balance of true positive and false positive rates. CNN (AUC = 0.97): The CNN model achieves an AUC of 0.97, showcasing robust performance. Though slightly behind the other two models, its results are still highly competitive, particularly given its simpler architecture. ResNet50 stands out with perfect AUC, making it the top-performing model. EfficientNetB0 and CNN also provide strong and reliable results, with CNN being a computationally lighter alternative for less resource-intensive scenarios.

The Grad-CAM visualizations shown in Figure 4 effectively illustrate the regions within the X-ray images that the model focuses on for its predictions. In the first image (a), the heatmap highlights concentrated activation around the lung regions, particularly in areas that may indicate abnormalities, suggesting

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the model is successfully identifying critical features. Similarly, the second image (b) shows widespread activation across the lungs, with notable focus near the ribcage and diaphragm, reflecting the model's effort to generalize its attention across the image. In the third image (Fold 2), the heatmap reveals precise activations in specific regions of the lungs, emphasizing potential abnormal areas and demonstrating the model's ability to narrow its focus to relevant features. Overall, these visualizations confirm that the model is attending to clinically significant regions, enhancing interpretability and reinforcing its reliability in decision-making.

DISCUSSION

This study aimed to evaluate the effectiveness of artificial intelligence (AI)-based systems, specifically convolutional neural networks (CNNs), in detecting pneumonia from chest X-ray (CXR) images. The study leveraged a dataset of 2,456 images, including both bacterial pneumonia and non-pneumonia cases, which were annotated by a physician and supplemented with additional images from a publicly available dataset. By utilizing deep learning approaches like CNN, ResNet50, and EfficientNetB0, we explored how these models could assist in pneumonia detection, particularly in a clinical decision-making context. The performance of all models—Proposed CNN, EfficientNetB0, and ResNet50—was evaluated using standard classification metrics, including accuracy, precision, recall, and F1-score. All models achieved an impressive overall accuracy of 97%, with each demonstrating strong performance in both the detection of bacterial pneumonia and non-pneumonia cases. For example, the Proposed CNN model achieved a precision of 1.00 and recall of 0.94

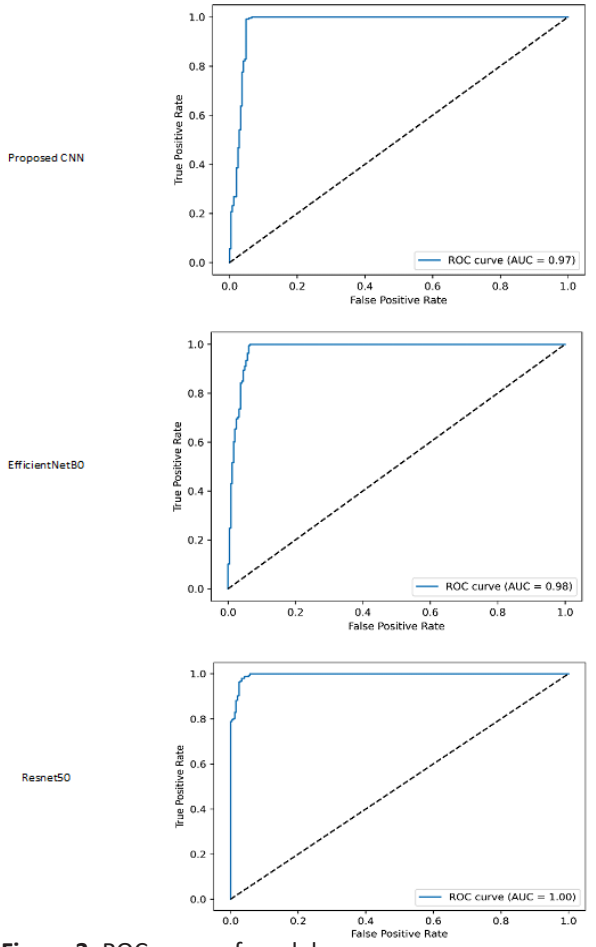

Figure 3. ROC curve of models

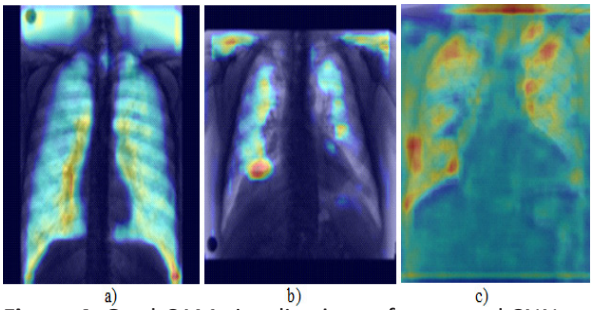

Figure 4. Grad-CAM visualizations of proposed CNN

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for the non-pneumonia class, and a precision of 0.95 and recall of 1.00 for pneumonia detection. Similarly, EfficientNetB0 and ResNet50 showed slightly varied results, but their performance remained robust, with high F1 scores across both classes. These findings suggest that the proposed AI-based systems are capable of providing accurate pneumonia detection, even in the presence of class imbalance (where non-pneumonia cases are more numerous). The use of a multi-model comparison, including well-established architectures like ResNet50 and EfficientNetB0, allowed us to understand how different deep learning models perform in medical image classification tasks. All three models demonstrated high precision and recall, ensuring reliable identification of both pneumonia and non-pneumonia cases. Moreover, the use of AI systems can serve as a valuable tool for clinicians, offering an additional layer of diagnostic verification. While AI cannot replace the expertise of healthcare professionals, it can assist in reducing diagnostic errors and enhance the efficiency of the clinical workflow, especially in environments with limited access to radiology specialists.

CONCLUSION

In this study, we demonstrated that deep learning-based models, particularly CNN, EfficientNetB0, and ResNet50, are effective in the detection of pneumonia from chest X-ray images. The models provided high accuracy, precision, and recall, making them suitable candidates for supporting clinical decision-making in pneumonia diagnosis. The results of this study suggest that AI can enhance diagnostic capabilities, offering reliable and accurate second opinions in clinical settings. The integration of AI in medical image analysis holds significant potential for improving the accuracy and efficiency of diagnoses, particularly in under-resourced healthcare settings. However, further validation with larger datasets and clinical trials is necessary to confirm the robustness and generalizability of these models in real-world scenarios. Future work could also explore the integration of AI systems with other diagnostic tools to create comprehensive, multi-modal decision support systems.

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The authors declare that they have no conflict of interest to disclose.

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ASSESSING THE POTENTIAL OF HYPOXIA-TARGETING AGENTS AS GSTP1 INHIBITORS IN OVERCOMING CANCER DRUG RESISTANCE

Kanser İlaç Direncini Aşmada Hipoksi Hedefli Ajanların GSTP1 İnhibitörleri Olarak Potansiyellerinin Değerlendirilmesi

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ABSTRACT

Objective: The persistent challenge of drug resistance in cancer therapy is closely linked to the detoxification activity of glutathione S-transferase P1 (GSTP1). This study aims to assess the potential of hypoxia-targeting agents as GSTP1 inhibitors to address drug resistance mechanisms in cancer.

Material and Methods: Molecular docking simulations were performed using the crystal structure of GSTP1 (PDB ID: 2GSS). Eight hypoxia-targeting agents were tested, including BAY 87-2243, Vadimezan, SLC-0111, Acriflavine, PX-478, Evofosfamide, Bevacizumab, and the reference GSTP1 inhibitor ethacrynic acid. Binding affinities were calculated using AutoDock Vina, and interaction profiles were visualized with Discovery Studio.

Results: Among the tested compounds, BAY 87-2243 exhibited the highest binding affinity to GSTP1 with a binding energy of -9.1 kcal/mol, surpassing ethacrynic acid (-6.7 kcal/mol). Vadimezan (-7.9 kcal/mol) and SLC-0111 (-7.2 kcal/mol) also demonstrated strong inhibitory potential. Key interactions included hydrogen bonds with residues GLN A:51 and ARG A:13 and hydrophobic interactions with PHE A:8. Other compounds displayed lower binding affinities, ranging from -6.6 to -5.7 kcal/mol.

Conclusion: Hypoxia-targeting agents, particularly BAY 87-2243, Vadimezan, and SLC-0111, show promising GSTP1 inhibition potential, offering dual functionality to modulate tumor hypoxia and counteract drug resistance. These findings warrant further in vitro and in vivo studies to explore their clinical application in cancer therapy.

Keywords: *Hypoxia; GSTP1; Drug Resistance; Molecular Docking*

ÖZET

Amaç: Kanser tedavisinde ilaç direncinin kalıcı zorluğu, glutatyon S-transferaz P1 (GSTP1) enziminin detoksifikasyon aktivitesi ile yakından ilişkilidir. Bu çalışma, kanser tedavisinde ilaç direnci mekanizmalarını hedeflemek amacıyla hipoksi odaklı ajanların GSTP1 inhibitörleri olarak potansiyelini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Moleküler yerleştirme simülasyonları, GSTP1'in kristal yapısı (PDB ID: 2GSS) kullanılarak gerçekleştirildi. BAY 87-2243, Vadimezan, SLC-0111, Akflavin, PX-478, Evofosfamid, Bevacizumab ve referans GSTP1 inhibitörü olan etakrinik asit dahil olmak üzere sekiz hipoksi odaklı ajan test edildi. Bağlanma afiniteleri AutoDock Vina kullanılarak hesaplandı ve etkileşim profilleri Discovery Studio ile görselleştirildi.

Bulgular: Test edilen bileşikler arasında BAY 87-2243, -9,1 kcal/mol bağlanma enerjisi ile GSTP1'e en yüksek bağlanma afinitesini gösterdi ve etakrinik asiti (-6,7 kcal/mol) geride bıraktı. Vadimezan (-7,9 kcal/mol) ve SLC-0111 (-7,2 kcal/mol) de güçlü inhibitör potansiyeli sergiledi. Önemli etkileşimler arasında GLN A:51 ve ARG A:13 kalıntıları ile hidrojen bağları ve PHE A:8 ile hidrofobik etkileşimler yer aldı. Diğer bileşikler, -6,6 ile -5,7 kcal/mol arasında değişen daha düşük bağlanma afiniteleri gösterdi.

Sonuç: Hipoksi odaklı ajanlar, özellikle BAY 87-2243, Vadimezan ve SLC-0111, GSTP1 inhibisyon potansiyeli göstererek tümör hipoksisini modüle etme ve ilaç direncini azaltmada çift işlevli bir yaklaşım sunmaktadır. Bu bulgular, kanser tedavisinde klinik uygulamalarını keşfetmek için ileri in vitro ve in vivo çalışmaların yapılmasını gerektirmektedir.

Anahtar Kelimeler: *Hipoksi; GSTP1; İlaç Direnci; Moleküler Yerleştirme*

INTRODUCTION

The persistent challenge of drug resistance in cancer therapy remains one of the most significant barriers to effective treatment. Among various mechanisms contributing to this resistance, the detoxification of chemotherapeutic agents by enzymes such as glutathione S-transferase P1 (GSTP1) has been extensively studied. GSTP1, a member of the glutathione S-transferase family, plays a crucial role in cellular defense against oxidative stress and toxic xenobiotics. By conjugating reduced glutathione to electrophilic compounds, GSTP1 facilitates the detoxification process, reducing the efficacy of many anti-cancer drugs (1, 2). Thus, targeting GSTP1 holds promise for overcoming drug resistance and enhancing therapeutic outcomes in cancer treatment.

Recent advances in cancer research have emphasized the importance of hypoxia as a central feature of the tumor microenvironment. Hypoxic conditions not only drive tumor progression but also contribute to resistance against conventional treatments, including chemotherapy and radiotherapy (3, 4). To address these challenges, researchers have explored hypoxia-targeting therapeutics as a novel strategy for cancer therapy. Compounds such as BAY 87-2243, Vadimezan, SLC-0111, Evofosfamide, PX-478, Acriflavine, and Bevacizumab have emerged as potential candidates for modulating the hypoxic tumor microenvironment (5-9). While these agents' primary mechanisms of action are well-documented, their possible interactions with GSTP1 remain an area of scientific curiosity and speculation.

BAY 87-2243 and Vadimezan are known for disrupting hypoxia pathways, but their potential roles in drug resistance mechanisms remain unclear (8, 10, 11). Similarly, SLC-0111, a carbonic anhydrase IX (CAIX) inhibitor, shows promise in targeting the acidic tumor microenvironment, yet its indirect effects on detoxification enzymes warrant further investigation (7, 12). Evofosfamide, a hypoxia-activated prodrug, demonstrates selective cytotoxicity under hypoxic conditions, raising questions about its impact on oxidative stress responses. Acriflavine and PX-478, both exhibiting antitumor activity through hypoxia-related mechanisms, underscore the importance of exploring their broader implications in resistance pathways (7). Bevacizumab, an anti-angiogenic agent targeting vascular endothelial growth factor (VEGF), is widely used in cancer therapy, but its role in hypoxia-driven resistance processes remains an important yet underexplored area (9). Investigating the interactions of these hypoxia-targeting agents with GSTP1, an enzyme prominently linked to drug-resistant cancer, could provide a foundation for overcoming and better understanding the mechanisms of drug resistance.

The intricate relationship between hypoxia, drug resistance, and GSTP1 remains a largely underexplored area in cancer research. While hypoxia-targeting compounds have demonstrated therapeutic efficacy in various preclinical and clinical settings, their potential to modulate GSTP1 activity indirectly has yet to be fully investigated. Understanding these interactions could pave the way for novel approaches to overcoming drug resistance and enhancing cancer therapies. In this study, molecular docking was utilized to analyze the binding affinities and interactions of hypoxia-targeting agents with GSTP1. Compounds such as BAY 87-2243, Vadimezan, and SLC-0111 emerged with promising GSTP1 inhibitor potential, surpassing the binding efficiency of ethacrynic acid, a known GSTP1 inhibitor. These findings suggest that hypoxia-targeting agents may play a dual role, influencing the tumor microenvironment and modulating key resistance pathways, offering valuable insights for future therapeutic strategies.

MATERIALS AND METHODS

The molecular structures of the selected compounds, along with the GSTP1 inhibitor ethacrynic acid, were obtained from the PubChem database (13). The compounds included BAY 87-2243 (PubChem CID: 67377767), Vadimezan (CID: 123964), SLC-0111 (CID: 310360), Acriflavine (CID: 6842), Bevacizumab (CID: 24801581), PX-478 (CID: 11234795), Evofosfamide (CID: 11984561), and Ethacrynic Acid (CID: 3278). Prior to molecular docking, energy minimization was conducted using Avogadro software to optimize the conformations of the compounds, ensuring their suitability for the docking process (14).

The crystal structure of Glutathione S-transferase P1 (GSTP1) was retrieved from the Protein Data Bank (PDB) with the ID 2GSS. This structure has a resolution

of 1.9 Å and R-factor and R-free values of 0.209 and 0.229, respectively (15). For docking preparation, water molecules and other non-protein components were removed, hydrogen atoms were added, and Gasteiger charges were applied to the protein to ensure accurate docking results. The active site of GSTP1 was identified by examining the binding pocket of ethacrynic acid, a known GSTP1 inhibitor. The active site coordinates were defined as x = 9.07595, y = 1.00542, and z = 26.9067. A cubic grid of 15 Å × 15 Å × 15 Å was centered around this region to facilitate the docking simulations. Docking was carried out using AutoDock Vina (version 1.2.5), applying the Lamarckian Genetic Algorithm with default settings to calculate the binding affinities of each ligand (16, 17).

After the docking analysis, the molecular interactions between GSTP1 and the compounds were examined in detail. Visualization and thorough analysis of these interactions were performed using Discovery Studio software. The focus was on identifying hydrogen bonds, hydrophobic interactions, and other significant binding interactions, which offered valuable insights into the molecular dynamics and binding characteristics between GSTP1 and the various compounds.

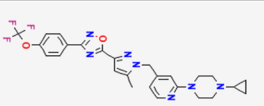
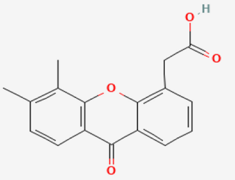
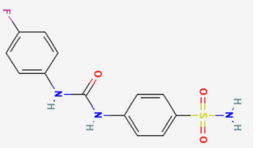
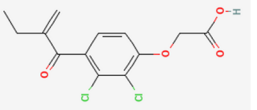
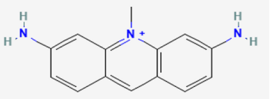
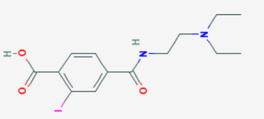
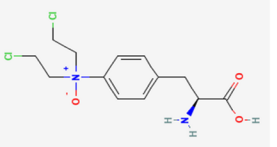
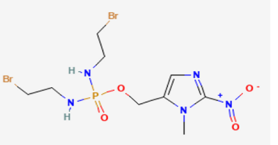
Energy minimization of the compounds was performed using Avogadro, which applies the default MMFF94 force field to optimize molecular geometries, ensuring stable conformations before docking. This process includes default statistical methods to assess the stability and energy profiles of the minimized structures. Docking analyses were conducted using AutoDock Vina, which uses its default Lamarckian Genetic Algorithm to compute binding affinities based on energy and geometric complementarity. The docking process also incorporated default statistical methods to evaluate the reliability and significance of the calculated binding affinities. Visualization of the docking results was done using Discovery Studio, which provides default features for assessing binding affinities and interaction frequencies. This software allows for the identification of key interactions, such as hydrogen bonds and hydrophobic contacts, while applying default statistical analyses to gain insights into the distribution and significance of these interactions.

This study was approved by the Non-Interventional Research Ethics Committee of Afyonkarahisar Health Sciences University (Meeting No: 2025/2, Date: 07.02.2025).

RESULTS

The binding energies of the compounds and ethacrynic acid to GSTP1 are presented in Table 1. Among the compounds tested, BAY 87-2243 showed the strongest binding affinity with a binding

Table 1. Binding energies of the compounds and ethacrynic acid to GSTP1

Compounds	Molecular structure	Binding energy (kcal/mol)
BAY 87-2243		-9.1
Vadimezan		-7.9
SLC-0111		-7.2
Ethacrynic acid		-6.7
Acriflavine		-6.6
Bevacizumab		-6.3
PX-478		-6.0
Evofosfamide		-5.7

energy of -9.1 kcal/mol, followed by Vadimezan at -7.9 kcal/mol and SLC-0111 at -7.2 kcal/mol. Ethacrynic acid, a known GSTP1 inhibitor, demonstrated a binding energy of -6.7 kcal/mol. Other compounds, including Acriflavine, Bevacizumab, PX-478, and Evofosfamide, exhibited progressively weaker binding affinities, with binding energies ranging from -6.6 to -5.7 kcal/mol. These results suggest that BAY 87-2243, Vadimezan, and SLC-0111 may have significant potential as GSTP1 inhibitors, surpassing the binding affinity of ethacrynic acid.

The molecular docking results display the binding interactions of various compounds with a target protein's active site, arranged in separate panels (Figure 1). The protein's secondary structure is depicted as brown ribbons, while the ligand molecules are highlighted in green stick representations for clarity. The compounds analyzed include BAY 87-2243, Vadimezan, SLC-0111, and Ethacrynic acid in the top row, alongside Acriflavine, Bevacizumab, PX-478, and Evofosfamide in the bottom row. Each ligand exhibits a distinct binding pose, aligning within the protein's binding pocket through molecular interactions such as hydrogen bonds, hydrophobic interactions, and other molecular forces. Ethacrynic acid, used as a reference inhibitor, demonstrates its specific positioning and interaction profile, serving as a comparison point for the other ligands. These results provide insights into the structural compatibility and potential inhibitory strength of each compound, contributing to a deeper understanding of their binding efficacy.

The interaction diagrams showcase the detailed molecular interactions of top hits compounds (BAY 87-2243, vadimezan, SLC-0111) and reference compounds (ethacrynic acid) with the active site of GSTP1 (Figure 2). Each compound forms specific bonds, including conventional hydrogen bonds, van der Waals forces, pi-anion, alkyl, and pi-sigma interactions, as indicated by color-coded lines. BAY 87-2243 establishes multiple hydrogen bonds with residues like GLN A:51 and ARG A:13, while also exhibiting alkyl and pi-anion interactions with residues such as PHE A:8 and VAL A:35. Vadimezan shows prominent pi-anion interactions with TYR A:108 and PHE A:8, alongside hydrogen bonds with ARG A:13 and TYR A:7, suggesting a balanced interaction network. SLC-0111 interacts extensively via hydrogen bonds with residues like ARG A:13, GLN A:51, and TYR A:108, while maintaining pi-anion interactions with PHE A:8. Finally, Ethacrynic acid displays multiple hydrogen bonds with residues such as TYR A:108 and ARG A:13, in addition to van der Waals interactions with surrounding residues. These results highlight

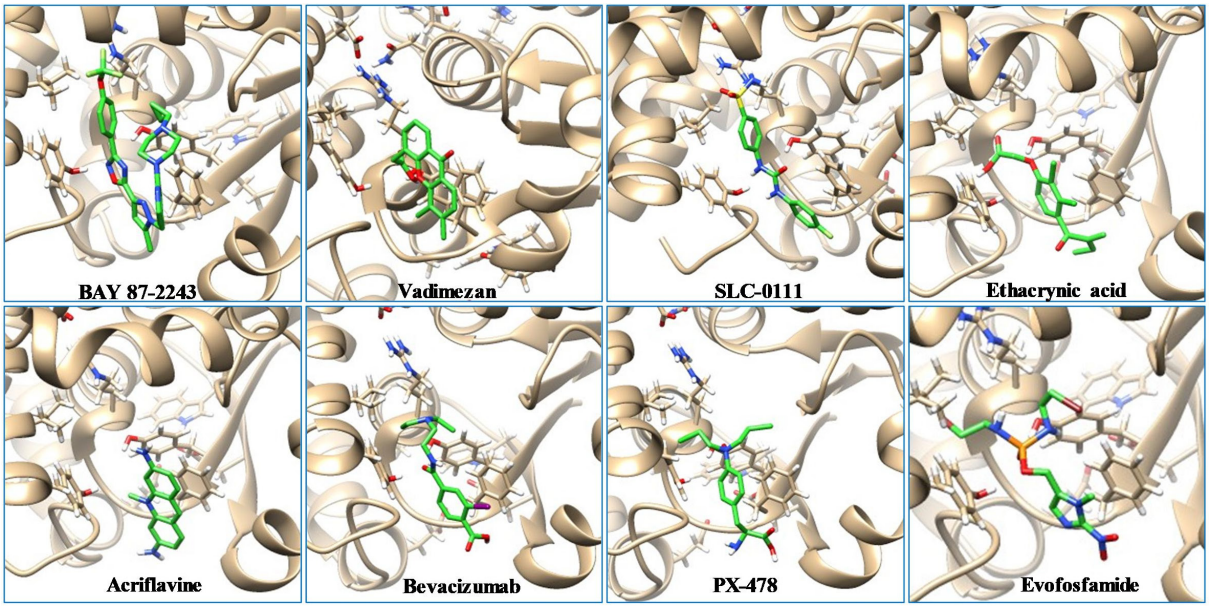


Figure 1. The arrangement of compounds (BAY 87-2243, vadimezan, SLC-0111 and ethacrynic acid) within the active site of GSTP1 (Glutathione S-transferase P1). The GSTP1 protein is illustrated in brown, with the compound structures displayed in green.

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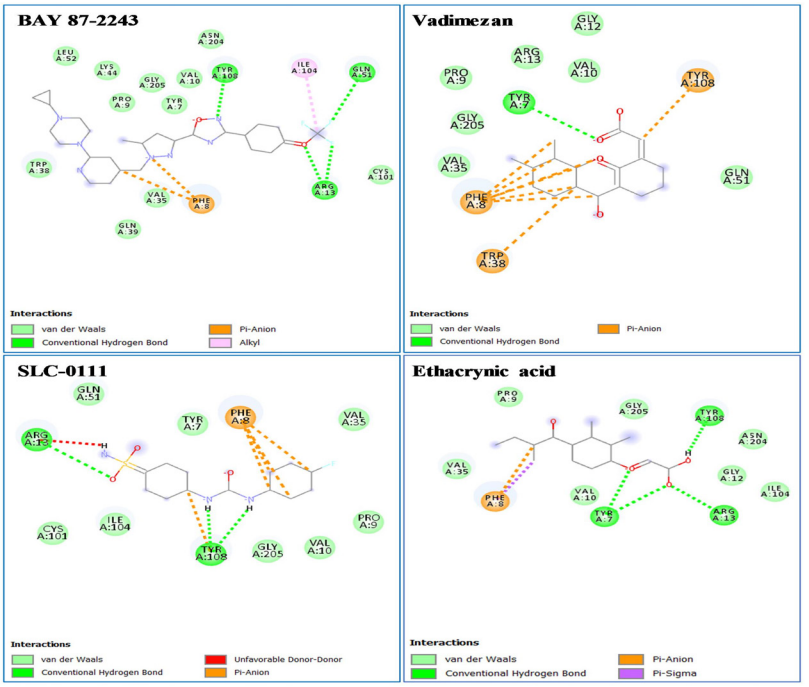

Figure 2. 2D Interaction diagrams of top hits (BAY 87-2243, vadimezan and SLC-0111) and reference compound (ethacrynic acid) with GSTP1 (Glutathione S-transferase P1). The amino acid residues involved in the interactions include Arginine (ARG), Asparagine (ASN), Cysteine (CYS), Glutamine (GLN), Glycine (GLY), Isoleucine (ILE), Leucine (LEU), Phenylalanine (PHE), Proline (PRO), Tyrosine (TYR), Tryptophan (TRP), and Valine (VAL).

each compound's unique binding characteristics and interaction strengths, emphasizing their potential to engage effectively with GSTP1's active site.

DISCUSSION

The findings of this study shed light on the potential dual functionality of hypoxia-targeting agents, not only as modulators of the tumor microenvironment but also as inhibitors of GSTP1, a pivotal enzyme in drug resistance mechanisms. GSTP1 has long been recognized for its role in detoxifying chemotherapeutic agents and reducing their efficacy (1, 2, 18-20). In this study, compounds such as BAY 87-2243, Vadimezan, and SLC-0111 demonstrated stronger binding affinities to GSTP1 compared to the reference inhibitor, ethacrynic acid. These results suggest that targeting hypoxia-associated pathways could inadvertently address resistance mechanisms mediated by GSTP1.

