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Indexing & Abstracting & Archiving

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Research Article

Anestezi Yoğun Bakım Ünitesinde Ekstübe Edilen Kardiyak Hastaların Retrospektif Analizi

A Retrospective Analysis of Cardiac Patients Extubated in the Anesthesia Intensive Care Unit

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Amaç: Bu çalışmada amacımız anestezi yoğun bakım ünitesi (YBÜ)'nde kardiyak kaynaklı mekanik ventilatör (MV) ile takip ettiğimiz ve ekstübe edilerek YBÜ ihtiyacı kalmayan hastaların kardiyoloji bölümüne nakledildikten sonraki süreçte uygulanan tedavilerin incelenmesidir.

Gereç ve yöntem: Çalışmaya anestezi YBÜ'de MV'de takip edilen kalp yetmezliği (KY) sebepli yatışı olan ve ani kardiyak arrest (AKA) sonrası başarılı kardiyopulmoner resüsitasyon (PRS) hastaları çalışmaya dahil edildi. Hastaların cinsiyetleri, başvuru sırasındaki yakınmaları, altta yatan sistemik hastalık öyküsü, kaç gün entübe vaziyette takip edildiği, ekstübe edildikten kaç gün sonra kardiyoloji servisine devredildiği, yapılan ve/veya önerilen medikal tedaviler, girişimsel tedaviler değerlendirildi.

Bulgular: Çalışmaya toplam 145 hasta dahil edildi ve yaş ortalaması 66.46 ± 13.8 idi. Hastaneye başvuru sebepleri sırasıyla %71 oranında dispne, %22,1 ile AKA sonrası PRS ve %13,8 ile kardiyak aritmiydi. Hastaların YBÜ ortalama yatış süreleri 8,7 gün, ekstübe edildikten sonra kardiyoloji bölümüne devredilme süresi ortalama 4,5 gündü. Hastaların %11'ine anjio-stent uygulandı. Hastaların %5,5'ine intrakardiyak defibrilatör (ICD) implante edildi. Hastaların %93,8'i taburcu olurken, %4,8'i eksitus oldu.

Sonuç: Kardiyak kaynaklı takip edilen hastalar ekstübe edildikten sonra primer etiyolojinin araştırılması açısından kardiyoloji kliniğine danışılması ve özellikle ventriküler artimi ve KY hastalarının ICD ve ilaç tedavilerinin düzenlenmesi, ST eleve olmayan myokard infarktüsü hastalarının anjiolarının planlanması ve ilaç tedavilerinin düzenlenmesi açısından değerlendirilmesinin oldukça önemli olduğunu unutmamak gereklidir.

Anahtar Kelimeler: Yoğun bakım ünitesi, Ani kardiyak ölüm, Kalp yetmezliği, Mekanik ventilasyon

Objectives: In this study, our aim is to examine the treatments administered during the period following the transfer of patients from the anesthesia intensive care unit (ICU), who are being monitored with cardiac-origin mechanical ventilation (MV) and no longer require ICU care after extubation, to the cardiology department.

Material and Method: Patients with heart failure (HF) admitted to the anesthesia ICU and those who underwent successful cardiopulmonary resuscitation (CPR) after sudden cardiac arrest (SCA) and followed up with MV were included in the study. Patients' gender, complaints at admission, underlying systemic disease history, duration of intubation, duration until transfer to the cardiology service after extubation, medical treatments administered and/or recommended, and interventional treatments were evaluated.

Results: A total of 145 patients were included in the study, with a mean age of 66.46±13.8. The reasons for hospital admission were dyspnea in 71% of cases, post-SCA CPR in 22.1%, and cardiac arrhythmia in 13.8%. The mean length of stay in the ICU was 8.7 days, and the mean time until transfer to cardiology department after extubation was 4.5 days. Angioplasty was performed in 11% of patients, and implantable cardioverter-defibrillator (ICD) was placed in 5.5%. While 93.8% of patients were discharged, 4.8% deceased.