The role of GSTP1 in cancer therapy has been extensively documented, with the enzyme often highlighted as a key player in cellular defense against oxidative stress and xenobiotics (1, 2). Ethacrynic acid, a well-known GSTP1 inhibitor, has been investigated in previous studies for its potential to combat drug resistance; however, its clinical application is still limited due to side effects. (21) . Compared to ethacrynic acid, BAY 87-2243 demonstrated a markedly higher binding affinity in this study, forming multiple hydrogen bonds and pi-anion interactions with key residues in the GSTP1 active site. These findings are consistent with the emerging literature emphasizing the need for more selective GSTP1 inhibitors with dual-targeting potential.

The interplay between hypoxia and drug resistance has been a growing focus in cancer research (22, 23). Hypoxia induces profound changes in tumor biology, including increased oxidative stress, activation of detoxification enzymes like GSTP1, and promotion of resistance to conventional therapies (20, 24) . BAY 87-2243, previously reported to inhibit hypoxia-inducible factor (HIF) activity and improve radiation response (8), demonstrated the strongest GSTP1 inhibition in this study. This suggests that the compound could act as a dual-function agent, targeting both the hypoxic

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environment and detoxification pathways, which could significantly enhance therapeutic outcomes.

Vadimezan, another hypoxia-targeting agent, also showed promising GSTP1 inhibitory potential in this study. Known for its vascular disrupting properties (6) , Vadimezan was previously thought to exert its antitumor effects primarily through vascular collapse. However, our results suggest that its interaction with GSTP1 could represent an additional mechanism of action. By forming hydrogen bonds and pi-anion interactions with residues such as TYR A:108 (25), Vadimezan could reduce GSTP1-mediated detoxification of chemotherapeutics, a concept not widely explored in the literature.

SLC-0111, a CAIX inhibitor targeting acidic tumor microenvironments, emerged as another strong GSTP1 interactor in this study. Carbonic anhydrase inhibitors like SLC-0111 have been shown to disrupt pH regulation in tumors, sensitizing them to chemotherapy (5). The observed GSTP1 inhibition by SLC-0111 suggests a potential synergistic mechanism, where both tumor acidification and detoxification pathways are simultaneously disrupted. This aligns with findings from Mokhtari et al. (12), who advocated for combination therapies targeting multiple resistance pathways. Such dual functionality could make SLC-0111 an attractive candidate for further preclinical investigation.

Combination therapy strategies often seek to exploit vulnerabilities in tumor biology while mitigating resistance mechanisms. This study's findings complement prior research advocating for the integration of hypoxia-targeting agents with conventional chemotherapeutics (7). Evofosfamide, a hypoxia-activated prodrug, was previously noted for its selective cytotoxicity under low-oxygen conditions but demonstrated weaker GSTP1 binding affinity in this analysis. Despite this, Evofosfamide's hypoxia activation may still contribute to overcoming GSTP1-related resistance when used in combination with stronger inhibitors like BAY 87-2243. Such strategies highlight the importance of designing multidimensional therapeutic regimens that address both the tumor microenvironment and intrinsic resistance pathways.

Molecular docking has become an indispensable tool in modern drug discovery, particularly in identifying and optimizing enzyme inhibitors. This computational approach enables screening potential drug candidates before costly and time-intensive in vitro and in vivo experiments (26, 27). In the context of GSTP1 inhibition, docking studies provide valuable insights into the binding interactions of hypoxia-targeting agents, facilitating the rational design of novel therapeutics. Recent molecular docking studies have identified promising GSTP1 inhibitors with improved selectivity and binding efficiency (28-30). By comparing our findings with these studies, we highlight the potential of hypoxia-targeting compounds as dual-function agents, reinforcing their relevance in overcoming drug resistance. Integrating molecular docking with experimental validation will further strengthen the translational value of this research.

While this study provides compelling evidence of GSTP1 inhibition by hypoxia-targeting therapeutics, several limitations warrant consideration. The findings are based on molecular docking simulations, which, while robust, require validation through in vitro and in vivo experiments to confirm enzyme inhibition and downstream effects on cancer cells (31). Additionally, the impact of these compounds on non-target tissues and their potential systemic toxicity must be thoroughly evaluated. Future research should explore the pharmacokinetics and pharmacodynamics of these agents in preclinical models, as well as their efficacy in overcoming resistance in various cancer types.

The integration of hypoxia-targeting therapeutics with GSTP1 inhibition represents a promising avenue for addressing the persistent challenge of drug resistance in cancer therapy. Expanding this line of research to include high-throughput screening of other hypoxia-targeting agents may yield additional candidates with superior binding properties and therapeutic potential. Ultimately, the development of dual-function compounds tailored to individual tumor profiles could pave the way for personalized cancer treatments with enhanced efficacy and reduced resistance.

CONCLUSION

This study underscores the potential of hypoxia-targeting agents such as BAY 87-2243, Vadimezan, and SLC-0111 as dual-function inhibitors that target the hypoxic tumor microenvironment while simultaneously inhibiting GSTP1-mediated detoxification pathways. By

demonstrating higher binding affinities than ethacrynic acid, these compounds offer novel opportunities to address both tumor hypoxia and drug resistance, two critical barriers in cancer therapy. Future preclinical and clinical studies should focus on validating these findings and exploring the therapeutic potential of combining hypoxia-targeting agents with existing chemotherapeutics to improve patient outcomes.

Acknowledgments

The authors declare that they have no conflict of interest to disclose.

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OCULAR TRAUMA PATIENTS ADMITTED TO A TERTIARY EMERGENCY DEPARTMENT: RETROSPECTIVE STUDY

Üçüncü Basamak Acil Servise Kabul Edilen Oküler Travma Hastaları: Retrospektif Çalışma

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ABSTRACT

Objective: This study aimed to retrospectively evaluate the demographic characteristics, causes of trauma, types of trauma, examination findings, and posttraumatic visual status of patients with ocular trauma admitted to the Emergency Department of Balıkesir University Hospital.

Material and Methods: The study retrospectively reviewed the file records of 402 ocular trauma patients admitted to Balıkesir University Hospital between January 1, 2020, and December 31, 2023, including mechanism, type, anatomical localization, associated injuries, examination findings, and visual status. Visual status was classified based on the clinical evaluation performed following ophthalmology consultation.

Results: The mean age of the patients was 44.10±20.64 years, and 75.12% were male. The most common settings of trauma were gardening/agricultural work (30.10%), home accidents (20.15%), and work accidents (11.19%). The most common type of trauma was blunt trauma (66.20%), followed by penetrating injuries and occupational accidents. Visual impairment (blurred vision/diminished vision) and vision loss were most commonly observed in isolated eye trauma and blunt trauma.

Conclusion: Eye traumas are frequently caused by preventable causes, and gardening and agricultural activities are important risk factors, especially in rural areas.

Keywords: *Ocular Injuries; Emergency Department; Visual Loss*

ÖZET

Amaç: Bu çalışmanın amacı, Balıkesir Üniversitesi Hastanesi Acil Servisi'ne başvuran göz travmalı hastaların demografik özelliklerini, travma nedenlerini, travma türlerini, muayene bulgularını ve travma sonrası gelişen görme durumlarını retrospektif olarak değerlendirmektir.

Gereç ve Yöntemler: Çalışma, 1 Ocak 2020- 31 Aralık 2023 tarihleri arasında Balıkesir Üniversitesi Hastanesi'ne başvuran 402 göz travmalı hastanın dosya kayıtlarının retrospektif olarak incelenmesiyle gerçekleştirildi. Travmanın mekanizması, türü, anatomik lokalizasyonu, eşlik eden yaralanmalar, muayene bulguları ve görme durumu analiz edildi. Görme durumu, oftalmoloji konsültasyonunu takiben yapılan klinik değerlendirmeye göre sınıflandırıldı.

Bulgular: Hastaların yaş ortalaması 44,10±20,64 olup, %75,12'si erkekti. Travmaların en sık meydana geldiği ortamlar bahçe-tarım işleri (%30,10), ev kazaları (%20,15) ve iş kazaları (%11,19) idi. En yaygın travma türü künt travmalar (%66,20) olup, bunu penetran yaralanmalar ve iş kazaları izledi. Görme bozukluğu (bulanık görme/görmede azalma) ve görme kaybı en sık olarak izole göz travması ve künt travmalarda gözlendi. Görme kaybına en çok neden olan muayene bulguları ise kornea perforasyonu, total hifema ve korneaskleral perforasyondu.

Sonuç: Göz travmaları sıklıkla önlenebilir nedenlere bağlı gelişmekte olup, özellikle kırsal bölgelerde bahçe ve tarım faaliyetleri önemli bir risk faktörüdür.

Anahtar Kelimeler: *Göz Travması; Acil Servis; Görme Kaybı*

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INTRODUCTION

Ocular trauma is a significant public health problem worldwide and a leading cause of preventable monocular vision loss (1,2). Eye trauma is an important cause of visual impairment, accounting for approximately 3% of emergency department visits (3,4). According to the World Health Organization (WHO) Prevention of Blindness Programme, it is estimated that approximately 55 million people experience ocular trauma or disability each year. Approximately 19 million of these cases involve unilateral blindness, 2.3 million involve bilateral reduced visual acuity, and 1.6 million involve blindness due to traumatic causes requiring hospitalization (5).

The prevalence of eye trauma among patients admitted to emergency departments is relatively high. The most common causes of eye injuries among these patients include foreign objects in or near the eye, motor vehicle accidents, falls, and domestic accidents. Studies have shown that young adult males and elderly individuals are at higher risk (3,5–7). The main types of eye trauma include orbital fractures and open globe injuries, which can lead to severe visual loss (8,9).

Timely and accurately evaluating ocular trauma in emergency departments is crucial for early diagnosis and effective treatment. However, since ocular traumas often occur with other associated injuries, they may sometimes be overlooked in emergency departments, resulting in delays in diagnosis and intervention. This can lead to permanent visual impairment and other serious consequences (9,10).

In conclusion, adopting a multidisciplinary approach in emergency departments is crucial for effectively managing ocular trauma. Strengthening the coordination and cooperation between ophthalmologists and other related specialties is essential for the early diagnosis of trauma cases, determining appropriate intervention methods, and minimizing long-term complications. Therefore, increasing the training of emergency service teams on ocular trauma and establishing effective interdisciplinary communication mechanisms will significantly contribute to preserving visual functions and improving patients' quality of life.

MATERIALS AND METHODS

This retrospective study was conducted among patients from the Balıkesir University Medical Faculty Emergency Department from January 1, 2020, to December 2023.

The study analyzed data from the hospital's automation system and patient records. This included various information such as the date of admission, age, gender, type of eye complaints (monocular or bilateral), type and mechanism of trauma, any concomitant injuries, the diagnosis made in the emergency department, whether an orbital Computed Tomography (CT) scan was performed, whether a consultation was conducted with the Ophthalmology department, and the discharge status of the patients.

In this study, we considered demographic characteristics such as age and gender, trauma mechanisms, types of trauma, injury localization, associated injuries, and hospitalization status as independent variables. The dependent variable was visual impairment and loss due to trauma.

The patients' demographic and clinical admission data were obtained retrospectively from the hospital data processing service. Records of 582 patients were reviewed; 180 patients with no ocular trauma or missing data were excluded. A total of 402 patients were included in the study.

Mechanisms of trauma were categorized as gardening and agricultural activities, home accidents, falls, occupational accidents, assault, traffic accidents, sports injuries, animal injuries, and gunshot wounds. Types of traumas were categorized as blunt, penetrating, piercing-cutting instrument, chemical, thermal trauma, and presence of foreign bodies.

Localization of the trauma (right, left, or bilateral), concomitant traumas (head trauma, multitrauma, etc.), need for consultation, ocular examination findings, and patient outcomes (discharge, ward admission, intensive care unit admission, referral, and refusal of treatment) were evaluated in detail.

Visual status was evaluated jointly by emergency physicians and ophthalmologists based on bedside gross visual assessments performed during emergency department consultations. In cases where standard visual acuity measurement (e.g., Snellen chart) was not feasible, alternative clinical assessments were used, including the patient's ability to count fingers, detect hand motion, perceive light, or respond to bright light

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exposure. Based on these evaluations and intraocular findings, patients were categorized as having normal vision, reduced vision, permanent vision loss, transient vision loss, or unassessable vision.

Data was analyzed using SPSS 26.0 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.). Continuous variables are presented as means, standard deviations, minima, and maxima, while categorical variables are shown as counts and percentages.

This study was conducted according to the principles outlined in the Declaration of Helsinki. Due to the study's retrospective nature, written informed consent was waived. Institution: Balıkesir University Health Sciences Non-Interventional Ethics Committee Date: 25.06.2024 Approval no: 2024/97.

RESULTS

The mean age of the 402 patients included in the study was 44.10±20.64 years, and 38.06% were between 36 and 59 years. Of all patients, 75.12% (n=302) were male, and 24.88% (n=100) were female. According to the localization of the trauma, 50.25% of the injuries were isolated in the left eye (n=202), 45.02% were isolated in the right eye (n=181), and 4.73% were bilateral (n=19). Orbital CT was used in 73.13% (n=294) of patients, and 92.79% (n=373) were referred to the ophthalmology department. Regarding hospitalization status, 63.93% (n=257) of the patients were discharged, 28.86% (n=116) were hospitalized in the ward, 1.99% (n=8) were followed up in the ICU due to multitrauma/traffic accident, 2.99% (n=12) were referred to an advanced center and 2.24% (n=9) refused treatment. The most common cause of trauma was gardening- an agricultural environment and work (30.10%; n=121) due to the impact of wood and tree branches. This was followed by home environment accidents due to glass, bottle caps, iron, and wire (20.15%; n=81), falls (11.19%; n=45), occupational accidents (9.20%; n=37), battery (7.46%; n=30), and motor vehicle accidents (6.21%; n=25). Less common causes of trauma included animal-related injuries (4.97%; n=20), sports accidents (2.24%; n=9), and gunshot wounds (1.24%; n=5) (Table 1). A statistically significant association was found between the trauma mechanism and the visual outcome ($p<0.05$).

Blunt trauma (66.20%; n=266) was the most common type. This was followed by occupational accidents (7.70%; n=31), traffic accidents (6.50%; n=26), and intraocular foreign body injuries (6.50%; n=26). Penetrating injuries (6.70%; n=27) and penetrating sharp injuries (4.70%; n=19) were less common.

In visual function evaluations, 49.25% (n=198) had normal vision, 36.07% (n=145) had blurred vision or decreased vision, 12.19% (n=49) had visual loss, 0.75% (n=3) had transient visual loss, and 1.74% (n=7) were intubated and could not be evaluated. The most common causes of vision loss (12.19%; n=49), decreased vision, and blurred vision (36.07%; n=145) were isolated eye trauma and blunt trauma. Most of the patients had isolated eye trauma (74.90%; n=301). When organ and system injuries accompanying ocular trauma were analyzed, the most common causes were head trauma (15.7%; n=66) and multitrauma (8.00%; n=32) (Table 2). A statistically significant association was found between the presence of concomitant injuries and the visual outcome ($p<0.05$).

Although subconjunctival hemorrhage and periorbital ecchymosis/hematoma were the most common ocular examination findings after injury, hyphema and epithelial defect were the most common findings causing visual impairment (decreased/blurred vision). Corneal perforation, total hyphema, and corneascleral perforation were the most common findings causing visual loss (Figure 1).

DISCUSSION

Traumatic eye injuries are one of the most common causes of preventable visual impairment and blindness worldwide. These injuries can occur due to many causes, including accidents, sports injuries, workplace accidents, and daily activities. The frequency and mechanism of injury also vary according to geography, demographics, and age groups (8,11). Eye traumas cause serious social and psychological problems in individuals and, as a result, can have permanent consequences that negatively affect quality of life. However, many of these injuries can be prevented by identifying risk factors, increasing social awareness, and taking protective measures, especially in specific environments such as the home, workplace, and school (12,13).

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Table 1. Distribution of demographic and clinical characteristics of patients according to place of trauma

	Farm	Home	Fall	Work	Assault	Motor Vehicle Crash	Animal-Caused	Sports	Gunshot	Other	Total N (%)
Gender											
Female	32	18	18	1	7	3	9	0	0	12	100 (24.88%)
Male	89	63	27	36	23	22	11	9	5	17	302 (75.12%)
Age(Years)											
1-17	6	14	5	2	3	2	0	3	0	9	44 (10.95%)
18-35	15	25	7	14	8	10	3	5	3	10	100 (24.88)
36-59	47	33	11	16	13	8	13	1	2	9	153 (38.06%)
≥60	53	9	22	5	6	5	4	0	0	1	105 (26.12%)
Affected Eye											
Left	64	44	22	20	15	7	10	5	1	14	202 (50.25%)
Right	56	36	19	12	14	11	10	4	4	15	181 (45.02%)
Bilateral	1	1	4	5	1	7	0	0	0	0	19 (4.73%)
Orbital CT	86	56	38	25	28	25	17	4	5	10	294 (73.13%)
Consultation	116	77	37	33	29	22	18	7	5	29	373 (92.79%)
Patient Outcome											
Discharged	78	52	26	22	23	12	15	8	0	21	257 (63.93%)
Hospitalization	41	24	13	15	6	3	5	0	5	4	116 (28.86%)
ICU	0	1	1	0	0	6	0	0	0	0	8 (1.99%)
Transfer	1	2	4	0	0	3	0	0	0	2	12 (2.99%)
Treatment Refused	1	2	1	0	1	1	0	1	0	2	9 (2.24%)
Total	121	81	45	37	30	25	20	9	5	29	402 (100%)

ICU: Intensive Care Unit; CT: Computed Tomography

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Table 2. Vision examination findings according to the type of trauma and concomitant trauma

	Normal	Blurred Vision/Reduced Vision	Vision Loss	Temporary Vision Loss	Unevaluable	Total N (%)
Type Of Trauma						
Blunt Injury	128	104	28	3	3	266 (66.20%)
Work Accident	20	6	5	0	0	31 (7.70%)
Penetrating Injury	8	7	12	0	0	27 (6.70%)
Traffic Accident	15	5	2	0	4	26 (6.50%)
Intraocular Foreign Body	13	12	1	0	0	26 (6.50%)
Penetrating And Sharp Instrument Injury	10	8	1	0	0	19 (4.70%)
Chemical Injury	4	2	0	0	0	6 (1.50%)
Thermal Injury	0	1	0	0	0	1 (0.20%)
P Value (Chi-Square)				P<0.001*		
Concomitant Trauma						
Isolated Eye Trauma	136	122	39	3	1	301 (74.90%)
Head Trauma	42	12	7	0	0	66 (15.7%)
Multitrauma	17	11	1	0	3	32 (8.00%)
Extremity Trauma	2	0	2	0	1	5 (1.20%)
Chest Trauma	1	0	0	0	0	1 (0.20%)
P Value (Chi-Square)						p<0.001*
Total	198(49.25%)	145(36.07%)	49(12.19%)	3(0.75%)	7(1.74%)	402 (100%)

*Chi-square test, p<0.05 considered significant.

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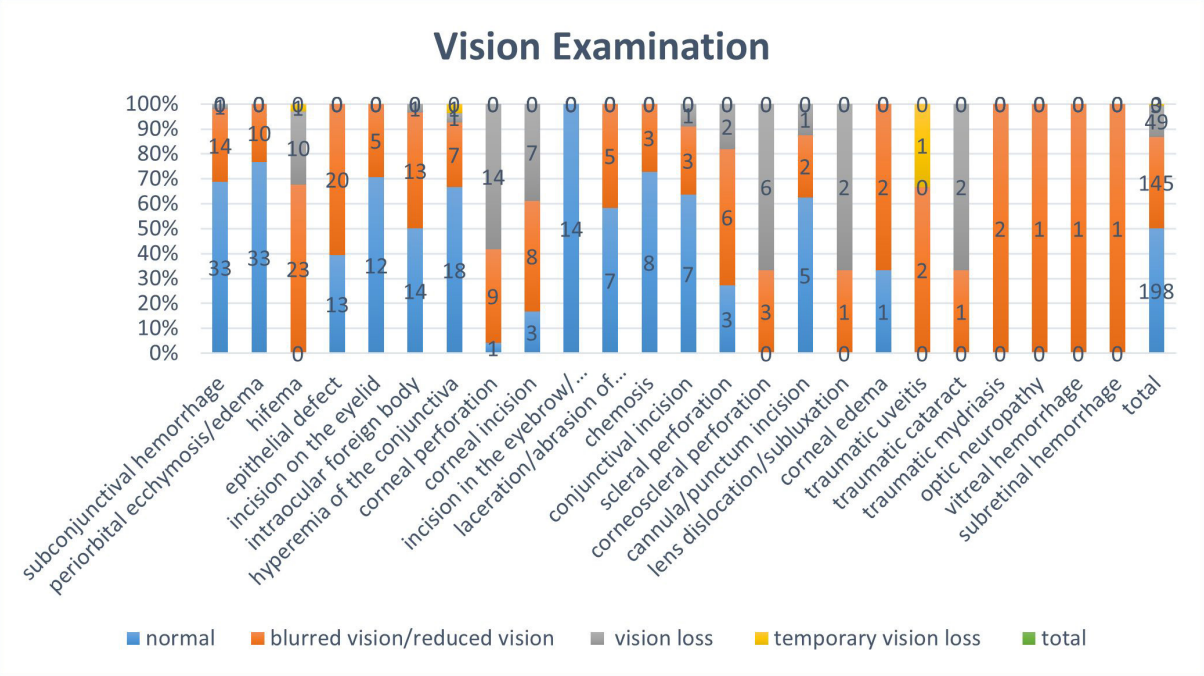

Figure 1: Vision examination findings

Balıkesir University Hospital, where our study was conducted, provides tertiary emergency health services in its region and serves as the referral center for eye trauma in Balıkesir province. This situation causes the trauma cases admitted to the hospital to vary in mechanism and type.

Research conducted by Li et al. regarding global ocular injuries found that the occurrence was more prevalent among males across all age categories, with injuries often observed in the younger and middle-aged groups (25-49 years) (12). In our study, the most common age group was 36-59 years (38.06%), followed by 18-35 years (24.88%). The high incidence of trauma is explained by the fact that men are more likely to be involved in risky working environments, traffic, renovation work, and sports activities. In our study, 72.12% of the patients admitted with eye injuries were males, similar to the literature (1,10–13).

May et al. reported that the most common causes of serious eye injuries were home accidents, work accidents, accidents on the street, and sports injuries, respectively (14). He et al. reported that the most common cause of eye trauma was falls; however, the mechanism, localization, and severity of trauma varied according to age, gender, and ethnicity (15). In our study, the most common settings of trauma were gardening/agricultural work (30.10%), home accidents (20.15%), and workplace accidents (11.19%). In addition, in our study, it was observed that patients who were consulted for trauma and underwent CT scans for the presence of foreign bodies/fractures were most frequently injured during gardening and agricultural work. In alignment with our study, Shrestha et al. identified gardening and agricultural work as the predominant cause of injury, particularly involving materials like branches and wood. This finding reflects the specific characteristics of the region where their research took place, contrasting with numerous studies conducted in Western countries (16). These findings suggest that rural characteristics and socioeconomic conditions may be determinants among the factors affecting the mechanism of eye trauma.

When the etiologic distribution of traumas in our study was analyzed, blunt traumas were the most common, followed by occupational accidents, penetrating injuries, and traffic accidents, respectively. This situation has been reported similarly in many previous studies (8,12). The majority of cases with visual loss were observed to have isolated eye trauma. It is known that blunt trauma can cause severe damage to deep

structures such as the retina and lens, leading to complications such as traumatic retinopathy and traumatic cataracts, which may result in visual loss (16). Similarly, in penetrating injuries, disruption of the integrity of the eye and complications such as endophthalmitis and retinal detachment can lead to permanent visual loss (17). In addition, it has been found that anatomical and functional outcomes in open-eye injuries with orbital fracture are pretty poor, and especially the presence of retinal detachment is an important marker for unfavorable prognosis (18). All these data suggest that not only the etiologic distribution but also the clinical outcomes of the types of trauma should be taken into consideration.

This study's single-centered and retrospective design limits the generalization of findings to larger populations or different geographical regions. Additionally, it is possible that some clinical parameters (Such as visual acuity at the time of trauma, duration of symptoms, and pre-traumatic eye health status) were recorded incompletely or inadequately due to the nature of retrospective data collection.

The treatment approach for eye injuries is influenced by various factors, including the mechanism of injury, the presence of associated conditions, and the duration since the injury occurred. Simple injuries are typically treated with conservative methods, whereas more complex cases may necessitate surgical intervention and a multidisciplinary approach. Kaplan et al. reported that 41.7% of patients were found to have corneal and extracorneal foreign bodies, with 81.1% of cases being discharged after treatment (19). In our study, 63.93% of patients were discharged following diagnosis and treatment, while 28.86% required admission to relevant departments for surgical intervention.

Alpay et al. reported that in the Western Black Sea Region, trauma related to wooden objects was the most common cause of injury in rural areas. Conversely, work-related injuries were most prevalent among males aged 30–50. Furthermore, corneal-scleral lacerations were identified as the most severe ocular injuries, impacting both initial and final visual acuity (20). In our study, the predominant cause of trauma was injuries incurred during agricultural activities. This prevalence can be linked to insufficient protective equipment and a lack of awareness in rural communities. When considering vision loss, it was found that penetrating injuries were correlated with a greater severity of vision impairment.

Doğan et al. reported that the most prevalent causes of eyelid injuries include sharp object injuries (33%), blunt trauma (30%), falls (22%), and traffic accidents (15%). Furthermore, foreign bodies were found at the wound site in 11.1% of cases, and concomitant canalicular lacerations were observed in 22.2% of instances (20 lower eyelids and 10 upper eyelids). A range of additional ocular findings was noted, including conjunctival lacerations (17%), open globe injuries (10.3%), corneal epithelial defects (7.4%), vitreous hemorrhage (6.6%), hyphema (4.4%), and retinal detachment (3.7%) (21). Our study similarly observed concomitant orbito-ocular pathologies in several cases, particularly in penetrating injuries associated with more severe intraocular complications. These findings underscore the importance of not only considering the etiological distribution of injuries but also evaluating the clinical outcomes of various types of trauma. Additionally, the lack of long-term follow-up data limits our ability to assess late post-traumatic complications and determine final visual outcomes.

CONCLUSION

Ocular traumas globally are primarily caused by preventable factors, highlighting the necessity for effective prevention strategies and enhanced public awareness. Promoting the use of personal protective equipment, enhancing educational initiatives, and establishing prompt diagnosis and intervention protocols, particularly in high-risk activities, will play a crucial role in reducing vision loss due to trauma. Our findings can inform public health policies that should be implemented locally and nationally.

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The authors declare that they have no conflict of interest to disclose.

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IS MYOMA SIZE IMPORTANT IN CAESAREAN MYOMECTOMY OPERATION?

Sezaryen Myomektomi Operasyonunda Myom Boyutu Önemli midir?

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ABSTRACT

Objective: The purpose of this study was to examine the impact of myoma size on intraoperative and postoperative clinical results among caesarean section (CS) patients who underwent myomectomy.

Material and Methods: The results of 34 cases who had caesarean myomectomy were analysed retrospectively. Patients' demographic, clinical, and pathological data was analysed in two categories based on the size of their myomas: those less than 5 cm, those 5 cm and greater than 5 cm. The study analysed many factors including maternal age, gravida, parity, history of abortions, gestational age at delivery, birth weight of the infant, duration of the operation, features of the myoma, pre- and post-operative haemoglobin levels, requirement for blood transfusion, and pathology results.

Results: Our study involved performing myomectomy operation concurrently with caesarean delivery in 17 pregnant patients with myomas measuring less than 5 cm and in 17 pregnant patients with myomas measuring greater than 5 cm. The most prevalent kind was corpus localised (79.4%), the most pathologically normal leiomyoma nodule (82.4%), and the most uncommon one was cellular leiomyoma (2.99%). Subserosal myoma was the most common kind, accounting for 64.7% of cases. There were no statistical differences seen between the two groups in terms of age, gestational age, infant weight at delivery, pre- and post-operative haemorrhage, requirement for blood transfusion, myoma location, myoma type, and pathological examination. Upon analysing all clinical data, a statistically significant difference was detected between the two groups when evaluating the operation duration of individuals with myomas measuring under 5 cm and those with myomas measuring 5 cm or greater (45.47±9.94 vs 52.88±11.09) (p=0.048).

Conclusion: In proficient medical facilities, the practice of conducting myomectomy during caesarean delivery, irrespective of the size of the myoma, may be regarded as a secure and efficient method in selected patients. It is important to acknowledge that the duration of the operation may be extended as the size of the myoma grows.

Keywords: *Caesarean Section; Caesarean Myomectomy; Myoma Uteri; Myoma Size; Operation Time*

ÖZET

Amaç: Sezaryen operasyonu sırasında myomektomi yapılan olgularda myom boyutlarının intraoperatif ve postoperatif klinik sonuçlar üzerine etkisinin araştırılması amaçlandı.

Gereç ve Yöntemler: Sezaryen myomektomi yapılan 34 olgunun sonuçları retrospektif olarak incelendi. Hastaların demografik, klinik ve patolojik verileri olgular myom boyutuna göre 5 cm altı ve 5 cm ve üstü olarak iki grup olarak incelendi. Anne yaşı, gravida, parite, abortus, doğumdaki gebelik haftası, bebek doğum kilosu, operasyon süresi, myom özellikleri, operasyon öncesi ve sonrası hemoglobin değerleri, transfüzyon ihtiyacı, patoloji sonuçları karşılaştırıldı.

Bulgular: Çalışmamızda myom boyutları 5 cm altı 17 gebe hastaya ve 5 cm ve üstü olarak 17 gebe hastaya sezaryen esnasında myomektomi operasyonu aynı anda uygulandı. En sık korpus yerleşimli (%79,4), patolojik olarak en sık normal leiomyoma nodülü (%82,4) en az ise sellüler leiomyoma (%2,99) izlendi. En sık myoma çeşidi ise %64,7 oranında subserozal yerleşimli olarak görüldü. iki grup arasında yaş, gebelik haftası, doğumda bebek kilosu, operasyon öncesi ve sonrası kanama, transfüzyon ihtiyacı, myom yerleşimi, myom çeşidi ve patolojik inceleme açısından istatistiksel olarak farklılık saptanmadı. Tüm klinik veriler incelendiğinde ise 5 cm altı ve 5 cm ve üstü iki grup operasyon süresi açısından değerlendirildiğinde iki grup arasında istatistiksel olarak anlamlı farklılık izlendi (45,47±9,94 vs 52,88±11,09) (p=0,048).

Sonuç: Tecrübeli kliniklerde, sezaryen sırasında myom boyutundan bağımsız olarak myomektomi yapılması seçilmiş hastalarda güvenli ve etkin bir yöntem olarak kabul edilebilir. Operasyon süresinin myom boyutu arttıkça uzayabileceği unutulmamalıdır. Uygun yerleşimli myomlarda sezaryen sırasında myomektomi yapılması maternal morbidite ve mortaliye artırmamaktadır.

Anahtar Kelimeler: *Sezaryen Doğum; Sezaryen Myomektomi; Myoma Uteri; Myom Boyutu; Operasyon Süresi*

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INTRODUCTION

Leiomyomas, which are also diagnosed as fibroids, are the most prevalent benign gynaecological tumours among women of reproductive age (1). Leiomyomas are smooth muscle cell-derived monoclonal tumoral formations (2). Typically, they manifest without apparent symptoms and are identified through routine gynaecological examinations (3).

Myoma incidence during pregnancy ranges from 3 to 10% (3). During pregnancy, hormonal changes and increased blood flow to the uterus cause these hormone-sensitive benign tumours to become larger. These lesions, which are typically asymptomatic, result in pelvic pain as a consequence of degeneration induced by estrogenic alterations in the body during pregnancy. Additionally, they may result in complications during pregnancy. Specifically, they can induce complications such as threatening miscarriage, preterm delivery, ectopic pregnancy, premature membrane rupture, placental abruption, placental location abnormalities, antenatal haemorrhage, and, in rare cases, high blood pressure during pregnancy (4).

Pregnancies at an advanced age are on the rise at present. Furthermore, concerning birth, it is regrettable to report that the incidence of operative births (caesarean sections) continues to rise on a daily basis. In underdeveloped countries, the caesarean section (CS) rates are around 6%, in developed countries 27.2%, and when looking at the world average, it is approximately 18.6%; however, these rates continue to increase (5).

As the incidence of myoma rises with age and the number of pregnancies in older women grows, there is a corresponding increase in the number of pregnancies identified with myoma and associated problems. Hence, it is important to diagnose and treat complications that may arise as a result of myoma during a caesarean birth (5, 6). The incidence of complications associated with myomas is rising as a result of an increasing number of births at advanced maternal age and the higher rates of caesarean deliveries. Clinicians continue to be concerned about performing myomectomy, particularly after caesarean birth, due to the increased problems that may ensue. Myomectomy, particularly when done during caesarean birth, can lead to serious complications including heightened bleeding, uterine atony, and infertility due to the need for a hysterectomy. Due to these many factors, it is not advisable to do a myomectomy as routine procedure during a caesarean delivery. Myomectomy is not suggested during caesarean birth if it is suspected to create serious complications, particularly if it is located in the lower portion of the uterus or the posterior wall (7, 8, 9).

We know that there is 3-4 times increase in uterine blood flow due to physiological changes that occur during pregnancy. Consequently, it is established that there is a physiological enhancement in the blood supply to the fetus and placenta within the uterus, as well as an increase in blood flow to the myoma. During caesarean sections and myomectomy surgeries, a lack of clinical knowledge and ineffective control of bleeding might lead to a higher demand for blood and blood product transfusions in around 20-25% of cases. This might result in an increase in serious complications, and which might lead to severe problems such as infertility due to hysterectomy. It is important to remember that including myomectomy during caesarean delivery has serious potential complications owing to physiological and pathological alterations. Therefore, it is advisable to only do this procedure in carefully chosen patients, after acquiring the required expertise and taking appropriate precautions (10, 11).

Recent literature indicates that myomectomy performed during caesarean section is a secure surgical procedure for specific patient populations in medical facilities with clinical expertise. This procedure has been found to yield positive results in subsequent pregnancies by reducing complications, the need for additional surgeries, and associated risks. Based on the findings of these studies, it is concluded that myomectomy operation can be performed during caesarean delivery, particularly for patients who meet the acceptable criteria (12-15).

Our study examined the clinical and pathological characteristics of patients who had a myomectomy during caesarean delivery. We identified and discussed the potential complications that can occur during or after the procedure, based on existing literature. Additionally, we aimed to analyse the impact of myoma sizes on the clinical results.

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MATERIAL AND METHOD

The scope of our study encompasses pregnant women who have been diagnosed with myoma uteri and have applied to the same clinic from November 2017 to 2023. After obtaining authorization from the local ethics council (dated 18.04.2025 and numbered 4/10), a retrospective examination was conducted on the files of pregnant patients who were above 34 weeks and underwent caesarean section for various reasons, as well as those who received myomectomy simultaneously. The study comprised 34 cases, which were categorised into two groups based on the size of the myoma: cases with a size below 5 cm and cases with a size of 5 cm and greater. The study comprised cases that had myomectomy during caesarean section. Myomas detected incidentally were operated on during planned cesarean section under normal elective conditions and in cases with appropriate emergency cesarean section indications. Patients who experienced bleeding during pregnancy, patients who were diagnosed with placenta adhesion and placement problems, patients who had previously undergone myomectomy, patients with a history of gynaecological surgery in the pelvic region, patients who declined to participate in the study, patients with pre-eclampsia or eclampsia, patients with Hellp syndrome, patients with acute fatty liver disorder during pregnancy, cases of immune thrombocytopenic purpura, patients who had serious comorbidities, cases of premature delivery before 28 weeks' gestation, and cases with coagulation problems or the use of anti-coagulant medication were not included in the study. The patient files were reviewed to evaluate various factors including maternal age, previous pregnancy history, gestational week, preoperative and postoperative haemoglobin levels, baby weight at birth, operation time, location of the myoma nodule, pathological diagnosis, type according to location, whether blood transfusion was performed, history of postoperative complications, and the sizes and locations of the removed myomas during caesarean section.

The caesarean section and simultaneous myomectomy procedure were carried out by the same proficient surgical team. All caesarean section surgeries were conducted through a lower uterine segment incision at a single centre with expertise with postpartum haemorrhage and access to blood and blood supplies. If the myomectomy was performed simultaneously, the serosal incision and/or caesarean section was operated on and removed from the incision line if it was close to the incision line. All patients received an oxytocin infusion and a methylergonovine injection as part of their routine care to promote uterine contractions during and after a normal caesarean birth.

The excised myoma nodules were assessed by proficient pathologists within the same clinic. The largest diameter measured in the pathological examination was analysed as the myoma size. All pathology reports evaluated yielded no indication of cancer.

The statistical analysis of the study's findings was conducted using the SPSS v22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) programme. During the evaluation of the study data, descriptive statistical methods such as the Mean and Standard deviation were employed. Additionally, the Mann Whitney U test was utilised to compare quantitative data and assess the differences in normally distributed parameters between two groups. The Wilcoxon test was employed to compare variables within the same group. The Chi-Square test and Fisher's Exact test were employed to compare qualitative data. The significance was assessed at a level of $p<0.05$.

RESULTS

Our study included 34 cases who had myomectomy during caesarean birth. In 17 cases, the diameter of the excised myoma was a smaller than 5cm, whereas in the remaining 17, it was 5cm or greater. The patients' ages varied from 25 to 45 years, with an average of 33.62±4.80. Pregnancy weeks range from 28 to 40 weeks, with an average of 37.50 ± 2.15 weeks. Preoperative Hgb values range from 11 to 14.9, with an average of 11.64 ± 2.97. Postoperative Hgb levels range from 10 to 13.6, with an average of 10.51±3.21. Baby weights range from 1330 to 4000 grams, with an average of 2983.5 ± 665.01 grams. Operation times range from 35 to 70 minutes, with an average of 49.18 ± 11.03 minutes. Myoma locations were corpus in 27 (79.4%) cases, fundus in 6 (17.6%) cases, and cellular leiomyoma in 1 (2.9%) case. When the pathological distribution is analysed, it is shown that Degenerate Leiomyoma is

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found in 5 (14.7%) cases, Leiomyoma in 28 (82.4%) cases, and Cellular Leiomyoma in 1 (2.9%) case. No blood transfusions were administered in any of the cases, and no postoperative fever was detected. Myoma type was intramural in 10 (29.4%) of the cases, intramural/subserous in 1 (2.9%), pedular in 1 (2.9%), and subserous in 22 (Table 1).

There is no statistically significant difference in gravida, parity, and abortion rates based on myoma diameter (p>0.05). There is no statistically significant difference in myoma locations based on myoma diameter, pathological diagnostic type, or myoma uteri kinds (p>0.05) (Table 2).

There is no statistically significant difference in average age, weeks of pregnancy, or weight of the baby at birth based on myoma diameter (p>0.05). There is a statistically significant difference between operation times based on myoma diameter (p <0.05). The group with larger myoma diameters had a longer operation time. There is no statistically significant difference between preoperative and postoperative Hgb levels based on myoma diameter (p>0.05). In the group with a myoma diameter smaller than 5 cm, the reduction in postoperative Hgb levels compared to preoperative Hgb levels was not statistically significant (p>0.05). In the group with a myoma diameter of 5 or greater, the reduction in postoperative Hgb levels compared to preoperative Hgb levels was not statistically significant (p>0.05) (Table 3).

Table 1. Clinical and demographic characteristics of the cases.

		Min-Max	Mean±SD
Age		25-45	33.62±4.80
Week of Pregnancy		28-40	37.50±2.15
Preop Hgb		11-14.9	11.64±2.97
Postop Hgb		10-13.6	10.51±3.21
Baby Weight (gr)		1330-4000	2983.5±665.01
Operation time (min)		35-70	49.18±11.03
		n	%
Gravida	1	14	41.2
	2	4	11.8
	≥3	16	47
Parity	0	14	41.2
	1	6	17.6
	≥2	14	41.2
Abortion	0	13	65
	≥1	7	35
Myoma Location	Corpus	27	79.4
	Fundus	6	17.6
	Isthmus	1	2.9
Pathology	Degenerate Leiomyoma	5	14.7
	Leiomyoma	28	82.4
	Cellular Leiomyoma	1	2.9
Blood Transfusion	Not	34	100
Postoperative fever	Not	34	100
Myoma Type	Intramural	10	29.4
	Intramural/Subserous	1	2.9
	Pedunculated	1	2.9
	Subserous	22	64.7

Preop: preoperative, Postop: postoperative, Hgb: hemoglobin, gr: gram, min: minimum, max: maximum, SD: standard deviation, min: minute

Table 2. Evaluation of clinical characteristics of cases according to myoma diameter.

		Myoma Size< 5cm	Myoma Size≥ 5cm	P-value
		n; %	n; %	
Gravida	1	8;47.1	6;35.1	[3] 0.515
	2	3;17.6	1;5.9	
	3	3;17.6	5;29.4	
	≥4	3;17.6	5;29.4	
Parity	0	8;47.1	6;25.3	[2]0.751
	1	3;17.6	3;17.6	
	≥2	6;35.3	8;47.1	
Abortion	Not	6;66.7	7;63.6	[2]0.156
	Yes	3;33.3	4;36.4	
Myoma location	Corpus	13; 76.5	15; 88.2	[2]0.656
	Fundus	4; 23.5	2; 11.8	
Pathology	Degenerate Leiomyoma	3; 17.6	3; 27.6	[2]1.000
	Leiomyoma	14; 82.4	14; 82.4	
Myoma type	Intramural	4; 23.5	6; 35.3	[3]0.452
	Subserous	13; 76.5	11; 64.7	

[2]Fisher's Exact test, [3]Ki-Kare-test

Table 3. Characteristics of myomas in pregnant women who underwent cesarean section.

	Myoma size< 5cm	Myoma size≥ 5cm	P-value
	Mean±SD	Mean±SD	
Age	33.53±4.66	33.71±5.07	[1]0.917
Week of pregnancy	37.47±1.51	37.53±2.69	[1]0.938
Baby weight (gr)	2872.06±612.05	3095.0±715.04	[1]0.336
Operation time (min)	45.47±9.94	52.88±11.09	[1]0.048*
Pre-op Hgb	11.70±3.08	11.59±2.95	[1] 0.915
Post-op Hgb	10.94±2.91	10.07±3.52	[1] 0.441
Pre-op/ Post-op Hgb	[4] 0.404	[4] 0.179	

[1]Mann Whitney U test, [4] Wilcoxon test, *p<$^{0.05}$, Preop: preoperative, Postop: postoperative, Hgb: hemoglobin, gr: gram, min: minimum, max: maximum, SD: standard deviation

DISCUSSION

Our study analysed clinical, pathological, preoperative, and postoperative data from patients who received myomectomy during caesarean section. The cases who had myomectomy during caesarean section were divided into two groups based on myoma size: less than 5 cm and 5 cm or above. There was no statistically significant difference between the two groups when comparing age, gestational week, infant birth weight, uterine location of myomas, myoma kinds, pathological examination results, and preoperative and postoperative haemoglobin levels. However, it was discovered that the operation time in cases with myomas greater than 5 cm was statistically significant longer than in cases with myomas smaller than 5 cm (p=0.048). It demonstrates that the increases in myoma size between the two groups is unrelated to the increase in morbidity; the only difference is the increased operating time.

Gynaecological pathologies, particularly myoma, have become more common after surgical delivery in recent years as the number of advanced-age pregnancies and caesarean deliveries has increased worldwide. For all of these reasons, it is stated that performing a myomectomy operation during caesarean delivery has a positive effect on subsequent pregnancies and the

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patient's quality of life, the possibility of myoma re-developing is very low, and the risk of complications related to the operation is low (16, 17). However, it should be noted that myomectomy performed during caesarean delivery can result in serious morbidities such as postpartum bleeding and hysterectomy, including loss of fertility, so it is best to perform this procedure in effective centres with clinical experience and adequate blood and blood product replacement services. During our study, we did not administer any blood or blood products to 34 patients who underwent myomectomy during caesarean section. Furthermore, we did not observe any pathological findings that would lead to increased morbidity in the postoperative period, such as high fever or similar, in any of our patients' clinical vital signs.

Recently, it has been revealed that caesarean myomectomy is safe. Caesarean myomectomy is now widely regarded as an effective and safe procedure, particularly when performed by expert gynaecologists. Thus, the chance of repeat myomectomy surgery, the risks associated with repeat anaesthesia, and the expense are all decreased. Furthermore, the increased risk of pregnancy complications caused by mucosal-located myomas is reduced, and women's quality of life improves as a result of increased fertility after myomectomy and a decrease in clinical symptoms such as myoma-related pelvic pain and vaginal bleeding (18).

A study of 111 cases in which myomectomy was performed during caesarean section found that hysterectomy was never performed. Furthermore, there were no significant differences observed in terms of operation time, hospital stay, amount of bleeding, and rates of serious complications between the two groups (Those with myomectomy and those without). Caution is advised specifically while removing intramural deep-seated myomas, however it has been confirmed that myomectomy is generally safe regardless of the size and location of the myoma (12). None of the cases in our analysis required hysterectomy or any other surgical intervention to prevent bleeding, which is consistent with the results of all the cases that received myomectomy during caesarean delivery. There were no complications during or after the operation. Furthermore, it is worth noting that the majority of our cases exhibited myoma sizes of 5 cm or smaller and were located subserosally within the uterine corpus. As a result, the level of bleeding experienced was minimal, obviating the necessity for blood transfusion. Consequently, our incidence rates of fever and similar complications were lower in comparison to the existing body of literature (19).

When examining the literature, it is evident that myoma sizes play a crucial role in determining clinical and pathological results, as well as potential complications, in cases where caesarean myomectomy is performed. This highlights the significance of myoma sizes in all obstetric or gynaecological scenarios requiring myomectomy. However, we may conclude that there is no obvious cut-off value for myoma sizes. Upon reviewing the conducted studies, it was found that performing myomectomy during caesarean section is safe, regardless of the number, size, and location of myomas. This conclusion was based on a study that included cases with myoma sizes of 5 cm and above, where no complications were observed. Another study found no significant variation in the reduction of haemoglobin levels, length of hospital stays, and duration of surgery among patients with myomas larger than 5 cm who underwent caesarean myomectomy. The size and location of the myoma did not affect the feasibility of performing myomectomy (20).

A meta-analysis of 2301 cases was conducted, comparing cases with and without myomectomy after caesarean delivery. The average haemoglobin reduction in the caesarean myomectomy group was 0.25 mg/dL greater (95% [CI]: 0.06-0.45), and the requirement for blood transfusion was increased [OR]: 1.41; 95% [CI]: 0.96-2.07 (21). However, another retrospective cohort study published in 2019 reported no difference in average Hb decrease or blood transfusion rate between patients who received CS myomectomy and those who underwent CS alone (19). In our study, when we examined the cases who underwent myomectomy during caesarean section as below 5 cm and 5 cm and above, there was no difference between the two groups in terms of myoma location, pathological examination, myoma types, and amount of bleeding, and the operation time was only statistically significantly longer in cases with myomas

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of 5 cm and above. However, no increased bleeding, blood and blood product replacement, wound infection, or similar complication rates were found in any case related to the longer duration.

It is believed that myomectomy conducted after a caesarean delivery takes longer, regardless of the size of the myoma. It is stated that the difference in average operation times is statistically significant (22-24). Another study indicated that when myomectomy was performed during a caesarean section, the operation time was statistically significantly longer in the groups who had intramural and subserosal myomectomy than in the groups who did not (25).

A comparative analysis was conducted between 21 pregnant patients diagnosed with myoma uteri measuring above 5 cm and 68 pregnant patients with myoma uteri measuring under 5 cm. The analysis focused on evaluating the clinical, pathological, and complications following myomectomy performed during caesarean section. The operation time was found to be 13.1 minutes longer in the over 5 cm group, but it was stated that there was no statistically significant difference in terms of operation time between the two groups. In addition, the study reported that the duration of hospitalisation was 0.6 days longer in the group with myomectomy greater than 5 cm, but this was not statistically significant (26). Our study reveals that the average operation time was 7.41 minutes longer on average (52.88±11.09 compared to 45.47±9.94) in the group where myomectomy was performed over 5 cm, and this difference was statistically significant (p=0.048).

When myoma uteri is identified, particularly in gynaecology, despite the progress made in medical and surgical treatments, hysterectomy is still the preferred option over fertility-sparing surgery. Upon reviewing the literature, particularly regarding abdominal myomectomy operations, it has been reported that there is a transition to hysterectomy in % 2cases due to bleeding and similar serious complications, especially due to inadequate haemostasis. Despite retrospective studies indicating a 0% rate of serious complications, such as loss of fertility or hysterectomy, after caesarean myomectomy, clinicians continue to avoid this procedure due to concerns about potential risks (19, 27, 28). In this study, we did not develop any potentially serious complications in all myomectomy cases in which 5 cm below or above 5 cm were removed in the CS. Furthermore, we did not have any cases in which a hysterectomy was conducted in a manner that would result in a loss of fertility.

When examining the studies overall, a comparison was made between the operation times in cases with and without myomectomy during caesarean section. It was noted that the operation times were generally longer, ranging from 5 to 15 minutes, in the myomectomy group. It is stated that this difference in operation times is of no importance, because it has been stated that the group without myomectomy may need a second operation later, which causes an increase in surgical and anaesthesia complications and an increase in cost (10, 29). In our study, myomectomy was conducted in all cases. In our study, myomectomy was conducted in all cases, and when these cases were reviewed in terms of myoma size, we can conclude that it is important since it is the first clinical study to indicate that the operation duration may rise as the myoma size grows.

The primary concern during a myomectomy operation performed during a caesarean section is the occurrence of post-myomectomy haemorrhage. Consequently, healthcare professionals universally refrain from doing myomectomy operations during caesarean sections. In reality, the contractility of the uterus is the most important predictor of the risk of bleeding in myomectomy surgery during caesarean section, both in gynaecological and especially in obstetric cases. Furthermore, it is important to acknowledge the physiological thrombogenic condition that occurs during pregnancy. This condition involves an elevation in coagulation factors that promote clotting, as well as an increase in the contractile capacity of the pregnant uterus. These physiological changes effectively prevent bleeding, despite the increased blood flow in the pregnant uterus. Upon completion of data analysis, a caesarean myomectomy operation may be advised in specific cases, conducted by skilled medical facilities and an experienced surgical team, while considering all protective and risky variables associated with pregnancy.

Our study has some limitations. The most important limitations of our study include its retrospective

nature, limited number of participants, absence of a control group comprising individuals diagnosed with myoma during caesarean section but not subjected to myomectomy, and the absence of long-term clinical monitoring and data on subsequent pregnancies. Furthermore, a relative decrease in morbidity may have been detected due to myoma location, size, and number, as well as clinical heterogeneity, and each case could not be examined individually in terms of potential complications. The fact that all our cases underwent myomectomy during caesarean section and the absence of a control group that did not do so may actually reduce the risk of bias, because in selected cases, the removal of single, millimetrically small and pedunculated or serosal myomas could have resulted in similar selection bias, as well as reducing morbidity. Moreover, the expertise of our centre in this field may have reduced the risk of complications.

Nevertheless, However, after the caesarean myomectomy operation performed in a single experienced centre by the same surgical team experienced in terms of postpartum bleeding, the fact that our clinical results support myomectomy during caesarean section, in line with the literature, can be seen as the most important strength. Furthermore, our study's strength is underscored when we consider the possibility that all myomas identified during caesarean section were removed without differentiation of their localised area, type, and size, and that if not eliminated, a subsequent operation may be necessary.