Conclusion: After extubation of patients followed up for cardiac reasons, it is important to consult the cardiology clinic for investigation of the primary etiology and, especially for patients with ventricular arrhythmias and HF, to evaluate the implantation of ICD and adjustment of drug treatments. It is crucial to evaluate planned angiography and adjustment of drug treatments for patients with non-ST elevated myocardial infarction.

Keywords: Intensive care unit, Sudden cardiac arrest, Heart failure, Mechanical ventilation

EXTENDED ABSTRACT

Objectives

Mechanical ventilation (MV) support is commonly applied to the majority of patients admitted to tertiary care intensive care units (ICUs), with cardiac patients and those with unknown cause sudden cardiac arrest (SCA) constituting one of the most frequently admitted patient groups. SCA is a significant health problem worldwide. Approximately 80% of SCAs are attributed to coronary heart disease (CHD), while other common causes include scar-related arrhythmias and cardiac pathologies that can potentially lead to fatal arrhythmias such as asystole and bradycardia. Another common reason for ICU admission due to cardiac causes is heart failure (HF), which leads to a significant morbidity and mortality. The aim of our study is to investigate the treatments administered to patients monitored with MV due to cardiac reasons in the anesthesia ICU who were extubated and transferred to the cardiology department.

Materials and Methods

The study was designed retrospectively and included 145 patients who were treated with MV in the Anesthesia ICU between January 2019 and April 2024, extubated during treatment, and transferred to the cardiology clinic. Cardiac patients included those with HF and those who underwent successful cardiopulmonary resuscitation (CPR) after SCA. Patient demographics, presenting complaints, underlying systemic disease history, duration of intubation, time to transfer to the cardiology service after extubation, medical treatments, interventional procedures, and length of stay in the cardiology department were recorded. These data were statistically analyzed.

Statistical Analysis

SPSS 20 (IBM SPSS Statistics Version 20.0; IBM Corp., Armonk, NY) was used for statistical analysis of the data. Qualitative data were expressed as numbers and percentages, while quantitative data were expressed as mean ± standard deviation (SD) and median (min, max).

Results

"A total of 145 patients were included in the study, with a mean age of 66.46 ± 13.8 years. Of these patients, 64.8% were female and 35.2% were male. The most common reason for hospital admission was dyspnea, accounting for 71% of cases. The second most common reason for admission was post-resuscitation syndrome (PRS) following SCA, at 22.1%, while cardiac arrhythmia accounted for 13.8% of cases. Other reasons included ST-elevation myocardial infarction (MI) at 9%, syncope at 4.1%, and postpartum patients at 0.7%. Patients with ST-elevation MI were intubated in the emergency department and transferred to the catheterization laboratory due to unavailability of space in the cardiology ICU. The most prevalent comorbidity was hypertension at 70.3%, followed by HF at 55.2%, and coronary artery disease (CAD) at 54.5%. Other comorbidities included diabetes mellitus, chronic obstructive pulmonary disease, cardiac arrhythmia, cerebrovascular events, and malignancy.

The average length of stay in the ICU was 8.7 days, while the mean duration from extubation to transfer to the cardiology department was 4.5 days. Among patients transferred to the cardiology service, 11% underwent angioplasty in the catheterization laboratory, and 3 patients were referred for coronary artery bypass graft (CABG) surgery. While 5.5% of patients received implantable cardioverter-defibrillator (ICD), transcatheter aortic valve implantation (TAVI) surgery was planned for 1 patient due to severe aortic stenosis. Of the 8 patients who received ICD due to ventricular arrhythmia (VA), 6 presented to the emergency department with a diagnosis of SCA, while 2 presented with isolated VA. Of the patients transferred to cardiology, 93.8% were discharged, while 4.8% died during hospitalization. Among the deceased patients, 2 had non-ST-elevation MI, 1 had an implanted ICD, 3 had HF, and 1 was planned for TAVI.