CONCLUSION

Performing a myomectomy during a caesarean section does not result in serious morbidity or mortality. There is a lengthening of the surgical procedure's duration, particularly in cases with large-sized myomas. However, this does not result in serious postoperative complications. Myomectomy operations can be successfully carried out during caesarean sections in skilled medical facilities.

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EVALUATION OF THE LEVELS OF ANXIETY AND SELF-ESTEEM EXPERIENCED BY EMERGENCY SERVICE PERSONNEL AT THE BEGINNING AND END OF THEIR SHIFT

Acil Servis Çalışanlarında Vardiya Başlangıcında ve Bitişinde Olan Anksiyete ve Benlik Saygısının Değerlendirilmesi

Meral YILDIRIM[1], Tuba SAFAK[2], Gulsah CIKRIKCI ISIK[3], Yunsur CEVIK[1]

ABSTRACT

Objective: This study aimed to evaluate changes in anxiety and self-esteem among emergency department (ED) staff at the beginning and end of their shifts.

Material and Methods: A cross-sectional study was conducted at a tertiary hospital's ED in between September 2022-March 2023.Participants, including all ED staff with more than 6 months of experience, completed the State-Trait Anxiety Inventory (STAI), Rosenberg's Self-Esteem Scale (RSES), and the Self-Esteem Rating Scale-Short Form (SERS-SF) at start and end of their shifts.Data were analyzed with comparisons made using paired t-tests and Wilcoxon tests for dependent groups and independent t-tests and Mann-Whitney U tests for independent groups.Correlations between STAI-2 and SERS-SF scores were examined using Spearman's correlation test.

Results: Mean STAI-2 score was 40±8, indicating moderate trait anxiety, while STAI-1 scores at shift start averaged 39±11 in 108 participants.Self-esteem scores, measured by SERS-SF (median 108) and RSES (median 3), were high.No significant changes in anxiety or self-esteem scores were observed.A weak negative correlation was found between STAI-2 and SERS-SF scores ($r = -0.484$, $p < 0.001$), but no correlation existed between STAI-2 and RSES.

Conclusion: ED staff experienced moderate levels of anxiety, which remained stable throughout their shifts. High self-esteem among participants may contribute to stable anxiety levels.

Keywords: *Anxiety; Emergency; Self-Esteem*

ÖZET

Amaç: Bu çalışmada acil servis (AS) çalışanlarının vardiyalarının başında ve sonunda anksiyete ve benlik saygılarındaki değişikliklerin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Eylül 2022-Mart 2023 tarihleri arasında üçüncü basamak bir hastanenin acil servisinde yapılan kesitsel bu çalışmada 6 aydan fazla deneyimi olan tüm acil servis personeli dahil olmak üzere katılımcılar, vardiyalarının başında ve sonunda Durumsal-Sürekli Kaygı Envanteri (STAI), Rosenberg Benlik Saygısı Ölçeği (RSES) ve Benlik Saygısı Derecelendirme Ölçeği-Kısa Formu'nu (SERS-SF) doldurdular. Veriler, bağımlı gruplar için eşleştirilmiş t-testleri ve Wilcoxon testleri, bağımsız gruplar için ise bağımsız t-testleri ve Mann-Whitney U testleri kullanılarak yapılan karşılaştırmalarla analiz edildi. STAI-2 ve SERS-SF puanları arasındaki korelasyonlar Spearman korelasyon testi kullanılarak incelendi.

Bulgular: Ortalama STAI-2 puanı 40±8 olup, orta düzeyde sürekli kaygıyı gösterirken, vardiya başlangıcında STAI-1 puanı 108 katılımcıda ortalama 39±11 idi. SERS-SF (ortanca 108) ve RSES (ortanca 3) ile ölçülen öz saygı puanları yüksekti. Kaygı veya benlik saygısı puanlarında anlamlı bir değişiklik gözlenmedi. STAI-2 ve SERS-SF puanları arasında zayıf bir negatif korelasyon bulundu ($r = -0,484$, $p < 0,001$), ancak STAI-2 ve RSES arasında bir korelasyon yoktu.

Sonuç: Acil servis personelinin, vardiyaları boyunca sabit kalan orta düzeyde kaygı yaşadığı görülmüştür. Katılımcılar arasındaki yüksek benlik saygı, stabil kaygı düzeylerinde katkısı olduğu düşünülmektedir.

Anahtar Kelimeler: *Anksiyete; Acil Servis; Benlik Saygısı*

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INTRODUCTION

Emergency departments (ED) are the most chaotic departments of hospitals. The necessity for immediate medical attention, coupled with the congestion that characterizes emergency departments, can precipitate a highly stressful environment for healthcare professionals. Furthermore, the frequent occurrence of traumatic events and deaths, coupled with the elevated prevalence of violence against healthcare workers in emergency departments, may serve as significant contributing factors to the development of anxiety and stress. Consequently, these adverse factors may have an impact on the physical and mental wellbeing of ED staff (1).

Stress is the most significant risk factor for depressive disorders, sleep disorders, substance abuse, and anxiety. The term 'anxiety' is defined in the updated literature as a high level of worry that is not accompanied by an objective danger. Anxiety can be classified into two categories: state anxiety and trait anxiety. State anxiety manifests when an individual encounters a dangerous and undesirable situation. In contrast, trait anxiety occurs independently or disproportionately from any objective reason and is characterized by a pervasive sense of worry or tension, which is associated with increased activity of the autonomic nervous system (2).

Work-related stress is a significant contributing factor to the development of anxiety disorders. Although anxiety is a necessary reflex for survival, it has the potential to negatively impact quality of life when it is excessive. Several studies have demonstrated that ED staff exhibit higher levels of anxiety than other healthcare providers. This is thought to be due to several factors, including working in shifts, irregular sleep habits and excessive workload (3). This may result in burnout and the dismissal of staff. One factor that protects an individual from burnout is self-esteem. Job dissatisfaction and low motivation can lead to a decrease in self-esteem (4, 5).

The objective of this study was to evaluate changes in anxiety and self-esteem among ED staff before and after shifts.

MATERIALS AND METHODS

This was a cross-sectional study conducted in an emergency department of a tertiary hospital with approximately one thousand daily admissions in the capital, between September 2022 and March 2023. Local ethics committee approval was obtained from Ethic Committee of Keçiören Training and Research Hospital at 26/02/2020.

Staff who had worked in the ED for more than 6 months in any role (doctor, nurse, security, medical secretary, etc.) were included in the study. Written informed consent was obtained from all participants. The State-Trait Anxiety Inventory (STAI), Rosenberg's Self-Esteem Scale (RSES) and the Self-Esteem Rating Scale-Short Form (SERS-SF) were administered to all participants at the beginning and end of their ED shift to assess anxiety and self-esteem. Demographic data and test scores were recorded on study forms. Participants who did not answer all questions on the forms or who did not attend before or after their shift were excluded.

The State-Trait Anxiety Inventory (STAI) was first developed by Spielberger et al in 1970, revised in 1983 and translated into Turkish by Öner and Le Compte in 1985. This scale has two subscales, the first part (STAI-1) measures the current level of anxiety (state) and the second part (STAI-2) assesses the relatively stable state of anxiety (trait). Each section consists of 20 questions answered on a 4-point Likert scale, so the total score of the STAI subscales can vary from 20 to 80. Average scores generally range from 36 to 41, with scores of 20-37 indicating no or low anxiety, 38-44 moderate anxiety, and 45-80 high anxiety (6, 7).

The Rosenberg’s Self-Esteem Scale (RSES) was developed by Rosenberg in 1965 and its Turkish adaptation was made by Çuhadaroğlu in 1986. It consists of ten sentences (the first 5 in a positive way, the last 5 in a negative way) using a 4-point Likert scale. High scores indicate high level of self-esteem and test group participants in three as high, medium and low level of self-esteem in the end (8). We coded the participants as 3, 2 and 1 for high, medium and low levels of self-esteem respectively.

The The Self Esteem Rating Scale-Short Form (SERS-SF) was first developed by Nugent and Thomas in 1993, and Lecomte et al. shortened it to 10 negative and 10 positive items, using a 7-point Likert scale (9). Thus, the original scores vary between (-10 to -70) for negative self-esteem and (+10 to +70) for positive

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self-esteem. In our study, to facilitate interpretation, a formulation was used: [(70 + total score in negative phrases) + (total score in positive phrases)], so our scores could be between 10 - 130, with higher scores indicating high levels of self-esteem.

Data were interpreted using SPSS 22.0 (Chicago, IL, USA). After analysing the distribution of normality with the Shapiro-Wilk test, normally distributed data were presented as mean ± standard deviation (SD) and non-normally distributed data were presented as median and interquartile range (IQR)25-75. Comparisons between independent groups were made using the Independent Sample t test for parametric variables and the Mann-Whitney U test for non-parametric variables. Comparisons between dependent groups were made using paired sample t-test for parametric variables and Wilcoxon test for non-parametric variables. Correlation between STAI-2 and SERS-SF was analysed by Spearman correlation test. $P<0.05$ was considered statistically significant for all tests.

RESULTS

The study included a total of 108 participants, of whom 23 were doctors, 33 were nurses and 52 were other ED staff. Fifty-seven of the participants were female and the mean age of the participants was 37±8 years. General characteristics of the participants are shown in Table 1.

The participants' anxiety and self-esteem were assessed using different scales. The mean STAI-2 score was 40±8, which means that the current anxiety level of the participants was at the moderate level. At the beginning of the shift, the mean STAI-1 score, which shows the current level of anxiety, was 39±11, which was similar to the STAI-2 score. In terms of self-esteem, the SERS-SF score was 108 (IQR 25-75%: 98 - 115.75) and the RSES score was 3 (IQR 25-75%: 3-3), indicating that their self-esteem was healthy and at a good level. We assessed these scores at the end of the shift and there was no difference in anxiety levels and self-esteem scores between the beginning and end of the shift (Table 2).

We also evaluated the anxiety and self-esteem scores according to a number of variables. Firstly, there was no difference in these scores between males and females; also, in the within-group comparisons, there was no difference between the scores at the beginning and end of the shift for either females or males. We divided the participants into two groups according to their role in the ED. Emergency physicians, junior doctors and nurses made up the first group, and other duties made up the second group. Anxiety and self-esteem scores were similar between the groups. The only difference between the groups was in the RSES

Table 1. General features of the participants

	N=108
Age (mean ± SD)	37±8
Gender (n)	
Female	57
Male	51
Duty (n)	
ED specialist	7
ED resident	16
Nurse	23
Medical secretary	22
Security	13
Cleaning staff	7
Servant	10
Time period on duty (n)	
6 month – 5 years	39
5 – 10 years	37
>10 years	32

Abbreviations: SD: Standart Deviation, ED: Emergency department

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score of the healthcare workers, which decreased at the end of the shift. We also analysed the scores according to the length of time they had worked in the ED, dividing the participants into two groups: those who had worked in the ED for less than 5 years and those who had worked in the ED for more than 5 years. Again, there was no difference between the groups according to length of time in the ED. In between group comparisons, the SERS-SF score at the end of the shift was increased in participants who had worked ≥5 years in the ED. (Table 3).

We analysed the correlation between anxiety and self-esteem scores. There was a weak negative correlation between STAI-2 and SERS-SF scores of the participants (p=<0.001 and r= -484). There was no correlation between the STAI-2 and the RSES.

DISCUSSION

In this study, in which anxiety and self-esteem were assessed in emergency service staff at the beginning and end of their shift in the ED, the results showed that there was no significant difference in participants' anxiety levels and self-esteem scores between the beginning and end of their shift. On the other hand, staff anxiety scores were generally at a moderate level and didn't differ according to participants' gender, role

Table 2. Anxiety and self-esteem scores of the participants at the beginning and end of the shift.

N=108	General score	Beginning of the shift	End of the shift	P value
STAI-2*	40.3±8.3			
STAI-1**		39.4±10.7	39.3±9.7	0.86
SERS-SF		108 (IQR 98 – 115.75)	110 (IQR 97 – 118)	0.12
RSES		3 (IQR 3 – 3)	3 (IQR 3 – 3)	0.22

*STAI-2 shows general anxiety level of the patient. **STAI-1 shows momentary anxiety level of the patient Abbreviations: STAI: State Trait Anxiety Inventory, SERS-SF: Self-esteem Rating Scale Short Form, RSES: Rosenberg Self-esteem Scale

Table 3. Anxiety and self-esteem scores of the participants according to variables

	STAI-2	STAI-1			SERS-SF			RSES		
	General score	Beginning of the shift	End of the shift	P1 (in group*)	Beginning of the shift	End of the shift	P1 (in group*)	Beginning of the shift	End of the shift	P1 (in group*)
Gender										
Female	41±7	39±10	39±10	0.839	106 (IQR 98-112)	107 (IQR 96-116)	0.422	3 (IQR 3- 3)	3 (IQR 3- 3)	0.48
Male	40±9	40±12	40±10	0.971	111 (IQR 98-116)	113 (IQR 98-118)	0.181	3 (IQR 3- 3)	3 (IQR 2- 3)	0.317
P2 (between groups**)	0.053	0.182	0.785		0.155	0.092		0.866	0.706	
Duty										
Health staff	39±7	39±11	39±11	0.550	108 (IQR 98-114)	111 (IQR 98-117)	0.053	3 (IQR 3-3)	3 (IQR 2.25-3)	0.034
Other staff	42±9	40±10	40±9	0.777	109 (IQR 98-118)	109 (IQR 96-120)	0.930	3 (IQR 3-3)	3 (IQR 3-3)	1.0
P2 (between groups)	0.116	0.388	0.05		0.389	0.944		0.228	0.862	
Tenure										
<5 years	39±8	39±11	37±10	0.284	106 (IQR 97-112)	107 (IQR 97-113)	0.338	3 (IQR 3-3)	3 (IQR 2-3)	1.0
≥5 years	41±8	40±11	41±9	0.665	109 (IQR 98-117)	112 (IQR 97-121)	0.01	3 (IQR 3-3)	3 (IQR 3-3)	0.134
P2 (between groups)	0.618	0.727	0.907		0.332	0.058		0.335	0.809	

*In group comparisons analyzed the difference between scores of the beginning and end of the shift, in that particular group. **Between group comparisons analyzed the difference between the scores according to gender, duty and seniority on duty of the groups. Abbreviations: STAI: State Trait Anxiety Inventory, SERS-SF: Self-esteem Rating Scale Short Form, RSES: Rosenberg Self-esteem Scale, P: p value, IQR: Inter Quartile Range

or tenure.

Anxiety is a state of worry, fear or apprehension that individuals often experience in response to threatening or stressful situations. These feelings can be a normal part of everyday life and are usually a temporary reaction. However, when anxiety becomes severe and persistent, it is considered a psychiatric disorder that affects the individual's quality of life (10). In emergency services, which are among the most demanding and intensive areas of health care, factors such as uncertainty, heavy workloads and night shifts are situations that increase anxiety levels in workers (1). In a study by Sonmez et al, emergency physicians were found to have low to moderate levels of anxiety and high levels of occupational burnout (11). In a study conducted in China, anxiety was found in 62% of night shift nurses, and factors influencing the level of anxiety were identified as busyness during night shifts, food intake during shift work, working > 40 h/week during shift work, and sleep quality before and after night shifts (12). Although there was no difference in state anxiety levels before and after shifts, the trait anxiety scores of the staff were at a moderate level, in accordance with the literature.

Self-esteem is a psychological state that expresses an individual's self-worth and respect. It determines how valuable and important a person feels about themselves, their own competence and how they see themselves in general (13). High self-esteem is known to make positive contributions in many areas, such as self-efficacy, positive emotionality and attachment security (14). Studies have also demonstrated that self-esteem is an important regulator of anxiety and emotion regulation (15). A study from India showed that health workers with low self-esteem were almost three times more likely to experience high stress, and those who were stressed were more than three times more likely to experience burnout (16). In our study, the participants' high self-esteem may have protected them from experiencing higher levels of anxiety.

The limitations of the study can be summarised as follows: The study only measured levels of anxiety and self-esteem at the beginning and end of the shift. This may not reflect daily variability and long-term trends. The study was conducted in a single centre and has limited generalisability. Each of the scales used has its own limitations. The simultaneous scoring of the two parts of the STAI, separating state and trait anxiety, may not reflect complex anxiety states in sufficient detail. The fact that the RSES and SERS-SF only measure self-esteem with specific statements may not capture all aspects of participants' self-esteem.

CONCLUSIONS

The present study evaluated anxiety and self-esteem among emergency service personnel. The findings indicated that the participants exhibited moderate anxiety levels, which remained consistent throughout the shift and were not influenced by gender, duty, or seniority. Conversely, the self-esteem scores were notably high, suggesting that this may serve as a protective factor for anxiety regulation.

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The authors declare that they have no conflict of interest to disclose.

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EXPLORING THE IMPACT OF ARTHROSCOPIC SURGERY ON SLEEP QUALITY AND CLINICAL RECOVERY IN CHRONIC LATERAL EPICONDYLITIS PATIENTS

Kronik Lateral Epikondilit Hastalarında Artroskopik Cerrahinin Uyku Kalitesi ve Klinik İyileşme Üzerindeki Etkisinin Araştırılması

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ABSTRACT

Objective: The purpose of the current study was to investigate the postoperative pattern of sleep quality and to evaluate the correlation between sleep quality and clinical scores in patients following arthroscopic surgery for chronic persistent lateral epicondylitis (ASCPLE).

Material and Methods: The current study included consecutive patients seeking lateral epicondylitis (LE) treatment at four orthopaedic outpatient clinics between 2020 and 2022 who failed to improve with conservative treatments and consented to ASCPLE. The current study evaluated patient demographics, the Pittsburgh Sleep Quality Index (PSQI), and patient-rated outcomes measures (PROMs) like the Disability of the Arm, Shoulder, and Hand (DASH) score and the Patient-rated Tennis Elbow Evaluation (PRTEE) score before and after ASCPLE surgery, with follow-up assessments at three weeks, three months, and six months.

Results: The study involved 28 patients aged 32-47 years. Statistically significant decreases were observed in the PSQI and DASH values at postoperative 3rd week, 3rd month, and 6th month compared to preoperative values ($p<0.05$). The PRTEE scoring showed a decrease in postoperative period and an increase in postoperative 6th month, albeit statistically lower than preoperative period. The present investigation revealed a significant correlation between preoperative PSQI scores and DASH and PRTEE scores, with a correlation of 71.9% and 67.3%, respectively.

Conclusion: ASCPLE significantly improves sleep quality and reduces clinical scores up to six months postoperatively, but caution is needed due to the potential risk of symptom recurrence and deteriorating sleep quality over time.

Keywords: *Elbow Tendinopathy; Sleep Quality; Arthroscopic Surgery*

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ÖZET

Amaç: Bu çalışmanın amacı kronik persistan lateral epikondilit (ASCPLE) nedeniyle artroskopik cerrahi uygulanan hastalarda ameliyat sonrası uyku kalitesi paternini araştırmak ve uyku kalitesi ile klinik skorlar arasındaki korelasyonu değerlendirmektir.

Gereç ve Yöntemler: Bu çalışmaya 2020-2022 yılları arasında dört ortopedi polikliniğinde lateral epikondilit (LE) tedavisi gören, konservatif tedavilerle iyileşme sağlanamayan ve ASCPLE'ye onay veren ardışık hastalar dahil edildi. Bu çalışmada, ASCPLE ameliyatı öncesinde ve sonrasında hasta demografisi, Pittsburgh Uyku Kalitesi İndeksi (PSQI) ve Kol, Omuz ve El Engelliliği (DASH) skoru ve Hasta Tarafından Değerlendirilen Tenisçi Dirseği Değerlendirmesi (PRTEE) skoru gibi hasta tarafından değerlendirilen sonuç ölçümleri (PROM'lar) üç hafta, üç ay ve altı aylık takip değerlendirmeleriyle değerlendirilmiştir.

Bulgular: Çalışmaya yaşları 32-47 arasında değişen 28 hasta dahil edildi. Postoperatif 3. hafta, 3. ay ve 6. ayda PSQI ve DASH değerlerinde preoperatif değerlere göre istatistiksel olarak anlamlı düşüşler gözlendi ($p<0,05$). PRTEE skorlamasında ameliyat öncesi döneme göre istatistiksel olarak daha düşük olmakla birlikte ameliyat sonrası dönemde azalma, ameliyat sonrası 6. ayda ise artış görüldü. Bu araştırma, ameliyat öncesi PSQI skorları ile DASH ve PRTEE skorları arasında sırasıyla %71,9 ve %67,3'lük bir korelasyon ile anlamlı bir ilişki olduğunu ortaya koymuştur.

Sonuç: ASCPLE, ameliyat sonrası altı aya kadar uyku kalitesini önemli ölçüde iyileştirmekte ve klinik skorları azaltmaktadır, ancak semptomların nüksetmesi ve zaman içinde uyku kalitesinin bozulması riski nedeniyle dikkatli olunması gerekmektedir.

Anahtar Kelimeler: *Dirsek Tendinopatisi; Uyku Kalitesi; Artroskopik Cerrahi*

INTRODUCTION

Lateral epicondylitis (LE), also referred to as tennis elbow, is a prevalent orthopaedic ailment that impacts approximately 1% to 3% of the overall population. It primarily affects individuals over the age of 40, with an equal distribution between genders (1,2). The available literature suggests that a significant proportion of LE cases, ranging from 70% to 90%, exhibit a clinical path characterised by either spontaneous remission or a positive response to conservative treatment strategies. These strategies often include rest, the administration of non-steroidal anti-inflammatory medicines, the use of orthotic devices, physical therapy interventions, and the application of injections (3). LE is a condition that arises due to the presence of overload, repetitive microtrauma, and degenerative alterations on the extensor carpi radialis brevis (ECRB) tendon. In cases where conservative care is not deemed effective, both arthroscopic and open surgeries are frequently considered as possible treatment options (4). The necessity of surgical treatment remains debatable and lacks a widely accepted consensus. However, surgical treatment, particularly using arthroscopic methods, is often beneficial for those experiencing prolonged and debilitating pain, even over six months of nonoperative therapy (5). Arthroscopic approaches offer advantages such as improved visualisation of intraarticular structures, shorter rehabilitation time, and reduced postoperative morbidity (6).

Sleep disruption is a commonly reported issue among people who have chronic pain (7-9). The relationship between persistent pain and sleep problems is reciprocal (10). Specifically, chronic pain may result in disruptions to sleep patterns, whereas those experiencing persistent insomnia are susceptible to developing chronic pain (8). Limited research exists on the association between chronic persistent LE and sleep quality (11). Nevertheless, a dearth of research exists in the scholarly literature regarding the investigation of alterations in sleep quality after arthroscopic surgery for chronic persistent lateral epicondylitis (ASCPLE). Hence, the current study aimed to investigate the potential enhancement of sleep quality and clinical outcomes in patients following ASCPLE. The hypothesis is that ASCPLE significantly improves sleep quality and reduces clinical scores up to six months postoperatively.

MATERIALS AND METHODS

Through clinical consultations and retrospective data analysis, an observational research was conducted. The current study reviewed the clinical records of patients who underwent ASCPLE at four orthopaedic outpatient departments between 2020 and 2022. The current study received approval from the ethics committee of the Fırat University Faculty of the Medicine (Approval Date: 27/09/2023, Approval Number: 2023/13-44). All patients provided the written informed consent form under with the ethical guidelines set forth by the hospital's committee. Patients who sought treatment for LE at two orthopaedic outpatient clinic between 2020 and 2022, attempted conservative treatments such as rest, splinting, and local injection therapy (steroid) without improvement, and consented to ASCPLE were included in the study. The exclusion criteria for the current study were as follows: individuals who had undergone prior surgical intervention in the elbow region for any reason; those who had not received conservative treatments (such as rest, splinting, and local injections) for LE for a minimum of 6 months; individuals with inflammatory disease in the elbow region; those with diabetes, sleep apnea syndrome, or restless leg syndrome; individuals with autoimmune disease; patients using medications for neuropathic pain; and patients using medications for narcolepsy. Patient demographics, the Pittsburgh Sleep Quality Index (PSQI), the patient-rated outcomes measures (PROMs) such as the Disability of the Arm, Shoulder, and Hand (DASH) score, and a Patient-rated Tennis Elbow Evaluation (PRTEE) score were collected prior to surgery. The participants were instructed to come back for a follow-up assessment on the PSQI, DASH, and PRTEE three weeks, three months, and six months after undergoing ASCPLE.

The PSQI is a validated instrument used for the evaluation of sleep quality (12). The assessment consists of a series of 19 questions that the patient answers, which are categorised into seven distinct sections: sleep quality, sleep onset latency, sleep duration, habitual sleep efficiency, presence of sleep disorders, use of sleep medicine, and daily functional impairment. Each part is assigned a numerical ranking ranging from 0 to 3, where a score of 0 indicates the absence of any disruption and a score of 3 indicates the

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lowest quality of sleep. The cumulative total of these seven sections determines the comprehensive PSQI score, whereby a higher score indicates worse sleep quality. A cumulative number over 5 indicates a state of sleep deprivation. There are five supplementary inquiries that pertain to the assessment of the patient's partner or roommate, which have no impact on the overall outcome.

The Patient-Rated Tennis Elbow Evaluation Scale (PRTEE) was used to assess levels of forearm discomfort and impairment in individuals diagnosed with LE. The scale is comprised of two distinct components, namely pain (consisting of five items) and functional activities (consisting of ten items). Each item is assigned a numerical value ranging from 0, indicating the absence of pain or difficulty in task performance, to 10, representing the most severe pain or complete inability to do the activity. The cumulative score is derived from the combination of the scores from both components (13,14).

The DASH is classified as a PROM because it solicits an individual's subjective evaluation of their recuperation following an upper-extremity injury (15). The injured individual is required to assess their condition by completing a 30-item questionnaire that measures their pain level and ability to perform various tasks. The International Classification of Functioning, Disability, and Health Framework (ICF) includes seven questions that assess pain intensity, falling under the category of body function and structure (16). Additionally, there are 23 items that evaluate an individual's ability to engage in different activities, categorised under Activity/Participation in the ICF.

All surgical procedures were conducted with general anaesthesia while the patient was positioned in the lateral decubitus posture. The surgical procedures were conducted by orthopaedic specialists who possessed a minimum of 5 years of expertise in the field and had sufficient experience in elbow arthroscopy. The elbow joint was filled with 15 ml of saline solution, resulting in the displacement of the brachial artery and median nerve in an anterior direction. Typically, two conventional arthroscopic portals were used. The proximal anteromedial portal is situated at a distance of roughly 2cm proximal and 2cm anterior to the medial epicondyle. Similarly, the proximal lateral portal is located around 2cm proximal and 2cm anterior to the lateral epicondyle in the region sometimes referred to as the 'soft spot'. The diagnostic arthroscopy is conducted via the medial viewing portal prior to establishing the lateral operating portal, using the 30 scope. This facilitates the visualisation of the anterior section of the elbow and enables a comprehensive assessment of the lateral tissues, particularly the ECRB tendon. A mechanical shaver with a diameter of 4.5 mm is introduced into the cannula, and the process is started. The distal excision of the radio-capitellar capsular complex was performed up to the standard annular ligament. Subsequently, an assessment of the radio-capitellar joint was conducted in both flexion and extension to verify the absence of any further impingement. The ECRB tendon's origin is located outside the joint and necessitates visualisation throughout the surgery. The ECRB tendon inside the joint capsule was excised using a shaver. Subsequently, the region situated immediately inferior to the superior capitellum is excised, a location that is in close proximity to the ECRB tendon. The resection procedure is terminated upon the visual identification of the extensor carpi radialis longus (ECRL) fibres. The decortication of the lateral epicondyle was not performed. A soft, thick dressing was put on the portals after they were stitched up. The patients were instructed to wear a splint for a duration of 2-3 days. They were advised to initiate elbow range of motion (ROM) exercises after the removal of the splint, and the ends of the sutures were then removed after a period of two weeks.

The statistical analyses in the current study were conducted using IBM SPSS Statistics 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) software. The normality of the parameters was assessed using the Shapiro-Wilks test. Descriptive statistical methods, such as mean, standard deviation, and frequency, were employed alongside the Friedman test to compare parameters that did not exhibit a normal distribution across different periods. The Wilcoxon sign test was utilised to identify the specific period that contributed to the observed differences. Spearman's rho correlation analysis was employed to examine the associations between non-normally distributed parameters. The

significance level was set at p<0.05.

RESULTS

The study included 28 patients, with ages ranging from 32 to 47 years. Of these patients, 15 (53.6%) were males and 13 (46.4%) were females. The mean age of the patients was 39.82±4.79 years. Patients' return to work was 36.2+8.6 days. The conservative follow-up period for the patients ranged from 8 to 12 months, with an average of 10.04±1.07 months and a median of 10 months (Table 1).

Statistically significant differences were observed in PSQI levels between preoperative, postoperative 3rd week, postoperative 3rd month, and postoperative 6th month (p<0.05). Statistically significant decreases were observed in the PSQI values at the postoperative 3rd week, 3rd month, and 6th month compared to preoperative values (p<0.05), based on pairwise comparisons. There was a statistically significant decrease in PSQI values at the 3rd month after surgery and a statistically significant increase in PSQI values at the 6th month after surgery, compared to the 3rd week after surgery (p1:0.040; p2:0.041; p<0.05). There was a statistically significant increase in PSQI values at the 6th month postoperative compared to the 3rd month postoperative (p:0.001; p<0.05) (Table 2) (Figure 1).

The analysis of DASH scores during the preoperative and postoperative periods revealed a decrease in scores after surgery, similar to the scoring of PSQI. However, unlike PSQI, there was no significant increase in DASH values observed in the sixth month after surgery (Table 3; Figure 1).

The analysis of PRTEE scoring revealed similar changes to the PSQI values. There was a significant decrease in the postoperative period and a significant increase in the postoperative 6th month, although the latter remained statistically lower than the preoperative period (Table 4; Figure 1).

Upon analysing the correlation between the three scores during the preoperative period, the present investigation revealed a significant association between preoperative PSQI scores and DASH and PRTEE scores, with a correlation of 71.9% and 67.3%, respectively (Table 5; Figure 1).

Table 1. Data on demographic characteristics of the patients

	Min-Max	Mean±SD
Age (year)	32-47	39.82±4.79
Return to work (day)	26-50	36.2+8.6
Conservative Follow-up time (month) $_{Median}$	8-12	10.04±1.07 (10)
Gender n,%		
Male	15	53.6
Female	13	46.4

Min: Minimum; Max: Maximum; SD: Standart Deviation.

Table 2. Analysing the changes in PSQI levels of patients over time

PSQI	Min-Max	Mean±SD (Median)
Preop	6-10	8.11±1.03 (8)
Postop 3.Weeks	4-7	5.32±0.72 (5)
Postop 3.Months	4-6	4.96±0.64 (5)
Postop 6.Months	4-7	5.68±0.77 (6)
p^1		0.001*
Preop-Postop 3.Weeks p^2		0.001*
Preop-Postop 3.Months p^2		0.002*
Preop-Postop 6.Months p^2		0.001*
Postop 3.Weeks-3.Months p^2		0.040*
Postop 3.Weeks-6.Months p^2		0.041*
Postop 3.Months-6.Months p^2		0.001*

p1: Friedman Test, p2: Wilcoxon Sign Test, *p<0.05, Min: Minimum; Max: Maximum; SD: Standart Deviation; Preop: Preoperative; Postop: Postoperative; PSQI: Pittsburg Sleep Quality Index.

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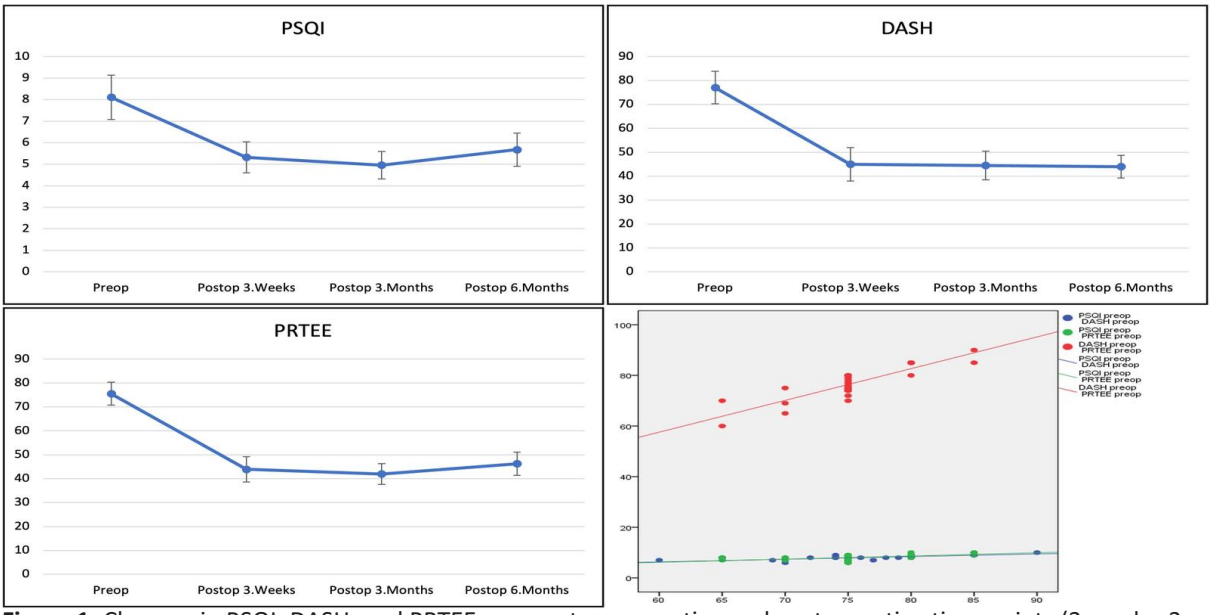

Figure 1. Changes in PSQI, DASH, and PRTEE scores at preoperative and postoperative time points (3 weeks, 3 months, and 6 months), along with correlations among their preoperative values.

Table 3. Investigation of the changes in DASH scores of patients over time

DASH	Min-Max	Mean±SD (Median)
Preop	60-90	77.07±6.83 (76.5)
Postop 3.Weeks	30-55	45±7.02 (45)
Postop 3.Months	34-55	44.5±5.97 (45)
Postop 6.Months	35-50	44±4.71 (45)
p^1		0.001*
Preop-Postop 3.Weeks p^2		0.001*
Preop-Postop 3.Months p^2		0.003*
Preop-Postop 6.Months p^2		0.001*
Postop 3.Weeks-3.Months p^2		0.572
Postop 3.Weeks-6.Months p^2		0.204
Postop 3.Months-6.Months p^2		0.349

p1: Friedman Test, p2: Wilcoxon Sign Test, *p<0.05, Min: Minimum; Max: Maximum; SD: Standart Deviation; Preop: Preoperative; Postop: Postoperative; DASH: Disabilities of the Arm, Shoulder and Hand.

DISCUSSION

The current study addresses a significant gap in the literature by examining the potential enhancement of sleep quality in patients following ASCPLE. The primary result of the current study was that patients who underwent ASCPLE experienced significant improvements in sleep quality at both the third week and the third month, as indicated by the analysis of PSQI values. Moreover, significant improvements were observed in the clinical outcomes of patients during the third week and third month when PROMs (DASH and PRTEE) were assessed. Upon evaluating all three scores in the current study, it was noted that the highest scores were achieved at the third month.

The authors suggested that the increase in nighttime pain levels is due to the increased levels of inflammatory cytokines associated with inflammation around tendon degenerative conditions (17,18). Inflammation is an important factor in LE, which is characterised by degeneration of the ECRB tendon (19). It is possible

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Table 4. Analysis of time-to-change in patients' PRTEE scores

PRTEE	Min-Max	Mean±SD (Median)
Preop	65-85	75.54±4.78 (75)
Postop 3.Weeks	35-55	43.93±5.33 (45)
Postop 3.Months	35-50	41.96±4.38 (40)
Postop 6.Months	35-55	46.25±4.84 (45)
p^1		0.001*
Preop-Postop 3.Weeks p^2		0.001*
Preop-Postop 3.Months p^2		0.003*
Preop-Postop 6.Months p^2		0.001*
Postop 3.Weeks-3.Months p^2		0.022*
Postop 3.Weeks-6.Months p^2		0.027*
Postop 3.Months-6.Months p^2		0.002*

p1: Friedman Test, p2: Wilcoxon Sign Test, *p<0.05, Min: Minimum; Max: Maximum; SD: Standart Deviation; Preop: Preoperative; Postop: Postoperative; PRTEE: Patient-Rated Tennis Elbow Evaluation.

Table 5. Evaluation of the correlation between PSQI, DASH and PRTEE preop values

Preop		PSQI	DASH
DASH	r	0.719	1.000
	p	0.001*	
PRTEE	r	0.673	0.864
	p	0.001*	0.001*

Spearman Rho Correlation Analysis; r: Correlation coefficient; p: Statistical significance level; *p<0.05. Preop: Preoperative; PSQI: Pittsburg Sleep Quality Index; DASH: Disabilities of the Arm, Shoulder and Hand; PRTEE: Patient-Rated Tennis Elbow Evaluation.

that the presence of inflammatory cytokines in such cases contributes to the pathophysiology of pain, especially during the night when repair processes and inflammatory responses may become more prominent without the distractions of daily activities. Therefore, while lateral epicondylitis is expected to affect sleep quality, this effect may be eliminated due to the removal of inflammatory degenerated tissues by arthroscopic surgery. In addition, when addressing the relationship between arthroscopic surgery for chronic persistent LE and sleep quality improvement, it is important to emphasise a few key considerations. The minimally invasive nature of this procedure may favour faster recovery times, allowing patients to return to their normal sleep patterns sooner.

Sağlam et al. conducted a study on chronic LE patients to assess their sleep quality (11). The findings revealed that 71.7% of the participants (n=33) had PSQI scores ≥5, indicating poor sleep quality. In a similar manner, all 28 patients in the present study had PSQI scores ≥5, indicating poor sleep quality during the preoperative period. Consistent with the present study, three previous studies on rotator cuff rupture (RCR) have examined the PSQI and have shown a statistically significant improvement in mean PSQI scores at the 6-month postoperative mark compared to preoperative levels (20-22). One study observed a significant improvement in PSQI scores that persisted for 12 months after RCR (6.6±3.6 to 4.2±3.3, P =0.006) (23). Another study reported a significant improvement in PSQI scores that lasted for more than 24 months after RCR (11.6±4.4 to 5.5±4.0; P <0.05) (22). In the current study, we observed a different pattern compared to the aforementioned studies. Specifically, we found that sleep quality improved progressively until the third month.

According to Herquelot et al., LE is more common among people who work with heavy lifting or repetitive movements (24). One of the most notable findings of this study was the statistically significant increase in the PSQI scores at the 6th month postoperative compared to the 3rd month postoperative. Initially, patients experienced an improvement in sleep quality, as evidenced by the lowering of PSQI scores

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from preoperative levels through the third month after surgery. This trend reflects the typical recovery trajectory where symptoms of pain and discomfort are mitigated, thereby allowing better sleep. However, this improvement plateaued and was followed by a worsening in sleep quality by the sixth month. Considering that the average return to work time of the patients in the current study was 36.2+8.6 days, this reversal can be attributed to several factors. As patients start to resume their usual activities, including returning to work, the exertion associated with these tasks can lead to a resurgence of pain and discomfort, particularly in jobs involving repetitive motions or heavy lifting. It is crucial to consider these risks when advising patients post-operatively, particularly when setting realistic timescales for return to work and managing expectations regarding sleep quality.

Clark et al. prospectively assessed the post-surgical outcomes of patients who underwent ASCPLE or open releases of the common extensor tendon (5). They utilised scoring systems including DASH, visual analogue scale (VAS) pain, and the PRTEE score. There were no statistically significant differences between the two techniques across all grading systems. In the current study, a control group was not included for the purpose of comparing clinical scores. Additionally, no alternative surgical treatment apart from arthroscopic surgery was considered. We believe that this represents a limitation of the current study. However, it is important to note that both groups demonstrated improvement in pain and function from the preoperative to postoperative evaluation in the study of Clark et al., which is in line with the current study (5). The utilisation of arthroscopic techniques in the management of LE, in addition to percutaneous and open techniques, has demonstrated favourable surgical outcomes in terms of pain reduction, functional improvement, resumption of normal activities, and restoration of grip strength after surgery. Nevertheless, arthroscopic intervention offers distinct advantages over the other two approaches (percutaneous and open techniques) due to its superior ability to visualise the entirety of intra-articular structures (1,2). Despite the prolonged learning process associated with the arthroscopic approach, an in-depth examination of the three surgical methods found that complications following surgery, including total or partial nerve damage and elbow joint instability, were comparable between the three approaches (25). No instances of nerve injury or elbow instability were seen in any patients who had ASCPLE in the current study. In the first year after the surgical procedure, revision ASCPLE was conducted on four individuals. We are now engaged in the assessment of the clinical outcomes of patients who have had revision ASCPLE.

The study conducted by Babaqi et al. reported the mean DASH and PRTEE scores during the preoperative period as 24.46±1.46 and 55.53±11.16, respectively (26). In the current study, the average DASH and PRTEE scores during the preoperative period were found to be 77.07±6.83 and 75.54±4.78, respectively. These values were notably higher compared to the existing literature (1). Out of the total sample size of 28 individuals, 22 participants reported being involved in physically demanding occupations, while the remaining 6 individuals specifically characterised their employment as including recurrent microtrauma. It is hypothesised that elevated preoperative values may contribute to a higher level of postoperative satisfaction. However, it should be noted that the current study did not assess satisfaction directly. Additionally, it is emphasised that careful patient selection is crucial in this particular patient population. Behazin et al. reported high DASH and PRTEE scores in the preoperative period, which aligns with the current study findings (27). In contrast to the present study, Behazin et al. reported a decline in clinical improvement and scores beyond the 6th month (27). In the current study, the PRTEE values at the 6th month were lower than the preoperative period but showed an increase compared to the 3rd month. When analysing the DASH scores, it was found that the clinical improvement plateaued at the 6th month. Patients who underwent ASPCLE experienced notable satisfaction until the 6th month. However, clinical complaints resurfaced after this time period. The majority of patients in this series experienced rapid recovery of movement, performance, and daily activities. They also reported a similar rate of early returns to their original employment and other activities. The potential consequences may arise from patients resuming physically demanding work in order to sustain themselves and the impact of prevailing

socioeconomic conditions.

The current study found a substantial correlation between preoperative PSQI scores and DASH and PRTEE scores, with values of 71.9% and 67.3%, respectively (Figure 1). The existing body of literature does not include any studies investigating the impact of LE on sleep quality. Furthermore, our search did not provide any papers that explore the potential relationship between PSQI values and DASH or PRTEE scores. The DASH and PRTEE measurements, which are found as LE-spesific PROMS exhibit a strong correlation with the PSQI (28). This indicates that the PSQI is a reliable indicator of sleep quality in individuals suffering from chronic persistent LE.

The data presented in the current study is subject to limitations, as is common with retrospective chart review studies. The data were not collected in a standardised manner using a prospective approach. Furthermore, the current study was designed as a multicenter study. Variability in surgical techniques and follow-up procedures among clinicians poses a risk to consistency. The investigation included a limited number of patients, and a power analysis was not conducted prior to the commencement of the study to identify the optimal sample size. Moreover, although patients were asked about any existing sleep disorders upon admission, no sleep polysomnography screening was performed before collecting the data. The absence of a control group in the present study precluded the comparison of clinical scores. Furthermore, arthroscopic surgery was the only surgical treatment option that was taken into account. However, the scales used in the current study were selected based on their frequent usage in the literature when analysing PROMs and sleep quality indexes (28,29). Therefore, these scales were chosen for use in the present study. Another limitation of the study is that it was not possible to clearly determine whether the improvement in sleep and pain scores in the early period was due to the surgical procedure or to the fact that the patients were kept away from their work. The major strength of the current study lies in addressing an important gap in the literature by examining the potential improvement of sleep quality in patients after ASCPLE. Furthermore, the PSQI demonstrates a robust association with the DASH and PRTEE, which are widely used PROMs in individuals with LE. This highlights the PSQI's efficacy as a reliable tool for evaluating sleep quality in LE patients.

CONCLUSION

In conclusion, ASCPLE significantly improves sleep quality and reduces clinical scores up to six months postoperatively. However, initial improvements in sleep quality and some clinical scores showed a decline at six months postoperatively, suggesting the potential for recurrence of symptoms over time. The DASH and PRTEE, two specific PROMs for LE, show a significant correlation with the PSQI. This suggests that the PSQI is a dependable measure of sleep quality in individuals with chronic persistent LE.

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BIBLIOMETRIC ANALYSIS OF ALGOLOGY THESES IN TÜRKİYE: RESEARCH TRENDS AND PUBLICATION OUTCOMES

Türkiye'deki Algoloji Tezlerinin Bibliyometrik Analizi: Araştırma Eğilimleri ve Yayın Sonuçları

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ABSTRACT

Objective: Algology is an evolving subspecialty within anesthesiology, neurology, and physical medicine and rehabilitation. Specialty theses are crucial for medical education and scientific progress. However, no systematic evaluation has been conducted on the distribution, thematic focus, or publication status of algology-related theses in Türkiye. This study aims to perform a bibliometric analysis of such theses, examining their distribution across disciplines, research trends, publication rates, and academic impact.

Material and Methods: This retrospective study utilized data from the National Thesis Center of Türkiye. Theses in anesthesiology, neurology, and physical medicine and rehabilitation were reviewed to identify those related to algology. Extracted data included thesis titles, research topics, study designs, advisor titles, institutional affiliations, publication status, and citation data. Descriptive statistics and comparative analyses were employed to assess differences across disciplines.

Results: Of 10505 specialty theses, 331 (3.2%) were related to algology. Neurology contributed the highest proportion (6.8%), followed by anesthesiology (2.3%) and physical medicine and rehabilitation (1.5%). Neurology focused on headache disorders (86.3%), anesthesiology on interventional techniques (20.3%), and physical medicine and rehabilitation on peripheral nerve blocks (24.3%). The overall publication rate was 34.1%, with significant differences across disciplines ($p = 0.048$). Neurology had the highest publication rate in SCI/SCI-E journals (60.3%).

Conclusion: This is the first comprehensive bibliometric analysis of algology-related theses in Türkiye. Findings highlight differences in research focus, publication rates, and methodologies, emphasizing the need for enhanced interdisciplinary collaboration and institutional support in pain medicine research.

Keywords: *Pain Management; Bibliometrics; Academic Dissertation; Anesthesiology; Neurology; Physical and Rehabilitation Medicine*

ÖZET

Amaç: Algoloji, anesteziyoloji, nöroloji ve fiziksel tıp ve rehabilitasyon alanlarında gelişmekte olan bir alt dal olup, tıpta uzmanlık tezleri eğitim ve bilimsel ilerleme açısından önemli bir bileşendir. Ancak, Türkiye'de algoloji ile ilgili tezlerin dağılımı, tematik odakları veya yayımlanma durumu üzerine sistematik bir değerlendirme yapılmamıştır. Bu çalışma, algoloji ile ilgili tezlerin disiplinler arası dağılımını, araştırma eğilimlerini, yayımlanma oranlarını ve akademik etkisini incelemeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu retrospektif kesitsel çalışma, Türkiye'nin Ulusal Tez Merkezi verilerinden elde edilen verilerle yapılmıştır. Anesteziyoloji, nöroloji ve fiziksel tıp ve rehabilitasyon alanlarındaki tezler incelenmiş ve algoloji ile ilgili olanlar belirlenmiştir. Çıkarılan parametreler arasında tez başlıkları, araştırma konuları, çalışma tasarımları, danışman unvanları, kurumsal bağlantılar, yayımlanma durumu ve atıf verileri yer almaktadır. Disiplinler arasındaki farklılıkları değerlendirmek için betimsel istatistikler ve karşılaştırmalı analizler kullanılmıştır.

Bulgular: Toplam 10505 uzmanlık tezinden 331'i (%3,2) algoloji ile ilgiliydi. En yüksek oran nörolojiye ait olup (%6,8), ardından anesteziyoloji (%2,3) ve fiziksel tıp ve rehabilitasyon (%1,5) gelmektedir. Nöroloji tezleri genellikle baş ağrısı bozukluklarına (%86,3), anesteziyoloji interdisipliner tekniklere (%20,3), fiziksel tıp ve rehabilitasyon ise periferik sinir bloklarına (%24,3) odaklanmıştır. Toplam yayımlanma oranı %34,1 olup, disiplinler arası farklılıklar istatistiksel olarak anlamlıdır ($p = 0,048$).

Sonuç: Bu çalışma, Türkiye'deki algoloji ile ilgili uzmanlık tezlerinin kapsamlı ilk bibliyometrik analizidir. Bulgular, araştırma odakları, yayımlanma oranları ve yöntemsel farklılıkları vurgulamakta ve ağrı tıbbı araştırmalarının akademik görünürlüğünü artırmaya yönelik daha fazla disiplinler arası iş birliği ve kurumsal destek gerekliliğini ortaya koymaktadır.

Anahtar Kelimeler: *Ağrı Yönetimi; Bibliyometri; Akademik Tez; Anesteziyoloji; Nöroloji; Fizik Ve Rehabilitasyon Tıbbı*

INTRODUCTION

Algology, also known as (interventional) pain medicine, is a dynamic and multidisciplinary branch of medical science that focuses on understanding, diagnosing, and treating chronic pain. In Türkiye and numerous European countries, this field initially emerged as a subspecialty of anesthesiology and reanimation, but is now also recognized as a subspecialty of neurology and physical medicine and rehabilitation (1,2). The first algology department in Türkiye was established in 1991 under the Department of Anesthesiology and Reanimation at Istanbul Faculty of Medicine (1,2).

Medical specialty training is a structured process designed to equip graduates with theoretical knowledge and practical skills in a specific field. According to the Regulation on Specialty Training in Medicine and Dentistry in Türkiye, completion of a specialty thesis is a mandatory requirement for obtaining specialization in a primary discipline. However, while subspecialty training does not necessitate thesis completion, specialty theses in anesthesiology and reanimation, neurology, and physical medicine and rehabilitation frequently address topics related to algology.

Although algology has gained increased popularity, no study has yet reviewed the range and quality of medical theses related to this field. These theses constitute valuable academic resources that reflect the evolution of pain medicine and its integration into various specialties. Scientific publishing is fundamental to academic advancement (3). Typically, medical doctors commence their academic careers through their specialty theses (4). A comprehensive bibliometric analysis of these theses can offer insights into research trends, methodological approaches, and implications for pain medicine practice in Turkey.

This study endeavors to address the existing gap by systematically analyzing theses related to algology archived at National Thesis Center. Through a comprehensive evaluation of research topics, methodological approaches, and their clinical relevance, this study aimed to elucidate the evolution of algology in Türkiye. By critically assessing the contributions and limitations of these theses, this study seeks to provide valuable insights that will guide future academic research and clinical advancements in pain medicine, addressing both its scientific and practical challenges.

MATERIALS AND METHODS

This study analyzed the distribution of specialty theses related to algology across three primary disciplines: anesthesiology and reanimation, neurology, and physical medicine and rehabilitation. A retrospective cross-sectional analysis was conducted to determine the proportion of algology-related theses in each specialty. The study was initiated after obtaining approval from the local ethics committee (registration date and number: 07.01.2025-2025/18).

Data were sourced from National Thesis Center by inputting the specialty field, thesis type, and year into the search interface (https://tez.yok.gov.tr/UlusalTezMerkezi/tarama.jsp). Data collection occurred in January 2025, and only completed theses available up to this date were included in the analysis. These theses were identified through a systematic review of their titles, abstracts, keywords, and full texts when accessible. The inclusion criteria comprised all theses explicitly related to algology, whereas those deemed irrelevant were excluded. Medical specialty theses directly related to the field of algology were included in the study if they contained the following keywords in the title, abstract, keyword section, or full text: algology, radiofrequency, neuromodulation, cancer pain management, chronic pain, radiculary pain, headache, migraine, trigeminal neuralgia, joint injections, regenerative therapies, and entrapment syndromes. For each identified thesis, additional parameters were recorded, including the year of completion, the institution where the thesis was conducted, the academic title of the advisor, study design and temporal characteristics, and whether the thesis had been published. If published, further details regarding journal indexing status and the number of citations were documented.