Conclusion

The diagnoses encountered in tertiary care ICUs exhibit a wide spectrum, reflecting the complexity of critical care medicine. Within this milieu, the

primary etiologies prompting MV in such settings display notable diversity. Among the myriad reasons necessitating ICU admission, pulmonary disorders, postoperative states, and cardiovascular maladies stand out as recurrent themes. HF looms large as a menacing condition, casting a shadow over public health landscapes globally. In confronting the exigencies posed by decompensated HF and acute respiratory failure, the prudent deployment of MV emerges as a pivotal therapeutic adjunct. The subset of patients mandating MV portends a prognosis marked by heightened mortality rates, underscoring the gravity of their clinical status.

SCA constitutes a poignant chapter in the narrative of adult mortality, exerting a profound impact on healthcare systems across the United States and Western Europe. Its grim toll, comprising approximately 15-20% of all natural deaths among adults and claiming roughly half of all cardiovascular fatalities, underscores the urgent imperative for effective interventions. Defibrillators emerge as frontline warriors in the battle against arrhythmic demise, embodying the vanguard of life-saving measures.

In conclusion, the post-extubation phase heralds a critical juncture in the trajectory of cardiac patients, demanding meticulous scrutiny of underlying etiologies prior to discharge. Of particular significance is the tailored management of patients afflicted with malignant ventricular arrhythmias and HF, necessitating deliberations on ICD placement and pharmacotherapeutic adjustments. Similarly, the strategic orchestration of angiographic interventions and pharmacologic titrations assumes paramount importance in the management of non-ST elevation MIs. These nuanced evaluations, far from being mere formalities, epitomize the cornerstone of comprehensive patient-centric care paradigms.

1. GİRİŞ

Üçüncü basamak yoğun bakım ünite (YBÜ)'nde yatan hastaların büyük çoğunluğuna mekanik ventilatör (MV) desteği uygulanmaktadır ve YBÜ'ne yatış endikasyonları çok çeşitlidir. En çok yatış yapılan hasta gruplarından biri de kardiyak kökenli hastalar ve nedeni bilinmeyen ani kardiyak arrest (AKA) hastalarıdır.[1,2] Bu hastaların MV ve YBÜ ihtiyaçları sonlandıktan sonra kardiyoloji hekimleri tarafından YBÜ'ne yatışına neden olan etiyolojinin saptanması ve tedavi edilmesi gerekmektedir.

Ani kardiyak ölüm (AKA), dünya ülkelerinde önemli bir sağlık problemidir ve Avrupa vatandaşlarında yılda 350.000-700.000 arasında görülürken bu hastaların yaklaşık %9'u hastaneden sağkalımla taburcu olmaktadır.[3] Bu AKA'lerin yaklaşık %80'i koroner kalp hastalığı (KKH)'na bağlıdır.[4] AKA'in diğer sebepleri ise skarla ilişkili aritmi ve ventriküler fibrilasyon, ventriküler taşikardi, asistol ve bradikardi gibi potansiyel olarak ölümcül aritmilere neden olan kardiyak patolojilerdir.[5] İmplante edilebilir kardiyak defibrilatörler (ICD)'ler teknolojik gelişmeler ve klinik kanıtlar doğrultusunda günümüzde AKA'lerin önlenmesinde standart tedavi olarak kullanılmaktadır.[6]

Diğer kardiyak nedenli yoğun bakım yatışı sebeplerinden biride kalp yetmezliği (KY)'dir. KY dünya genelinde sağlık sistemleri üzerinde önemli bir yük oluşturmakta ve önemli oranda morbidite ve mortaliteye neden olmaktadır.[7] Ayrıca, hastalığın şiddetinin artması ve KY tedavisindeki hızlı ilerlemelerle birlikte, KY hastaları sıklıkla YBÜ kaynaklarına ihtiyaç duymaktadır.[8] 65 yaş üstü hastane yatışlarının önemli bir kısmını akut KY hastaları oluşturmaktadır.[9] Bu başvurularda semptomlar farklılık göstermektedir. Şahin ve ark. KY hastalarında başvuruların %29,3'ünde plevral efüzyon, yüzde 13,3'ünde akciğer ödemi olduğunu göstermişlerdir. Kardiyojenik şok geçirenlerin hastaların ise %60'ının YBÜ'de eksitus olduğunu bildirmişlerdir.[10]

Bizim bu çalışmada amacımız üçüncü basamak anestezi YBÜ'de kardiyak kaynaklı MV ile takip ettiğimiz ve tedavi sürecinde ekstübe edilerek YBÜ ihtiyacı kalmayan hastaların kardiyoloji bölümüne nakledildikten sonraki süreçte uygulanan tedavilerin incelenmesidir.