The publication status of these theses was ascertained through a comprehensive search of multiple databases, including PubMed (https://pubmed.ncbi.nlm.nih.gov), Health Sciences University Library and Documentation Center Database (https://kutuphane.sbu.edu.tr/vetisbt), Turkish Academic Network and Information Center Turkish Database (ULAKBIM) (https://trdizin.gov.tr), and Google Scholar (https://scholar.google.com).

The indexation data of the scientific journals were also documented, encompassing journals indexed in the Scientific Citation Index/Scientific Citation Index-Expanded (SCI/SCI-E), Emerging Sources Citation Index (ESCI) and ULAKBIM, as well as those not indexed in SCI/SCI-E, ESCI, and ULAKBIM.

Statistical analyses were conducted using SPSS software version 27.0.1.0 (IBM Corp., Armonk NY, USA). Continuous variables were summarized as median, minimum, and maximum values, contingent upon the data distribution. Categorical variables are presented as frequencies (n) and percentages (%). For comparisons among three groups, Kruskal-Wallis test was used for non-normally distributed variables. Comparative analyses between two independent groups were conducted utilizing the Mann-Whitney U test for datasets that did not conform to a normal distribution. Categorical variables were examined using the chi-squared (χ^2) test and Fisher's exact test, as appropriate. Statistical significance was determined at a threshold of $p < 0.05$.

RESULTS

A comprehensive review was conducted on a total of 10,505 theses, comprising 5,694 from the fields of anesthesiology and reanimation, 2,361 from neurology, and 2,450 from physical medicine and rehabilitation. Of these, 133 theses (2.3%) in anesthesiology, 161 (6.8%) in neurology, and 37 (1.5%) in physical medicine and rehabilitation were focused on algology, representing 3.2% of the total theses. Additionally, 34.1% of the theses related to algology were subsequently published in scientific journals (Figure 1).

The descriptive statistics of the primary discipline distribution, advisor titles, institutional affiliations, research designs, and study topics are summarized in Tables 1 and 2. The majority of theses were conducted in university settings, most of which were supervised by professors. rofessors. Prospective study designs are common, particularly in the fields of neurology and physical medicine. The research topics varied, with neurology focusing on migraine and other headache (86.3%), anesthesiology on epidural injections (20.3%), neuromodulation (13.5%), physical medicine on peripheral blocks (24.3%), and prolotherapy (16.2%).

Publication rates varied significantly among the disciplines (p=0.048). Overall, 34.1% (n=113) of theses were published, whereas 65.9% (n=218) remained unpublished. Neurology had the highest publication rate (39.1%, n=63), followed by physical medicine and rehabilitation (40.5%, n=15) and anesthesiology (26.3%, n=35).

The distribution of publications in different journal indexes demonstrated a statistically significant difference among specialties (p<0.001). Neurology had the highest percentage of publications indexed to SCI/SCI-E (60.3%). In contrast, Anesthesiology and Physical Medicine and Rehabilitation displayed a more heterogeneous distribution across multiple indexing databases. Additionally, ESCI was more prominent in anesthesiology, with 51.4% of the publications indexed (Figure 2).

The distribution of advisor types differed significantly across specialties (p=0.025). Professors constituted the majority of all three fields, with the highest proportion in anesthesiology (63.8%). Associate and assistant professors were distributed more evenly. However, publication status did not differ significantly according to academic title (p =0.458).

The number of citations did not differ significantly across specialties (p=0.176).

The time to publication differed significantly across specialties (p<0.05). Pairwise comparisons using a post-hoc test showed a significant difference between anesthesiology and neurology (p=0.016), and between neurology and physical therapy (p=0.004), whereas no significant difference was found between anesthesiology and physical medicine (p=0.201) (Table 4).

The distribution of publications showed the highest contributions from Ankara (18.6%) and İstanbul (16.8%), followed by Elâzığ (8.8%) and Aydın (5.3%), whereas all other cities contributed less than 5%.

DISCUSSION

According to medical specialization regulations, completing a thesis is mandatory for specialization training. This thesis preparation provides medical doctors with scientific writing skills (5). However, they are not obligated to convert them into scientific publications (4,6).

This study represents the inaugural evaluation of the

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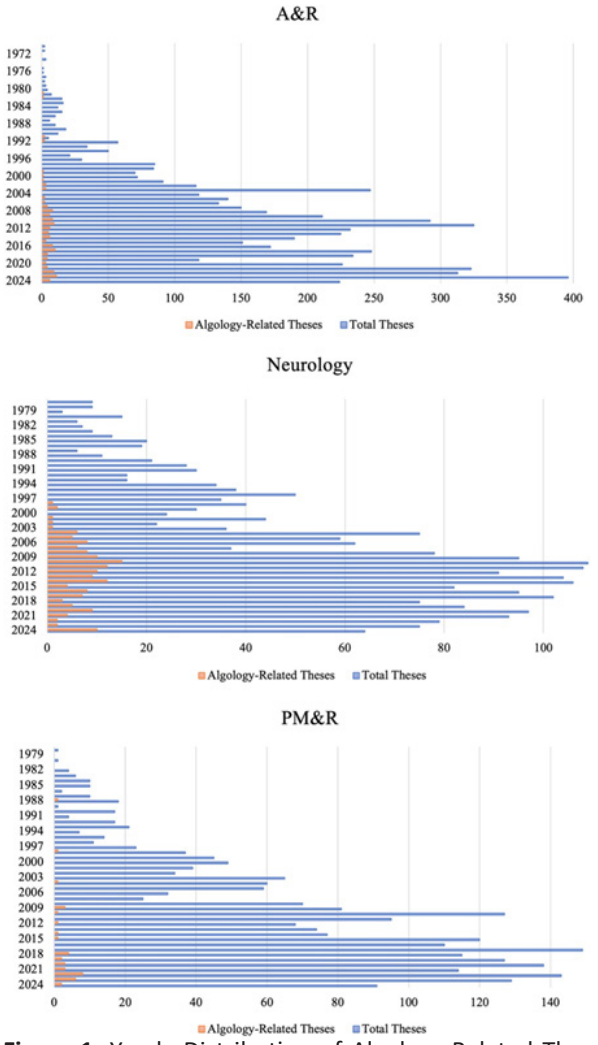

Figure 1. Yearly Distribution of Algology-Related Theses and Total Theses in A&R, Neurology and PM&R (A&R: Anesthesiology and Reanimation, PM&R: Physical Medicine and Rehabilitation)

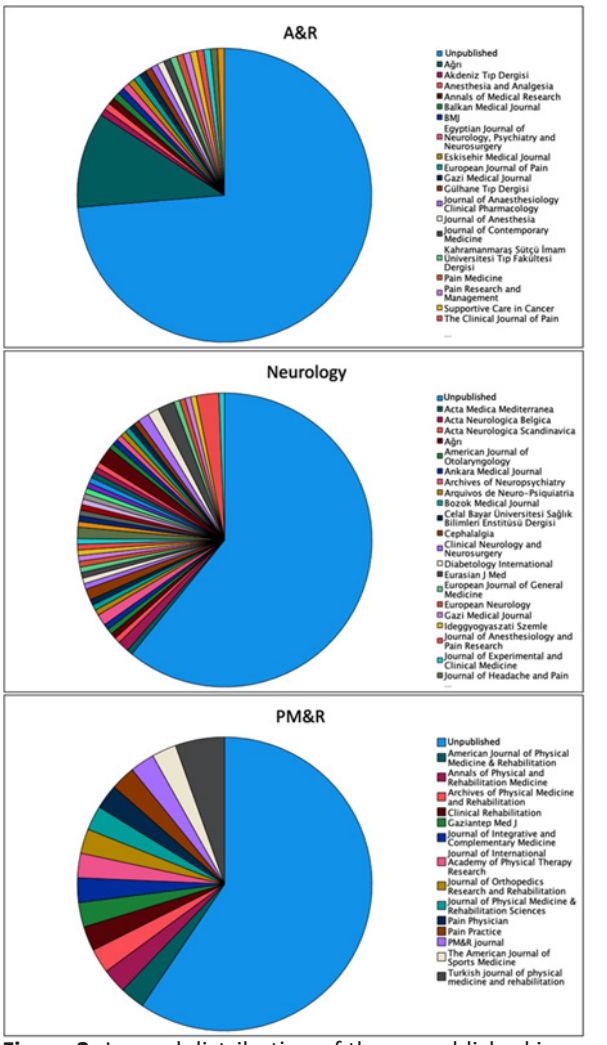

Figure 2. Journal distribution of theses published in three primary specialties

publication status of theses related to algology specialties in Türkiye, while also examining their thematic distribution and other pertinent characteristics. This research provides data on the distribution and role of algology theses in anesthesiology and reanimation, neurology and physical medicine and rehabilitation. The findings revealed significant disparities in research direction, publication trends, and methodological approaches within these specialties, highlighting the evolving nature of algology in medical specialty training.

The distribution of theses pertaining to algology exhibited notable variation across different disciplines (Table 1). Neurology accounted for the highest proportion of theses on algology (6.8%), followed by anesthesiology (2.3%) and physical medicine and rehabilitation (1.5%). The substantial prevalence of algology-related theses in neurology appears to correspond with the increasing interest in migraine and other headache disorders, which constitute the majority (86.3%) of pain-related theses in this field. Conversely, anesthesiology emphasizes interventional techniques, such as epidural injections (20.3%) and neuromodulation (13.5%), reflecting its focus on

interventional pain management (Table 2). In the domain of physical medicine and rehabilitation, emphasis on musculoskeletal pain has resulted in a higher number of theses on peripheral nerve blocks (24.3%) and prolotherapy (16.2%). These findings underscore the multidisciplinary nature of pain medicine.

The distribution of publications reflects the prominent roles of Ankara and İstanbul as academic centers, while other cities demonstrate comparatively limited contributions (Figure 3). The publication rate of algology-related theses was highest in physical medicine (40.5%), followed by neurology (39.1%) and anesthesiology (26.3%), with significant differences between the main disciplines (p=0.048) (Table 3). Variations in research culture and clinical practice across various disciplines may contribute to these observed differences. While scientific publications abroad are often conducted by teams of researchers in Türkiye, the need for individual efforts may negatively affect the transformation of theses into academic publications (4). In a questionnaire study by Saydam et al., which explored the necessity of writing a thesis, most participants with expert doctorates believed that requiring the composition of an article for publication would be more beneficial than mandating a thesis (7). Moreover, research conducted in both developed and developing countries has shown that the conversion rate of theses into publications is variable but generally remains low (8). Additionally, there were notable differences in the indexing distribution of published theses (p<0.001). Neurology had the highest proportion of SCI/SCI-E indexed publications (60.3%), whereas anesthesiology stood out with a significant presence in the ESCI index (51.4%) (Table 3). Based on a previous study, the publication rate of theses on Algology in SCI/SCI-E journals is higher than the total publication rate of theses in anesthesiology (9).

Key impediments to converting theses into publications include structural and administrative challenges within the research process, insufficient training in academic publishing, and linguistic barriers (10,11). Moreover, the substantial workload faced by physicians, coupled with the absence of effective publication incentive mechanisms, adversely affects this process (8,12,13).

Although professors predominantly served as thesis advisors across all three disciplines, this variable did not significantly influence the probability of publication (p=0.458) (Table 3). This indicates that although academic advising is crucial, other factors may have a more substantial influence on publication success.

The duration of thesis publication exhibited significant variation across different academic disciplines (p<0.05) (Table 4). Pairwise comparisons identified statistically significant differences between Anesthesiology and Neurology (p=0.016), and between neurology and physical medicine (p=0.004). These results suggest that theses in the field of neurology are published more expeditiously, possibly because of the higher prevalence of high-impact journals dedicated to research on migraines and other headaches. However, citation counts did not demonstrate significant differences across disciplines (p=0.176) indicating that, despite variations in publication rates and journal indexing, the overall impact of these studies on the scientific community may be comparable (Table 3).

In the analysis of citation impact, the study with the highest citation count was a clinical trial on joint injections within the domain of physical medicine (n=388), followed by a clinical trial addressing migraines in the field of neurology (n=264). The third most frequently cited study was an animal experiment exploring neuromodulation conducted in the field of anesthesiology and reanimation (n=211). This distribution indicates that clinical trials, especially those focusing on prevalent conditions, such as musculoskeletal disorders and migraines, tend to garner substantial academic attention. Additionally, experimental studies on neuromodulation within anesthesiology and reanimation have made a significant contribution to the field.

A significant strength of this study is its comprehensive analysis of 10505 theses across major disciplines, facilitating a detailed examination of topic trends in algology-related theses. Additionally, the investigation of academic advising roles and indexing distributions offers a thorough perspective on the published works.

However, this study had some limitations. First, National Thesis Center database aims to collect theses from university hospitals, excluding those written in health and research hospitals affiliated with the Ministry of Health until 2015 (9). This exclusion

Table 1. Distribution of Thesis Advisors, Institutional Affiliation, Study Designs and Temporal Characteristics Across Specialties

		A&R n (%)	Neurology n (%)	PM&R n (%)
Thesis Advisor	Professor	81 (63.8)	80 (50.6)	19 (51.4)
	Associate Professor	36 (28.3)	50 (31.6)	13 (35.1)
	Assistant Professor	5 (3.9)	25 (15.8)	5 (13.5)
	Other	5 (3.9)	3 (1.9)	0 (0.0)
Institutional Affiliation	University	124 (93.2)	146 (90.7)	23 (62.2)
	Ministry of Health	9 (6.8)	15 (9.3)	14 (37.8)
Types of Study Designs	Case Series	17 (13.0)	3 (1.9)	0 (0.0)
	Correlation Study	5 (3.8)	6 (3.7)	1 (2.7)
	Cross-Sectional Study	17 (13.0)	48 (29.8)	2 (5.4)
	Case-Control Study	2 (1.5)	48 (29.8)	0 (0.0)
	Cohort Study	30 (22.9)	21 (13.0)	1 (2.7)
	Animal Experiment	26 (19.8)	3 (1.9)	0 (0.0)
	Clinical Trial	31 (23.7)	30 (18.6)	33 (89.2)
	Validity Study	3 (2.3)	2 (1.2)	0 (0.0)
Temporal Characteristic	Prospective	63 (48.1)	98 (60.9)	32 (86.5)
	Retrospective	59 (45.0)	45 (28.0)	3 (8.1)
	Other	9 (6.9)	18 (11.2)	2 (5.4)

A&R: Anesthesiology and Reanimation, PM&R: Physical Medicine and Rehabilitation

Table 2. Distribution of Study Topics Across Specialties

Study Topic	A&R n (%)	Neurology n (%)	PM&R n (%)
Neuromodulation	18 (13.5)	0 (0.0)	2 (5.4)
Joint Injections	16 (12.0)	0 (0.0)	6 (16.2)
Demographic Studies	9 (6.8)	0 (0.0)	0 (0.0)
Epidural Injections	27 (20.3)	0 (0.0)	6 (16.2)
Medical Treatments	22 (16.5)	1 (0.6)	3 (8.1)
Cadaver Studies	2 (1.5)	0 (0.0)	0 (0.0)
Pain Physiology	6 (4.5)	1 (0.6)	0 (0.0)
Fibromyalgia	5 (3.8)	1 (0.6)	2 (5.4)
Migraine and Other Headaches	6 (4.5)	139 (86.3)	0 (0.0)
Intradiscal Procedures	4 (3.0)	0 (0.0)	0 (0.0)
Sleep Studies	3 (2.3)	0 (0.0)	0 (0.0)
Validity Studies	3 (2.3)	1 (0.6)	0 (0.0)
Imaging and Diagnostic Methods	2 (1.5)	2 (1.2)	1 (2.7)
Peripheral Blocks	2 (1.5)	0 (0.0)	9 (24.3)
Cancer Pain	4 (3.0)	0 (0.0)	0 (0.0)
Sympathetic Blocks and Radiofrequency	3 (2.3)	0 (0.0)	0 (0.0)
Phantom Pain	1 (0.8)	0 (0.0)	0 (0.0)
Trigeminal Neuralgia	0 (0.0)	2 (1.2)	0 (0.0)
Carpal Tunnel	0 (0.0)	6 (3.7)	2 (5.4)
Diabetic Neuropathy	0 (0.0)	7 (4.3)	0 (0.0)
Other Neuropathies	0 (0.0)	1 (0.6)	0 (0.0)
Prolotherapy	0 (0.0)	0 (0.0)	6 (16.2)

A&R: Anesthesiology and Reanimation, PM&R: Physical Medicine and Rehabilitation

Table 3. Publication Status, Index Distribution, Advisor Academic Titles and Citation Count by Specialty

Variables		A&R n (%)	Neurology n (%)	PM&R n (%)	Total n (%)	χ^2	p-value
Publication Status	Unpublished	98 (73.7)	98 (60.9)	22 (59.5)	218 (65.9)	6.079	0.048
	Published	35 (26.3)	63 (39.1)	15 (40.5)	113 (34.1)		
Index Type	SCI/SCIE	10 (28.6)	38 (60.3)	11 (73.3)	59 (52.2)	28.585	<0.001**
	ESCI	18 (51.4)	10 (15.9)	0 (0.0)	28 (24.8)		
	TR Dizin	7 (20.0)	13 (20.6)	1 (6.7)	21 (18.6)		
	Other International	0 (0.0)	2 (3.2)	3 (20.0)	5 (4.4)		
Academic Title	Professor	81 (63.8)	80 (50.6)	19 (51.4)	180 (55.9)	14.798	0.016*
	Associate Professor	36 (28.3)	50 (31.6)	13 (35.1)	99 (30.7)		
	Assistant Professor	5 (3.9)	25 (15.8)	5 (13.5)	35 (10.9)		
	Other	5 (3.9)	3 (1.9)	0 (0.0)	8 (2.5)		
	Total	127 (100.0)	158 (100.0)	37 (100.0)	322 (100.0)		
		Median (min-max)	Median (min-max)	Median (min-max)		H	p
Citation Count		2 (0-211)	6 (0-264)	2 (0-388)		3.480	0.176***
		Published n (%)		Unpublished (n (%)	Total n (%)	χ^2	p
Academic Title	Professor	124 (58.8)		56 (50.5)	180 (55.9)	2.597	0.458*
	Associate Professor	62 (29.4)		37 (33.3)	99 (30.7)		
	Assistant Professor	21 (10.0)		14 (12.6)	35 (10.9)		
	Other	4 (1.9)		4 (3.6)	8 (2.5)		
	Total	211 (100)		111 (100)	322 (100)		

A&R: Anesthesiology and Reanimation, PM&R: Physical Medicine and Rehabilitation, min-max: minimum and maximum values, χ^2: chi-square value, H: Kruskal-Wallis test value *Pearson chi-square, **Fisher-Freeman-Halton exact test, *** Kruskal-Wallis test p-values written in bold indicate statistical significance, with p<0.05 considered statistically significant, SCI: Science Citation Index, SCIE: Science Citation Index Expanded, ESCI: Emerging Sources Citation Index

Table 4. Descriptive Statistics of Publication Duration by Specialty

	A&R (n = 35)	Neurology (n = 63)	PM&R (n = 15)	H	p	Comparison of Groups	p
	Median (min-max)	Median (min-max)	Median (min-max)				
Publication Duration	3 (0-13)	4 (0-14)	2 (0-7)	11,409	0,003*	A&R<Neurology	0.016**
						A&R-PM&R	0.201**
						Neurology>PM%R	0.004**

A&R: Anesthesiology and Reanimation, PM&R: Physical Medicine and Rehabilitation, min-max: minimum and maximum values, H: Kruskal-Wallis test value, * Kruskal-Wallis test, **Post-hoc test p-values written in bold indicate statistical significance, with (*p<0.05, **p<0.017) considered statistically significant

created a gap in the dataset. Changing the associate professorship criteria made the publication of these mandatory. Additionally, some health and research hospitals previously under the Ministry of Health joined universities through affiliation processes or the establishment of the Health Sciences University (14).

Moreover, the study did not investigate whether thesis advisors were specialists in algology or whether the thesis authors pursued subspecialty training afterward. Therefore, the potential impact of theses in algology on the specialization process could not be assessed.

CONCLUSION

This study revealed significant interdisciplinary differences in the theses related to algology. Neurology exhibited the highest research activity and publication rates, whereas anesthesiology and physical medicine focused more on interventional pain management techniques. These findings suggest that enhancing interdisciplinary collaboration and providing structured academic support is essential for increasing the scientific visibility and impact of algology research.

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ÜNİVERSİTEDE EĞİTİM GÖREN KIZ ÖĞRENCİLERDE SOSYAL MEDYA BAĞIMLILIĞININ VE SAĞLIKLI BESLENMEYE İLİŞKİN TUTUMLARIN BEDEN MEMNUNİYETİ ÜZERİNE ETKİSİ

The Effect of Social Media Addiction and Attitudes Towards Healthy Nutrition on Body Satisfaction Among Female University Students

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ÖZET

Amaç: Bu çalışmada Üniversitede eğitim gören kız öğrencilerde sağlıklı beslenme tutumları ile sosyal medya bağımlılığının beden memnuniyeti üzerindeki etkisinin incelemesi amaçlanmıştır.

Gereç ve Yöntemler: Kesitsel ve tanımlayıcı tipte yapılan bu çalışma, Ocak-Şubat 2023 tarihleri arasında 356 kız öğrenci ile gerçekleştirilmiştir. Çalışmada öğrencilerle yapılan yüz yüze görüşmelerde öğrencilerin; demografik bilgileri, beslenme alışkanlıkları, bazı antropometrik ölçümleri sorgulanmıştır. Ayrıca öğrencilerin beden imajı durumlarını belirlemek için Stunkard Ölçeği, sosyal medya bağımlılık durumlarını tespit edebilmek için Sosyal Medya Bağımlılığı Ölçeği – Yetişkin Formu (SMBÖ-YF) ve sağlıklı beslenmeye ilişkin tutumlarını öğrenebilmek için de Sağlıklı Beslenmeye İlişkin Tutum Ölçeği (SBİTÖ) uygulanmıştır.

Bulgular: Beden memnuniyetsizliği olan kız öğrencilerin memnun olanlara göre, BKİ değerlerinin ve bel çevresi ölçümlerinin daha fazla olduğu ve bu değerler arttıkça beden memnuniyetlerinin daha azaldığı tespit edilirken, beden memnuniyetsizliğine sahip olanların daha fazla ara öğün yaptıkları, daha fazla diyet programına uydukları ve daha fazla besin etiketi okuma alışkanlığına sahip oldukları bulunmuştur ($p<0,05$). Ayrıca sosyal medyada en çok takip edilen konuların beden memnuniyeti üzerine etkisinin anlamlı olduğu tespit edilmiş olup; sosyal medyada yemek tarifleri, zayıflama ve sağlıklı beslenme+zayıflama konularını takip eden kız öğrencilerin sosyal medya konuları ile ilgilenmeyen öğrencilere göre beden memnuniyetsizliğinin istatistiksel olarak daha fazla olduğu bulunmuştur ($p<0,05$).

Sonuç: Üniversitede eğitim gören ve beden memnuniyetsizliğine sahip olan kız öğrencilerin genel ve santral obezite ölçümlerinin daha yüksek olduğu ve sağlıklı beslenmeye ilişkin tutumlarının ise daha düşük olduğunun tespit edilmesiyle birlikte sosyal medyada özellikle yemek tarifleri, zayıflama ve sağlıklı beslenme konularını takip etmenin de beden memnuniyetsizliği açısından bir risk faktörü oluşturabileceği tespit edilmiştir.

Anahtar Kelimeler: *Üniversite Öğrencileri; Beden Memnuniyetsizliği; Sosyal Medya Bağımlılığı; Beslenme Bilgi Düzeyi*

ABSTRACT

Objective: This study aimed to examine the effects of healthy eating attitudes and social media addiction on body satisfaction among female students studying at the university.

Material and Methods: This cross-sectional and descriptive study was conducted with 356 female students between January and February 2023. In the study, demographic information, eating habits, and some anthropometric measurements of the students were questioned in face-to-face interviews. In addition, the Stunkard Scale was applied to determine the students' body image status, the Social Media Addiction Scale - Adult Form (SMBO-YF) to determine their social media addiction status, and the Healthy Nutrition Attitude Scale (SBITS) to learn their attitudes towards healthy nutrition.

Results: It was found that female students with body dissatisfaction had higher BMI values and waist circumference measurements than those who were satisfied, and as these values increased, their body satisfaction decreased, while those with body dissatisfaction had more snacks, followed more diet programs, and had a habit of reading food labels more ($p<0.05$). It was also found that the most followed topics on social media had a significant effect on body satisfaction; it was found that female students who followed recipes, weight loss, and healthy nutrition+weight loss topics on social media had statistically higher body dissatisfaction than students who were not interested in social media topics ($p<0.05$).

Conclusion: It was determined that female students studying at university and having body dissatisfaction had higher general and central obesity measurements and lower attitudes towards healthy nutrition, and it was determined that following especially recipes, weight loss, and healthy nutrition topics on social media could also be a risk factor for body dissatisfaction.