2. MATERYAL VE METOD

Çalışma retrospektif olarak dizayn edilmiş olup, Helsinki Bildirgesi prensiplerine uygun bir şekilde Sakarya Üniversitesi Tıp Fakültesi Yerel Etik Kurul

(E-71522473-050.04-364003) onayı ile yapıldı. Çalışmaya Ocak 2019- Nisan 2024 tarihleri arasında Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi Anestezi YBÜ'de MV eşliğinde tedavi edilip tedavi sürecinde ekstübe edilip kardiyoloji kliniğine devredilen toplam 145 hasta dahil edildi. Anestezi YBÜ'de ekstübe edildikten sonra acil kardiyoloji kliniğine devredilemeden eve taburculuk gerçekleşen hastalar ise çalışma dışında bırakıldı. Hastaların verileri hastane elektronik veri tabanı sistemi olan KARMED üzerinden alındı. Kardiyak kaynaklı hastaları; KY sebepli yatışı olan hastalar ve AKA sonrası başarılı kardiyopulmoner resüsitasyon (PRS) hastaları oluşturdu. KY tanılı hastaları, kardiyoloji kliniği tarafından KY tanısı konulan ve acil başvurusu sırasında kardiyoloji tarafından KY semptomları olduğu belirtilen hastalar oluşturdu. AKA tanılı hastaları ise diğer AKA nedenleri dışlandıktan sonra kardiyoloji tarafından kardiyak nedenlerin dışlanamadığı hastalar oluşturdu. KY tanısı şüpheli olan hastalar ise çalışmaya dahil edilmedi.

Hastaların cinsiyetleri, başvuru sırasındaki yakınmaları, altta yatan sistemik hastalık öyküsü, kaç gün entübe vaziyette takip edildiği, ekstübe edildikten kaç gün sonra kardiyoloji servisine devredildiği, kardiyoloji servisinde yapılan ve/veya önerilen medikal tedaviler, girişimsel tedaviler ve kardiyoloji bölümündeki yatış gün sayıları kaydedildi. Bu veriler istatistiksel olarak değerlendirildi.

2.1. İstatistiksel analiz

Verilerin istatistiksel analizinde SPSS 20 (IBM SPSS Statistics Version 20.0; IBM Corp., Armonk, NY) paket programı kullanıldı. Niteliksel veriler sayı ve yüzde olarak, nicel veriler ortalama ± standart sapma (SS) ve ortanca (min, max) olarak belirtildi.

3. BULGULAR

Toplamda 178 kardiyak kökenli YBÜ yatışı yapılan ve ekstübe edilen hasta değerlendirilmiş, bu hastalardan 33'ü eve taburcu edildiğinden dolayı çalışma dışında bırakılmıştır. Kardiyoloji kliniğine devredilen 145 hasta ise çalışmamızın kapsamında yer almıştır. Bu hastaların yaş ortalaması 66.46 ± 13.8 idi. Hastaların %64,8'i kadın hasta iken, %35,2 ise erkek hasta idi (Tablo