Keywords: *University Students; Body Dissatisfaction; Social Media Addiction; Nutrition Knowledge Level*

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GİRİŞ

Adölesan ve yetişkinlik arasındaki geçiş dönemini işaret eden 18-30 yaş arasındaki dönem genç yetişkinlik dönemi olarak adlandırılmaktadır. Bağımsızlıklara yönelik yeni becerilerin geliştirildiği üniversite dönemi aynı zamanda yaşam deneyimi eksikliği nedeniyle savunmasız kalınan ve etkilenilebilen bir yaşam aşamasıdır (1). Üniversite dönemi sağlıklı besin seçimlerinin şekillendiği çok önemli bir zaman dilimi olup, bu dönemde olan genç yetişkinler çevresel faktörlerden etkilenebilmektedir (2). Üniversite öğrencileri sosyal çevre edinme, eğlenceli vakit geçirme ve bilgiye ulaşabilme/paylaşabilme gibi nedenlerle sosyal medya uygulamalarını sıklıkla kullanmaktadırlar. Sosyal medyada en çok araştırdıkları konuların başında ise sağlık ve beslenme konuları gelmektedir (3). Son on yılda sosyal medya kullanımındaki katlanarak artan büyüme nedeniyle, doktorlar, beslenme uzmanları ve sağlık kuruluşları, gençler ve yetişkinlerde sağlıklı besin seçimlerini ve beslenmeyle ilgili davranışları güçlendirmek için sosyal medyadan yararlanmaya çalışmaktadırlar (4). Ancak bu içerikler kurumsal markaların ve gıda endüstrilerinin gelişmiş sosyal pazarlama kampanyalarıyla rekabet etmek zorunda kalmaktadır (5). Sosyal medyada sunulan ürünlerin sağlık, güzellik ve başarı yanılması satmak için tasarlanmış akran elçilerinin ve ünlülerin onayları da dahil olmak üzere görüntüye dayalı pazarlama taktikleri kullanılarak genç yetişkinlerin sosyal güvenlik açıklarından yararlanıldığı bilinmektedir (5). Bu tür içeriklerin özellikle genç yetişkin kadınlarda beden imajı üzerine olumsuz etkiler oluşturduğuna dair kanıtlar bulunmaktadır (6). Sosyal medyada kalınan sürenin artması sosyal medya bağımlılığının oluşmasının yanı sıra yanlış beslenme alışkanlıklarının kazanılmasına, obezite varlığının oluşmasına ve beden memnuniyetsizliğine neden olabilmektedir (7).

Beden memnuniyetsizliği ise bir bireyin istediği vücut şekli ile gerçek vücut şekli arasında bir tutarsızlık olduğunda yaşanmakta olup, Batı toplumlarında daha yaygın olmakla birlikte kadınların %60'ını ve erkeklerin ise %30'unu etkilediği tahmin edilmektedir (8). Üniversite döneminin popülasyonunu oluşturan genç yetişkinlerde ise, kadın popülasyonu daha baskın olmak üzere, beden imajı süreklilik içerisinde deneyimlenerek değişmektedir (9). Bir birey bedeni hakkında ne kadar memnuniyetsizlik hissederse bireyin benlik saygısı depresyonuna sahip olmasının yanı sıra uzun vadeli olumsuz sağlık sonuçlarına yol açan sağlıklı beslenme alışkanlıkları da olumsuz yönde etkilenebilmekte ve bu durumda kısır döngü oluşturarak bireylerin beden imajına zarar verebilmektedir (10). Sosyal medya etkileşimi ile beden imajı arasındaki ilişki sosyal karşılaştırma teorisine dayanmaktadır ve genellikle daha ince ve daha güzel akranlarla yapılan karşılaştırmalar beden memnuniyetsizliğinin yerleşik bir habercisi olarak görülmektedir (6). Sosyal medya ve beden imajı ile ilişkilendirilen kanıtlara ve beden memnuniyetsizliğinin sağlık üzerindeki olumsuz etkilerine rağmen, bugüne kadar genç yetişkinlerde sosyal medya ve beden memnuniyetsizliği arasındaki doğrusal ilişkiyi kanıtlayan sınırlı sayıda çalışma bulunmaktadır (7, 11). Bu konuda yapılan, deneysel ve gözlemsel literatürün sistematik incelemesi olan bir çalışmada sosyal medya platformlarına maruziyetin, topluluk, ergenlik, üniversite ve genç yetişkin popülasyonlarında beden memnuniyetsizliği ile düzensiz ve sağlıksız yeme davranışı gibi olumsuz beslenme alışkanlıkları arasında doğrusal bir ilişki olduğu bildirilmiştir (11).

Bu konuda literatürü desteklemek amacıyla yapılan bu çalışmada Üniversitede eğitim gören kız öğrencilerde sosyal medya kullanımına dair özellikler ile beden memnuniyeti ve sağlıklı beslenme tutumları arasındaki ilişkinin değerlendirilmesi ve sağlıklı beslenme ile sosyal medya kullanım durumlarının beden memnuniyeti üzerindeki etkisinin incelemesi amaçlanmıştır.

GEREÇ VE YÖNTEMLER

Kesitsel ve tanımlayıcı tipte yapılan bu çalışma, Ocak-Şubat 2023 tarihleri arasında Toros Üniversitesi'nde eğitim gören 356 kız öğrenci ile gerçekleştirilmiştir. Çalışmaya dahil edilme kriterleri cinsiyetlerinin kız olması, 18 yaş üzeri olmaları, Beck Depresyon Ölçeği (BDÖ) puanları ≤8 olması, çalışmaya gönüllü katılım sağlamış olmaları ve en az bir sosyal medya platformunu kullanıyor olmaları iken üniversitede okumayan, gebe ve emzikli olanlar, kronik ve psikiyatrik hastalığı olanlar, herhangi ilaç, vitamin-mineral ve besin desteği kullanan ve erkek cinsiyetine sahip olan öğrenciler çalışma dışında bırakılmışlardır.

Örneklem sayısı için G*Power yazılımı ile alfa (α)=0,05,

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güç (1-β)=0,95 ve orta düzey etki büyüklüğü (d=0,50) alınarak güç analizi yapılmıştır. Analiz sonucunda bu çalışmada toplam 200 gözlemle çalışıldığı takdirde yaklaşık %100 düzeyinde bir test gücüne ulaşılacağı belirlenmiştir. Bu çalışma Dünya Tıp Birliği Helsinki Bildirgesi'nin etik ilkeleri çerçevesinde yürütülmüş olup, çalışma için 26.12.2022 tarih 188 nolu karar ile Toros Üniversitesi Bilimsel Araştırmalar ve Yayın Etik Kurulu'ndan etik kurulu izni alınmış ve çalışmaya katılan tüm öğrencilerden çalışma öncesi onam alınmıştır.

Çalışmada öğrencilerle yapılan yüz yüze görüşmelerde öğrencilerin; demografik bilgileri (yaş, medeni durum, okuduğu bölüm), beslenme alışkanlıkları (ana öğün, ara öğün tüketim durumları, alkol ve su tüketimleri), antropometrik ölçümleri (vücut ağırlığı, boy uzunluğu ölçümleri) sorgulanmıştır. Ayrıca öğrencilerin beden imajı durumlarını belirlemek için Stunkard Ölçeği, sosyal medya bağımlılık durumlarını tespit edebilmek için Sosyal Medya Bağımlılığı Ölçeği – Yetişkin Formu (SMBÖ-YF) ve sağlıklı beslenmeye ilişkin tutumlarını öğrenebilmek için de Sağlıklı Beslenmeye İlişkin Tutum Ölçeği (SBİTÖ) uygulanmıştır (12-14).

Vücut ağırlığı, boy uzunluğu ölçümleri araştırmacı tarafından yüz yüze yapılan görüşmelerde ölçülmüştür (15). Vücut ağırlığı ve boy uzunluğu ölçümlerinden Beden Kütle İndeksi (BKİ) değerleri (vücut ağırlığı (kg) / boy uzunluğu (m^2)) hesaplanmış ve Dünya Sağlık Örgütü (DSÖ) sınıflamasına (zayıf (<18,5 kg/m^2); normal (18,5-24,9 kg/m^2); hafif şişman (25,0-29,9 kg/m2); Obez (>30,0 kg/m^2)) göre değerlendirilmiştir (16). Santral obezitenin değerlendirilmesinde ise ölçülen bel çevresi ve kalça çevresi ölçümlerinden bel/kalça oranı hesaplanmış bu değer de DSÖ sınıflandırmasına (kadınlarda ≥0,85, erkeklerde ise ≥0,90) göre değerlendirilmiştir (16).

Beden İmajı Ölçeği, 1983'te erkeklerde ve kadınlarda beden memnuniyetsizliğini belirlemek için Stunkard tarafından geliştirilmiştir (12). Ölçekte aşırı zayıflıktan aşırı şişmanlığa kadar değişen 9 kadın ve 9 erkek şematik görsel bulunmakta olup bireylerden hem mevcut vücut boyutunu hem de ideal vücut boyutunu en iyi yansıtan görselleri seçmeleri istenerek puanlama yapılmaktadır. Bireylerin beden memnuniyet puanı ise ideal vücut görseli puanından mevcut vücut görselin puanı düşürülerek hesaplanmaktadır. Elde edilen 0 ve 1 puan beden memnuniyetini, >1 puan ise beden memnuniyetsizliğini ifade etmektedir (12).

Sosyal Medya Bağımlılık Ölçeği, 18-60 yaş grubundaki yetişkinlerin sosyal medya bağımlılığını belirlemeye yönelik bir ölçek olarak geliştirilmiş olup Şahin ve Yağcı tarafından Türkçe geçerlilik ve güvenilirliği yapılmıştır. Ölçek 5'li likert tipte 20 sorudan oluşmaktadır ve bu maddeler arasından 5. ve 11. maddeler ters puanlanmakta olup ölçekten alınabilecek en yüksek puan 100, en düşük puan ise 20'dir. Puanın yüksek olması bireyin kendisini "sosyal medya bağımlısı" olarak algıladığı biçiminde değerlendirilmektedir (13).

Dört alt boyuttan (Beslenme Hakkında Bilgi (BHB), Beslenmeye Yönelik Duygu (BYD), Olumlu Beslenme (OB) ve Kötü Beslenme (KB)) ve 5'li likert tipte cevaplanan 21 maddeden oluşan bu ölçek Demir ve Cicioğlu (14) tarafından geliştirilmiş olup, yine aynı araştırmacılar tarafından Türkçe geçerlilik ve güvenilirliği yapılmıştır. Ölçekten alınabilecek en düşük puan 21 en yüksek puan ise 105'tir. Bireylerin ölçekten alacağı 21 puan çok düşük, 23-42 puan düşük, 43-63 puan orta, 64-84 puan yüksek ve 85-105 puan ise ideal düzeyde yüksek sağlıklı beslenmeye ilişkin tutuma sahip oldukları şeklinde değerlendirilmektedir (11).

Çalışmada, sosyal medya bağımlılığı ve sağlıklı beslenmeye ilişkin tutum ölçeklerinin güvenilirliği Cronbach Alfa ile değerlendirilmiştir. Ölçeklerin iç tutarlılık açısından yüksek düzeyde güvenilir olduğu tespit edilmiştir. Beden imajına göre normallik, Kolmogorov-Smirnov testiyle incelenmiştir (n>50). Normal dağılmayan verilerde Mann Whitney U testi kullanılmıştır. Kategorik verilerde, beklenen gözlem değeri 5'ten büyükse ki-kare testi, küçükse Fisher testi uygulanmıştır. Çoklu karşılaştırmalar Bonferroni düzeltmeli Z testi ile yapılmıştır. Beden imajına etkileyen faktörler hiyerarşik lojistik regresyonla analiz edilmiştir. Modeller arasındaki değişim Akaike Bilgi Kriteri (AIC) ile incelenmiştir. Tüm analizler R yazılımı ve yazılımında bulunan temel stats paketi ve ek olarak pscl paketleri kullanılarak yapılmıştır. İstatistiksel anlamlılık p<0,05 olarak kabul edilmiştir.

BULGULAR

Tablo 1'de çalışmaya dahil edilen öğrencilerin tanımlayıcı özellikleri verilmiştir. Kız öğrencilerin yaş ortalamalarının 21,3±3,4 yıl olduğu ve %71,9'unun ise sağlık bilimleri alanında eğitim aldığı görülürken; BKİ

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değerlerinin 21,7±3,8 kg/m2, bel çevresi ölçümlerinin 72,1±10,9 cm olduğu görülmektedir. Kız öğrencilerin günlük uyku süresi ortalamalarının 8,4±1,7 saat olduğu, %26,7'sinin düzenli egzersiz yaptığı bulunmuştur. Öğrencilerin %57,0'sinin ana öğün, %74,2'sinin ise ara öğünleri atladığı belirlenirken; %8,1'inin diyet programı uyguladığı, %42,1'inin ise besin etiketi okuma alışkanlığı olduğu belirlenmiştir.

Kız öğrencilerin beden imajı ölçeği puan ortalamalarının -0,7±1,2 olduğu ve %50,6'sının ise beden memnuniyetsizliğine sahip olduğu tespit edilmiştir.

Kız öğrencilerin SBİTÖ toplam puan ortalamasının 67,8±9,8 olduğu, ölçeğin alt boyutları olan beslenme hakkına bilgi boyutu ortalamasının 19,6±5,6, beslenmeye yönelik duygu boyutu ortalaması 17,6±3,7, olumlu beslenme boyutu ortalaması 19,2 ± 5,1 ve kötü beslenme boyutu ortalaması ise 11,3±4,3 olduğu bulunurken, öğrencilerin %58,3'ünün sağlıklı beslenmeye ilişkin tutum düzeylerinin yüksek düzeyde olduğu da saptanmıştır.

Kız öğrencilerin %28,9'unun sosyal medya konuları ile ilgilenmediği görülürken, %29,8'inin sosyal medyada en çok yemek tarifi konularını takip ettiği görülmektedir. Ayrıca kız öğrencilerin SMBÖ toplam puan ortalamasının 54,2±13,8 olduğu; ölçeğin alt boyutları olan sanal tolerans boyutu ortalaması 32,3±8,2 ve sanal iletişim boyutu ortalamasının ise 21,9±7,3 olduğu belirlenmiştir.

Çalışmaya dahil edilen kız öğrencilerin beden imajına göre demografik ve antropometrik özellikleri, egzersiz, uyku, beslenme ve sosyal medya alışkanlıkları Tablo 2'de sunulmuştur.

Kız öğrencilerin beden memnuniyeti durumlarına göre BKİ, bel çevresi ölçümleri arasında istatistiksel olarak anlamlı bir fark tespit edilirken; beden memnuniyetsizliği olan kız öğrencilerin hem BKİ değerlerinin hem de bel çevresi ölçümlerinin memnun olanlara göre istatistiksel olarak daha yüksek olduğu tespit edilmiştir (p <0,001).

Kız öğrencilerin beden imajlarına göre ara öğün atlama durumu, öğün sayısı, diyet yapma ve besin etiketi okuma alışkanlığı durumları arasında istatistiksel olarak anlamlı bir fark olduğu bulunurken; beden memnuniyetsizliği olan kız öğrencilerin memnun olanlara göre daha fazla ara öğün yaptığı, daha az öğün sıklığına sahip olduğu, daha fazla diyet programına uyduğu ve daha fazla besin etiketi okuma alışkanlığına sahip olduğu bulunmuştur (sırasıyla p=0,005, p<0,001, p=0,004 ve p=0,029).

Kız öğrencilerin beden imajına göre SBİTÖ toplam puanı ve ölçek alt boyutlarından beslenmeye yönelik duygu, olumlu beslenme puanları arasında istatistiksel olarak anlamlı bir fark elde edilmiş olup, beden memnuniyeti olan kız öğrencilerin ölçek toplam puan ve alt boyutlara ait ortanca değerlerinin memnun olmayanlara göre daha yüksek olduğu saptanmıştır (sırasıyla p=0,001, p=0,039, p=0,001). Ayrıca kız öğrencilerin beden imajlarına göre sağlıklı beslenmeye ilişkin tutum düzeyleri arasında da istatistiksel olarak anlamlı bir fark saptanmış olup, bu farklılığın orta düzey tutum sergileyen öğrenciler arasında olduğu saptanmıştır (p=0,011).

Kız öğrencilerin beden memnuniyetine göre sosyal medyada en çok takip edilen konu dağılımları arasında istatistiksel olarak anlamlı bir fark olduğu (p<0,001), bu farklılığında beden memnuniyetsizliği olan kız öğrencilerin memnun olanlara göre zayıflama konulu içerikleri daha fazla oranda takiplerinden kaynaklandığı tespit edilmiştir.

Tablo 3'te kız öğrencilerin beden memnuniyeti ile ilişkili faktörlerin etkisi incelenmiştir. Üç modelden oluşan hiyerarşik lojistik regresyon analizi bulguları incelendiğinde, tüm modeller istatistiksel olarak anlamlı bulunmuştur (Model 1 ki-kare: 121,550, Model 2 ki-kare: 152,170, Model 3 ki-kare: 172,200; p<0,001). AIC değerleri incelendiğinde ise; antropometrik ölçümler, beslenme ve sosyal medya alışkanlığı değişkenleri arasındaki etkilerin dahil edilmesi ile model 1 ve model 2'ye göre model 3'te daha düşük bir AIC değeri elde edilmiştir. Bu sonuçlar model 3'ün daha iyi bir model uyumu sağladığını göstermektedir.

Model 1'de antropometrik ölçümlerin etkisi değerlendirilirken, model 2'de antropometrik ölçümlere beslenme alışkanlıklarının etkisi de dahil edilmiştir. Elde edilen bulgular incelendiğinde her iki modelde de BKİ ve bel çevresi ölçümlerinin beden memnuniyeti üzerine olan etkisinin anlamlı olduğutespit edilmiş olup; BKİ ve bel çevresi değerleri arttıkça, beden memnuniyetinin azaldığı saptanmıştır (Model 1 sırasıyla OR: 0,728 ve OR: 0,934; p<0,001, p<0,05; model 2 sırasıyla OR: 0,765 ve OR: 0,922; p<0,001, p<0,05).

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Tablo 1. Kız Öğrencilerin Tanımlayıcı Özellikleri

	n / +SS	% / Ortanca (alt-üst)	Cronbach Alfa
Yaş (yıl)	21,3 ± 3,4	21 (18 - 41)	
Medeni Durum			
Evli	23	6,5	
Bekar	333	93,5	
Eğitim alanı			
Sağlık Bilimleri	256	71,9	
Sosyal Bilimler	100	28,1	
BKI (kg/m²)	21,7 ± 3,8	21 (13,5 – 40,6)	
Bel Çevresi (cm)	72,1 ± 10,9	70 (50 - 126)	
Kalça Çevresi (cm)	96,1 ± 10,1	96 (40 - 140)	
Bel/kalça	0,74 ± 0,08	0,73 (0,58 -1,25)	
Düzenli Egzersiz			
Evet	95	26,7	
Hayır	261	73,3	
Günlük Uyku Süresi (saat)	8,4 ± 1,7	8 (5 - 13)	
Ara Öğün Atlama			
Evet	264	74,2	
Hayır	92	25,8	
Kaç Öğün Yemek	2,8 ± 1,1	3 (1 - 6)	
Diyet Programı Durumu			
Evet	29	8,1	
Hayır	327	91,9	
Besin Etiketi Okuma Alışkanlığı			
Evet	150	42,1	
Hayır	206	57,9	
Beden İmajı Ölçeği Puanı	-0,7 ± 1,2	0 (-4 - 2)	
Beden İmajı			
Memnun Değil	180	50,6	
Memnun	176	49,4	
SBİTÖ			
-Beslenme Hakkında Bilgi	19,6 ± 5,6	20 (5 - 71)	0,456
-Beslenmeye Yönelik Duygu	17,6 ± 3,7	18 (8 - 26)	0,699
-Olumlu Beslenme	19,2 ± 5,1	19 (6 - 30)	0,719
-Kötü Beslenme	11,3 ± 4,3	11 (4 - 20)	0,782
Toplam Puan	67,8 ± 9,8	67 (43 - 115)	0,653
Sağlıklı Beslenmeye İlişkin Tutumları			
Orta	127	35,8	
Yüksek	207	58,3	
İdeal	21	5,9	
En Çok Takipteki Konular			
İlgilenmiyorum	103	28,9	
Sağlıklı Beslenme	62	17,4	
Yemek Tarifleri	106	29,8	
Zayıflama	30	8,4	
Sağlıklı Beslenme+Zayıflama	27	7,6	
Sağlıklı Beslenme+Yemek Tarifleri	28	7,9	
SMBÖ			
-Sanal Tolerans	32,3 ± 8,2	33 (12 - 51)	0,783
-Sanal İletişim	21,9 ± 7,3	22 (8 - 45)	0,836
Toplam Puan	54,2 ± 13,8	55 (21 - 92)	0,871

BKİ: Beden Kütle İndeksi; SBİTÖ: Sağlıklı Beslenmeye İlişkin Tutum Ölçeği; SMBÖ: Sosyal Medya Bağımlılık Ölçeği; kg: kilogram; cm: santimetre; m: metre; $\bar{X}$+SS: Ortalama Standart sapma

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Tablo 2. Kız öğrencilerin beden imajı ile demografik özellikleri, antropometrik ölçümleri ve sosyal medya alışkanlıkları arasındaki ilişkilerin incelenmesi

	Memnun Değil (n=180) Ortanca (alt-üst)	Memnun (n=176) Ortanca (alt-üst)	p
Yaş (Yıl)	20,5 (18 - 41)	21 (18 - 34)	0,157[m]
Medeni Durum			
Evli	13 (7,2)	10 (5,7)	0,583[f]
Bekar	167 (92,8)	166 (94,3)	
Eğitim Alanı			
Sağlık Bilimleri	124 (68,9)	132 (75)	0,200[x]
Sosyal Bilimler	56 (31,1)	44 (25)	
BKI (kg/m^2)	22,4 (16,4 - 40,6)	19,6 (13,5 - 29)	<0,001[m]
Bel Çevresi (cm)	73 (57 - 126)	67 (50 - 85)	<0,001[m]
Kalça Çevresi (cm)	98 (72 - 140)	92 (40 - 110)	<0,001[m]
Bel/kalça	0,75 (0,60-1,10)	0,71 (0,58-1,25)	<0,001[m]
Düzenli Egzersiz			
Evet	48 (26,7)	47 (26,7)	1,000[x]
Hayır	132 (73,3)	129 (73,3)	
Günlük Uyku Süresi	8 (5 - 11)	8 (5 - 13)	0,127[m]
Ara Öğün Atlama			
Evet	145 (80,6)	119 (67,6)	0,005[x]
Hayır	35 (19,4)	57 (32,4)	
Kaç Öğün Yemek	2 (1 - 6)	3 (1 - 6)	<0,001[m]
Diyet Programı Durumu			
Evet	22 (12,2)	7 (4,0)	0,004[x]
Hayır	158 (87,8)	169 (96,0)	
Besin Etiketi Okuma Alışkanlığı			
Evet	86 (47,8)	64 (36,4)	0,029[x]
Hayır	94 (52,2)	112 (63,6)	
SBİTÖ			
-Beslenme Hakkında Bilgi	20 (5 - 44)	20 (5 - 71)	0,360[m]
-Beslenmeye Yönelik Duygu	18 (8 - 26)	18 (9 - 26)	0,039[m]
-Olumlu Beslenme	18.5 (6 - 30)	20 (6 - 30)	0,001[m]
-Kötü Beslenme	11 (4 - 20)	11.5 (4 - 20)	0,291[m]
Toplam Puan	66 (43 - 92)	69 (50 - 115)	0,001[m]
Sağlıklı Beslenmeye İlişkin Tutumları			
Orta	77 (42,8)[a]	50 (28,6)[b]	0,011[x]
Yüksek	96 (53,3)[a]	111 (63,4)[a]	
İdeal	7 (3,9)[a]	14 (8)[a]	
En Çok Takipteki Konular			
İlgilenmiyorum	46 (25,6)[a]	57 (32,4)[a]	<0,001[f]
Sağlıklı Beslenme	25 (13,9)[a]	37 (21)[a]	
Yemek Tarifleri	53 (29,4)[a]	53 (30,1)[a]	
Zayıflama	26 (14,4)[a]	4 (2,3)[b]	
Sağlıklı Beslenme+Zayıflama	18 (10)[a]	9 (5,1)[a]	
Sağlıklı Beslenme+Yemek Tarifleri	12 (6,7)[a]	16 (9,1)[a]	
SMBÖ			
-Sanal Tolerans	32 (17 - 51)	33 (12 - 49)	0,997[m]
-Sanal İletişim	22 (8 - 45)	22 (9 - 45)	0,916[m]
Toplam Puan	55 (27 - 88)	55 (21 - 92)	0,737[m]

BKİ: Beden Kütle İndeksi; SBİTÖ: Sağlıklı Beslenmeye İlişkin Tutum Ölçeği; SMBÖ: Sosyal Medya Bağımlılık Ölçeği; kg: kilogram; cm: santimetre; m: metre; m: Mann Whitney U testi, x: Pearson ki-kare testi, f: Fisher's exact testi, a-b: Aynı harfe sahip gruplar arasında fark yoktur (Bonferroni düzeltmeli Z testi)

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Tablo 3. Kız öğrencilerin beden imajını etkileyen faktörlerin hiyerarşik lojistik regresyon analizi ile incelenmesi

	Model 1	Model 2	Model 3
	OR (%95 CI)	OR (%95 CI)	OR (%95 CI)
Antropometrik ölçümler			
BKI	0,728 (0,634 - 0,827)**	0,765 (0,661 - 0,876)**	0,767 (0,659 - 0,885)**
Bel Çevresi	0,934 (0,888 - 0,980)*	0,922 (0,872 - 0,972)*	0,918 (0,866 - 0,969)*
Kalça Çevresi	1,001 (0,961 - 1,042)	0,981 (0,939 - 1,025)	0,979 (0,935 - 1,025)
Beslenme Alışkanlıkları			
Ara Öğün Atlama (Ref: Hayır)		1,535 (0,791 - 3,018)	1,82 (0,903 - 3,726)
Öğün Sayısı		1,157 (0,890 -1,515)	1,147 (0,870 - 1,522)
Diyet Programı Durumu (Ref: Hayır)		2,452 (0,815 - 8,047)	2,015 (0,552 - 7,975)
Besin Etiketi Okuma Alışkanlığı (Ref: Hayır)		1,771 (0,994 - 3,183)	1,687 (0,905 - 3,172)
Beslenmeye Yönelik Duygu		1,062 (0,963 - 1,171)	1,089 (0,981 - 1,208)
Olumlu Beslenme		1,074 (0,996 - 1,159)	1,063 (0,980 - 1,154)
SBİTÖ Toplam Puan		1,015 (0,975 - 1,058)	1,032 (0,988 - 1,080)
Sosyal Medya Alışkanlıkları			
En Çok Takipteki Konular (Ref: İlgilenmiyorum)			
Sağlıklı beslenme			0,576 (0,236 - 1,387)
Yemek tarifleri			0,275 (0,125 - 0,584)*
Zayıflama			0,139 (0,033 - 0,477)*
Sağlıklı beslenme+Zayıflama			0,216 (0,069 - 0,647)*
Sağlıklı beslenme+Yemek tarifleri			0,594 (0,184 - 1,907)
Model Chi-Square (df)	121,550 (3)**	152,170 (10)**	172,200 (15)**
McFadden's pseudo R2	0,246	0,308	0,349
AIC	379,9286	363,307	353,278

AIC: Akaike Bilgi Kriteri; BKİ: Beden Kütle İndeksi; CI: Confidence Interval; OR: Odds Ratio; Ref: Referans; SBİTÖ: Sağlıklı Beslenmeye İlişkin Tutum Ölçeği; *p<0,05; **p<0,001

Model 3'te elde edilen bulgular incelendiğinde ise antropometrik ölçümler ve sosyal medyada en çok takip edilen konuların beden memnuniyeti üzerine etkisinin anlamlı olduğu tespit edilmiş olup; BKİ ve bel çevresi değerleri arttıkça, beden imajı memnuniyetinin azaldığı (sırasıyla OR:0,767 ve OR:0,918; p<0,001, p<0,05); ancak beslenme alışkanlıkları durumlarının beden memnuniyetine olan etkisinin istatistiksel olarak anlamlı olmadığı bulunmuştur (p>0,05). Sosyal medyada yemek tarifleri, zayıflama ve sağlıklı beslenme+zayıflama konularını takip eden kız öğrencilerin ise sosyal medya konuları ile ilgilenmeyen öğrencilere göre beden memnuniyetsizliğinin istatistiksel olarak daha fazla olduğu bulunmuştur (sırasıyla OR:0,275 OR:0,139 ve OR:0,216, p<0,05).

TARTIŞMA

Bu çalışmada Üniversitede eğitim gören kız öğrencilerde sosyal medya kullanımına dair özellikler ile beden memnuniyeti ve sağlıklı beslenme durumları arasındaki ilişkinin değerlendirilmesi ve sağlıklı beslenme ile sosyal medya kullanım durumlarının beden memnuniyeti üzerindeki etkisinin incelemesi amaçlanmış olup, üniversitede eğitim gören kız öğrencilerde genel ve santral obezite risk faktörleri ile sağlıklı beslenmeye ilişkin tutumların ve bazı sosyal medya takip konularının beden memnuniyeti üzerinde olumsuz etki oluşturabileceği bulunmuştur.

Üniversite dönemine denk gelen genç yetişkinlik dönemi bağımsızlıklara yönelik yeni becerilerin geliştirildiği bir dönem olduğu için beslenme alışkanlıklarının en çok etkilendiği dönemler arasında gösterilmektedir. Bu dönemde yetişkinler sosyal çevre edinme, eğlenceli vakit geçirme ve bilgiye ulaşabilme/paylaşabilme gibi nedenlerle sosyal medyayı aktif olarak kullanmaktadırlar (17). Hızla yaygınlaşan ve giderek günlük yaşamın vazgeçilmezi haline gelen sosyal medyanın kullanımı etkileşim üzerindeki olumlu etkileriyle beraber paylaşılan bilgilerin güvensizliği ve kontrolsüzlüğü açısından benzer oranda da risklere

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sahip olabilmektedir (7). Bu dönemi oluşturan popülasyonun sosyal medyada en çok araştırdıkları konuların başında ise sağlık ve beslenme konuları gelmektedir (18). Önemli bir geçiş dönemi olan üniversite döneminde sosyal medyanın kontrolsüz ve aşırı kullanımı sosyal medya bağımlılığı oluşturmasının yanı sıra beden imajı kaygısını ve buna istinaden beslenme durumunu olumsuz yönde etkileyebilmektedir (19). Yakın tarihte yapılan sistematik bir incelemede sosyal medyanın yeni bir bağımlılık olarak sınıflandırıldığı ve sosyal medyanın yoğun kullanımının beden memnuniyetsizliği, düşük öz saygı ve yeme bozukluklarıyla ilişkili olduğu tespit edilmiştir (20). Literatürde, beden imajı üzerine yapılan çalışmalar genellikle kadın cinsiyetine odaklanmaktadır (21, 22). Lisans öğrencileri arasında vücut ağırlığı ve beden memnuniyetsizliğinin incelendiği bir çalışmada, kız öğrencilerde erkek öğrencilere kıyasla daha fazla beden memnuniyetsizliğinin olduğu ve normal vücut ağırlığına sahip olan kız öğrencilerin bile daha hafif ve daha ince bir vücuda sahip olmayı istedikleri görülmüştür (23). Ülkemizde ise üniversite öğrencileriyle yapılan bir çalışmada öğrencilerin orta düzeyde sosyal medya bağımlılığına sahip oldukları bulunurken, beden memnuniyetsizliği olan üniversite öğrencilerinin daha fazla sosyal medya bağımlılığına sahip oldukları ve sosyal medya bağımlılığının beden memnuniyetsizliği için bir risk faktörü olduğu bulunmuştur (24-25). Suudi Arabistan'da yapılan başka bir çalışmada ise üniversitede eğitim gören ve beden memnuniyetsizliğine sahip olan kız öğrencilerin zayıflama, yemek tarifleri, egzersiz ve diyetlerle ilgili konuları sosyal medyada takip edenlerin beslenme alışkanlıkları olumsuz yönde etkilendiği saptanmıştır (26). Bu çalışmada da literatürü destekleyecek şekilde sosyal medyada yemek tarifleri, zayıflama ve sağlıklı beslenme+zayıflama konularını takip eden kız öğrencilerin, sosyal medya ile ilgilenmeyen öğrencilere göre beden memnuniyetsizliği riskinin istatistiksel olarak daha fazla olduğu bulunmuştur ($p<0,05$) (Tablo 3).

Beden memnuniyetsizliği ile ilişkilendirilen beden imajı kaygısı ise, vücut görüntü bileşenlerindeki rahatsızlıkları tanımlayan genel bir terim olup, bu konuda yapılmış birçok çalışmada beden imajındaki kaygının kronik diyet yapma durumuyla ya da bu düşünceye yoğun bir şekilde bağlı kalmayla, vücut ağırlığı üzerindeki kontrol dışı davranışlarla, düşük benlik saygısıyla, depresyonla, obezite ve yeme bozukluklarıyla ilişkili olduğu gösterilmektedir (10, 27). Üniversite dönemi popülasyonunu oluşturan genç yetişkinlerde, kadın popülasyonu daha baskın olmak üzere, beden imajı süreklilik içerisinde deneyimlenerek değişmektedir (6). Bir bireyin bedeni hakkındaki memnuniyetsizlik hissiyatı arttıkça bireyin benlik saygısının olumsuz yönde etkilenmesiyle birlikte uzun vadeli olumsuz sağlık sonuçlarına yol açan sık aralıklarla yapılan diyetler, yoğun besin etiketi okuma ve kalori sayımı, aşırı yeme ya da öğün atlama gibi yanlış yeme alışkanlıkları oluşarak, bireylerin sağlıklı beslenme alışkanlığı bozulabilmekte ve bu durumda bireylerin beden memnuniyetsizliğini daha da arttırabilmektedir (28). Vereecken ve ark'nın kızların vücut görünümlerine erkeklerden daha fazla önem verdiklerinden ve ideal vücut görünümlerine ulaşmak için daha fazla zaman harcama olasılıkları sahip olduklarından daha sık kahvaltı ve diğer öğünleri atladıkları saptanmıştır (29). Beden imajı ve beslenme düzeni ilişkisinin saptanması amacıyla yapılan bir çalışmada da sosyal medyaya ve diyetle ilgili içeriğe yoğun oranda maruz kalmanın, bireylerin beslenme alışkanlıklarını, öğün sıklığını ve vücutlarının nasıl göründüğü hissiyatını önemli ölçüde değiştirmeye katkıda bulunduğu belirlenmiştir (30). İngiltere'de yapılan bir çalışmada ise besin etiketleriyle ilgili deneyimlerin beden imajı endişeleriyle şekillenebileceği ortaya koyulurken, Raffoul ve ark'ın karma yöntemli çalışmasında da, düşük beden saygısına sahip bireylerin besin etiketlerini diğerlerinden farklı algıladıkları da ortaya koyulmuştur; bu da besin etiketlerine okuma farkındalığının bireylerin beden algıları ile ilişkili olduğu anlamına gelmektedir (31). Buna karşılık, Lillico ve ark. öğrencilerde besin etiketlerinin düzensiz yeme düşünceleri veya davranışları üzerinde hiçbir etkisi olmadığını bulmuşlardır (32). Bu çalışmada da Vereecken ve ark çalışmasına benzer şekilde beden memnuniyetsizliği olan kız öğrencilerin memnun olanlara göre daha fazla ara öğün yaptığı, daha az öğün sıklığına sahip olduğu, daha fazla diyet programına uyduğu ve daha fazla besin etiketi okuma alışkanlığınasahip olduğu bulunmuştur (sırasıyla $p=0,005$, $p<0,001$, $p=0,004$ ve $p=0,029$) (Tablo 2) (29). Modern kültürün zayıflığı güzellik olarak vurgulaması,

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vücut ağırlığı fazla olan bireyleri etiketlemesi, obez bireylerin bu kültürel mesajları içselleştirmelerine ve fiziksel görünümleri konusunda kötü hissetmelerine neden olmaktadır (33). Aslında, birçok çalışmada, BKİ ile beden memnuniyetsizliği arasında pozitif bir ilişki bulunmuştur (34, 35). Divecha ve ark yapmış oldukları bir çalışmada BKİ değerleri ile beden memnuniyetsizliği arasında anlamlı ve doğrusal bir ilişki bulunmuştur (36). Yakın zamanda yapılan bir meta-analizde ise obez bireylerin normal vücut ağırlığı olan bireylere göre daha fazla beden memnuniyetsizliğine sahip oldukları bulunmuştur (37). Bu çalışmada da beden memnuniyetsizliğine sahip olan bireylerin hem BKİ hem de bel çevresi ölçümlerinin daha yüksek olduğu belirlenirken ($p<0,001$), BKİ ve bel çevresindeki artışların beden memnuniyetsizliği riskini anlamlı şekilde arttırdığı da belirlenmiştir (sırasıyla $p<0,001$, $p<0,05$) (Tablo 3). Bu sonuçlar literatürü destekler niteliktedir. Bu çalışmanın güçlü yönleri arasında doğrulanmış anketlerin kullanılması ve çeşitli fakültelerden rastgele bir örneklem alınması yer almaktadır. Ek olarak, sosyal medya kullanımın daha yaygın olduğu üniversite çağındaki bireyler hedeflenmiştir. Ancak çalışmanın bazı kısıtlılıkları da bulunmaktadır. Bunlardan ilki çalışma kesitsel bir tasarıma sahip olduğu için genellemeye imkan vermemesi iken, diğerleri ise çalışmaya erkek öğrencilerin dahil edilmemesi ve üniversitede sadece sağlık ve sosyal bilimler alanındaki öğrencilere ulaşılabildiği için diğer bölümlerin değerlendirilememesidir.

SONUÇ

Sonuç olarak üniversite öğrencilerinde sosyal medya bağımlılığı, beden memnuniyeti ve beslenme alışkanlıkları karşılıklı olarak birbirini etkileyebilmektedir. Sosyal medyada idealize edilen zayıf beden imajına kız öğrenciler daha duyarlı olmakta; bu nedenle, bu ideale ulaşma çabası onları sağlıklı beslenme alışkanlıklarından daha kolay uzaklaştırabilmektedir. Bu çalışmada da üniversitede eğitim gören ve beden memnuniyetsizliğine sahip olan kız öğrencilerin genel ve santral obezite ölçümlerinin daha yüksek olduğu ve sağlıklı beslenmeye ilişkin tutumlarının ise daha düşük olduğunun tespit edilmesiyle birlikte sosyal medyada özellikle yemek tarifleri, zayıflama ve sağlıklı beslenme konularını takip etmenin de beden memnuniyetsizliği açısından bir risk faktörü oluşturabileceği tespit edilmiştir. Bu nedenle sosyal medya kullanımının yaygın olduğu bu dönemdeki öğrenciler için beden memnuniyetini olumsuz yönde etkileyen risk faktörlerine yönelik taramalar yapılmasının ve sağlıklı beslenme ile normal düzeyde BKİ değerlerinde olmanın farkındalığını arttıran eğitim ve müdahalelerin gerekliliği büyük önem taşımaktadır.

Tasdik ve Teşekkür

Yazarlar arasında herhangi bir çıkar çatışması bulunmamaktadır.

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SPINAL ACCESSORY NERVE PALSY AND WINGED SCAPULA CAUSED BY REPETITIVE STRAIN: A CASE REPORT

Tekrarlayan Gerilme Sonucu Oluşan Spinal Aksesuar Sinir Felci ve Kanat Skapula: Bir Olgu Sunumu

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ABSTRACT

Scapular winging is a rare disorder that causes functional limitation of the upper extremity. It may develop due to many pathological conditions that can cause paralysis in the serratus anterior, trapezius and rhomboid muscles (which are innervated by the long thoracic nerve, spinal accessory nevre, and dorsal scapular nerve, respectively). Diagnosis is made by imaging and electrodiagnostic studies after physical examination. In this case, it is aimed to present the diagnosis and treatment stages of the patient who developed shoulder pain, muscle weakness, and scapular winging, due to injury to the spinal accessory nerve, which is the 11th cranial nerve and provides pure motor innervation to the trapezius muscle. Although scapular winging is not a condition we frequently encounter in clinical practice, it is important due to its potential for disability that may affect the quality of life.

Keywords: *Scapular Winging; Spinal Accessory Nerve; Electrodiagnostic Assessment*

ÖZET

Amaç: Skapular kanatlanma, üst ekstremitede fonksiyonel kısıtlılığa neden olan nadir bir hastalıktır. Serratus anterior, trapezius ve rhomboid kaslarında (sırasıyla long torasik sinir, spinal aksesuar sinir ve dorsal skapular sinir tarafından innerve edilir) felce neden olabilen birçok patolojik duruma bağlı olarak gelişebilir. Tanı, fizik muayene sonrası görüntüleme ve elektrodiagnostik çalışmalarla konulur. Bu olguda, 11. kranial sinir olan ve trapezius kasına saf motor innervasyon sağlayan spinal aksesuar sinirin yaralanması sonucu omuz ağrısı, kas güçsüzlüğü ve skapular kanatlanma gelişen hastanın tanı ve tedavi aşamalarını sunmak amaçlanmıştır. Skapular kanatlanma klinik pratikte sıklıkla karşılaştığımız bir durum olmasa da yaşam kalitesini etkileyebilecek sakatlık potansiyeli nedeniyle önemlidir.

Anahtar Kelimeler: *Skapular Kanatlanma; Spinal Aksesuar Sinir; Elektrodiagnostik Değerlendirme*

INTRODUCTION

Wing scapula (scapula alata) is a clinical condition characterized by the medial edge of the scapula moving away from the thorax, which often develops due to the dysfunction of the serratus anterior, trapezius, and rhomboid muscles, which are the scapulothoracic stabilizing muscles (1, 2). It may cause a decrease in shoulder muscle strength due to disruption of scapulohumeral rhythm, a decrease in joint range of motion, pain, and asymmetry due to tension and spasm in the periscapular muscles (3, 4). It is divided into three groups according to etiological factors: primary, secondary, and voluntar. In the primary wing scapula, the factors are neurological, bony, and surrounding soft tissue pathologies in the scapulothoracic joint, and in the secondary wing scapula, the factors are glenohumeral and/or subacromial pathologies. Voluntary wing scapula is less common and is thought to have a psychological origin (5).

The spinal accessory nerve (SAN), which provides innervation to the trapezius, is superficial as it passes through the posterior cervical triangle. There is a high risk of injury during minor surgical interventions (biopsies) and radical neck dissections in this area. The nerve may also be exposed to blunt trauma and repetitive strain injuries in this region (6). After an accessory nerve lesion, patients develop periscapular pain in a short time. In chronic pathologies, pain can be felt in the forearm, hand, face, head,

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and opposite upper extremities. The patient's scapula slides laterally and the inferior angle turns outward. The patient's functions in daily life begin to be restricted, and the pathological condition and clinical picture may not appear immediately due to overwork of the compensatory muscles at the beginning of the acute period. When muscle fatigue begins, the affected shoulder falls downward, and shoulder asymmetry is evident. There is trapezius atrophy and wing scapula appearance develops.

Functionally, elevation and abduction are limited. To make a diagnosis, anamnesis, physical examination, radiological examination and (Electromyography) EMG must be performed. In a study, it was observed that 71% of the cases with SAN injury were iatrogenic and 24% were trauma-related. Spontaneous or idiopathic cases are extremely rare (7). Here, the diagnosis and treatment stages of a case that developed SAN damage after excessively repetitive stretching exercises are presented.

CASE REPORT

A 25-year-old male patient applied to our outpatient clinic with complaints of right shoulder pain, drooping of the right shoulder and thinning of the right shoulder muscles. He stated that his shoulder pain increased, especially during abduction and activity. There was no complaint of numbness or tingling. There was no additional disease, trauma, medication use, surgical history, or family history. In his history, it was learned that the patient had repeated this neck stretching movement to the left excessively, as he was relieved of neck pain that had been occurring intermittently for the last year, especially when he moved his neck to the left lateral flexion. In the physical examination of the patient, there was asymmetry between the shoulders, a drop in the right shoulder, atrophy in the upper part of the right trapezius muscle, and a winged scapula on the right side, which became evident with right shoulder abduction and disappeared at rest (Fig. 1 and 2).

Neurological examination revealed muscle weakness of 4/5 of the right shoulder abductor muscles and +3/5 of the right trapezius muscle. Cranial nerve examination, sternocleidomastoideus (SCM), and other muscle strengths were normal. Superficial sensory examination and deep tendon reflexes were within normal limits. Laboratory examinations and imaging methods were also evaluated as normal. (Routine hemogram, biochemistry tests, vitamin B12 level, thyroid function tests, shoulder, cervical, and lung radiographs were normal.) EMG showed normal right upper extremity median and ulnar nerve motor and sensory conduction studies. Right SAN - trapezius muscle recording - motor response could not be obtained. In needle EMG, the right SCM, deltoid, supraspinatus, infraspinatus, serratus anterior, levator scapula, and rhomboid major muscles were evaluated as normal. Spontaneous

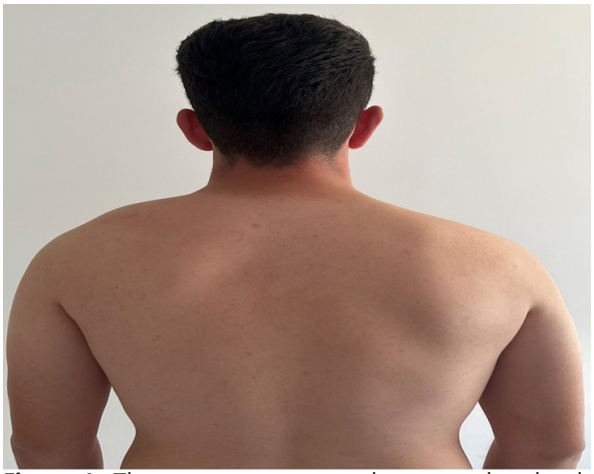

Figure 1. There was asymmetry between the shoulders, a drop in the right shoulder, atrophy in the upper part of the right trapezius muscle, and a winged scapula on the right side.

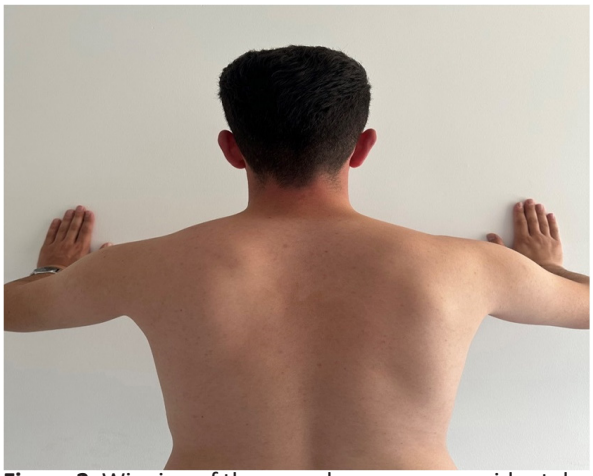

Figure 2. Winging of the scapula was more revident during wall push-up.

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activity in the upper, middle, and lower parts of the right trapezius muscle, an increased polyphasic motor unit potentials in mild contraction, and a dilution in the interference pattern in full contraction were detected. These findings were interpreted as compatible with partial axon damage in the branch of the right accessory nerve leading to the trapezius muscle. In parallel with the rehabilitation program planned for the patient, a 15-minute hot pack application and conventional (Transcutaneous Electrical Nerve Stimulation) TENS application were performed on the right shoulder. Electrostimulation was applied to the trapezius muscle in atrophy mode. An active assistive and resistive exercise program was applied gradually. At the same time, a home exercise program was organized. After the 4-week rehabilitation program, a significant improvement in shoulder abductor muscle strength was observed. In the follow-up examination performed 6 months later, it was observed that the trapezius atrophy partially continued, muscle strength almost had fully recovered, and joint range of motion was normal. He had no complaints other than shoulder pain that occurred with strenuous activities.

DISCUSSION

The trapezius muscle is between the cervical and thoracic vertebrae and the spina scapula and acromion. The upper fibers of the trapezius muscle contribute to scapulothoracic movement by moving the shoulder downwards with scapula elevation, the middle fibers with scapula rotation, and the lower fibers with scapula retraction. The upper and lower fibers cause upward rotation and abduction of the scapula in the horizontal plane (8). After passing through the jugular foramen, the SAN gives branches to the sternocleidomastoid (SCM) muscle. It enters the posterior neck triangle space and stimulates the upper fibers of the trapezius muscle and the middle and lower fibers along with the branches of the cervical plexus (9,10). The superficial course of the nerve makes it more prone to injury during posterior cervical region traumas, cervical lymph node dissection, and mass excision. SAN damage occurring during neck surgery has decreased in recent years due to the development of new techniques. Although it is rarely seen spontaneously or idiopathically, there are cases described as an occupational disease in carpenters, car mechanics, welders, and tailors (9).

Trapezius muscle paralysis is often neurogenic and develops due to SAN damage. In SAN paralysis, with abduction of the arm, the wing scapula becomes prominent, and the scapula moves upward. In SAN damage, the trapezius muscle appears atrophic, there is a steep slope between the neck and the shoulder, and the shoulder falls down. The distance of the scapula to the vertebra decreases. If the SAN lesion site is proximal, difficulty is observed in turning the head and lifting the shoulder to the opposite side of the lesion. If the lesion is distal, the SCM is preserved, and weakness in shoulder elevation and abduction is observed. In our case, there was trapezius muscle failure due to SAN damage, shoulder drop, and lateral winging that became evident when the arm was in abduction. The preservation of the SCM muscle, the presence of trapezius muscle atrophy, and limitation of shoulder elevation and abduction indicate that the SAN is affected distally. In its physiopathology, it is thought that neuropraxia develops in the nerve due to repetitive trauma. Fibrosis, microvascular insufficiency, and resulting neuropathy develop in the fascia of the muscle (1).

Although wing scapula developing due to SAN damage is rare, it is a clinical condition that limits the patient's upper extremity functions and whose etiology can be very diverse. The fact that it can mimic many diseases can make diagnosis difficult and lead to a delay in diagnosis (11). For a correct diagnosis, a good clinical examination is first required. EMG is the gold standard in diagnosis and is very important in identifying different peripheral neurological conditions, including compressive syndromes, and in showing nerve damage (1). In the treatment, pain control, electrical stimulation, and early joint range of motion exercises, scapular stabilization exercises, and strengthening exercises (trapezius, rhomboids and levator scapula muscles) are given. A significant improvement was observed after rehabilitation in our case which developed wing scapula due to SAN damage caused by excessively repetitive exercises.

CONCLUSION

In conclusion, although this case report is extremely rare in the literature, it draws attention to the fact

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that fibrosis and microvascular insufficiency in the fascia of the muscle due to repetitive trauma may cause neuropraxia in the nerve. Disability of patients can be prevented with early diagnosis and effective rehabilitation programs.

Acknowledgment

The authors declare that they have no conflict of interest to disclose.

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CATEGORIES OF ARTICLES

Original Research Articles:

Original prospective or retrospective studies of basic or clinical investigations in areas relevant to medicine.

Content: - Abstract (200-250 words; the structured abstract contain the following sections: Objective, material and methods, results, conclusion; both in Turkish and English)
- Introduction
- Material and Methods
- Results
- Discussion/ Conclusion
- Acknowledgements
- References

*Original articles should be no longer than 5000 words and should include no more than 6 figures / tables and 40 references.

Review Articles

The authors may be invited to write or may submit a review article. Reviews including the latest medical literature may be prepared on all medical topics. Authors who have published materials on the topic are preferred.

Content: - Abstract (200-250 words; without structural divisions; both in Turkish and English)
- Titles on related topics
- References

* These manuscripts should be no longer than 5000 words and include no more than 4 figures and tables and 100 references.

Short Communications

It should be no longer than 2000 words and include no more than 2 figures and tables and 20 references.

Case Reports

Brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens. They should include an adequate number of photos and figures.

Content: - Abstract (average 100-150 words; without structural divisions; both in Turkish and English)
- Introduction
- Case report
- Discussion
- References

Letter to the Editor

These are the letters that include different views, experiments and questions of the readers about the manuscripts that were published in this journal in the recent year.

Content: - There's no title, abstract, any figures or tables
- It should be no more that 500 words, the number of references should not exceed 5.
- Submitted letters should include a note indicating the attribution to an article (with the number and date) and the name, affiliation and address of the author(s) at the end.
- The answer to the letter is given by the editor or the author(s) of the manuscript and is published in the journal.

Checklist

The manuscript should be prepared as separate files in the following order:

1. Cover Letter
2. Title Page
3. Abstract
4. Main Text (text, acknowledgments, references, tables, and figure legends)
5. Figures
6. Copyright Form