1). En sık hastaneye başvuru sebebi %71 oranında dispneydi. İkinci en sık yatış nedeni %22,1 ile AKA sonrası PRS, üçüncü en sık neden ise %13,8 ile kardiyak aritmiydi. Diğer sebepler sırasıyla %9 ST eleve MI, %4,1 senkop, %0,7 ile postpartum hastaydı. ST eleve MI hastaları entübe vaziyette acil servisten katater labaratuvarına alınarak acil anjio-stent uygulanan ve kardiyoloji YBÜ'de yer olmadığı için anestezi YBÜ'nde yatan hastalar idi (Tablo 1). En sık görülen ek hastalık %70,3 ile hipertansiyon, ikinci en sık ek hastalık %55,2 ile KY iken üçüncü en sık ek hastalık ise %54,5 ile koroner arter hastalığı (KAH) idi. Diğer ek hastalıklar ise sırasıyla diabetes mellitus, kronik obstrüktif akciğer hastalığı, kardiyak aritmi, serebrovasküler olay ve maligniteydi (Tablo 1).

Tablo 1.

Demografik veriler

	Tüm hastalar, n=145
Yaş, Ort±SD	66.46 ± 13.8
Cinsiyet, n (%)	
Kadın	94 (% 64,8)
Erkek	51 (% 35,2)
Etyoloji, n (%)	
Dispne	103 (% 71)
PRS	32 (% 22,1)
Aritmi	20 (% 13,8)
ST Eleve MI (yatış öncesi)	13 (% 9)
Senkop	6 (4.1)
Postpartum	1 (0.7)
Ek hastalık, n (%)	
HT	102 (% 70,3)
KKY	80 (% 55,2)
KAH	79 (% 54,5)
DM	42 (% 29)
KOAH	13 (% 9,0)
Aritmi	11 (% 7,6)
SVO	11 (% 7,6)
Malignite	6 (% 4,1)
Postpartum	1 (% 0,7)

PRS: Başarılı kardiyopulmoner resüsitasyon, MI: Myokard infarktüsü, HT: Hipertansiyon, KY: Kalp yetmezliği, KAH: Koroner arter hastalığı, DM, Diabetes mellitus, KOAH: Kronik obstrüktif akciğer hastalığı, SVO: Serebrovasküler olay

Hastaların YBÜ yatışı sırasında ortalama yatış süreleri 8,7 gün iken ekstübe edildikten sonra kardiyoloji bölümüne devredilme süresi ortalama 4,5 gündü. Kardiyoloji servisine devredilen hastalardan %11'ine katater labaratuarında anjio uygulanırken, 3 hasta koroner arter baypas greft cerrahisi (CABG) operasyonuna yönlendirildi.

Hastaların %5,5'ine ICD takılırken 1 hastaya ise ciddi aort darlığı nedeniyle TAVİ operasyonu planlandı. Ventriküler aritmi (VA) nedeniyle ICD takılan 8 hastadan 6 hasta AKA tanısı ile acile gelirken, 2 hasta ise acil servise başvuru sebebi izole VA idi. Kardiyolojiye devredilen hastaların %93,8'i taburcu olurken, %4,8'i eksitus oldu (Tablo 2). Eksitus olan hastalardan 2 hasta NST-MI, 1 hasta ICD takılan, 3 hasta KY, 1 hasta ise TAVİ planlanan hasta idi.

Tablo 2.

Hastalara uygulanan tedaviler ve sonlanım noktaları

	Tüm hastalar, n=145
Kardiyoloji serviste uygulanan işlemler, n (%)	16 (% 11)
Anjio stent	1 (% 0,7)
TAVİ	3 (% 2,1)
CABG	8 (% 5,5)
ICD	
Anestezi ybü de yatış gün	8,7 ± 7,4
Yatış öncesi anjio uygulanan hasta yatış gün	9,23 (2-35)
Extübasyon sonrası anjio yapılan hasta yatış gün	5,23 (1-25)
Ekstübasyon sonrası devir gün	4,5 ± 3,9
Sonuç, n (%)	
Taburcu	136 (% 93,8)
Eksitus	7 (% 4,8)
Nefroloji	1 (% 0,7)
Tekrar YBÜ	1 (% 0,7)

Ort ± SD, Ortanca (min, max), TAVİ: Transkateter aort kapak implantasyonu, CABG: Koroner arter baypas greft cerrahisi, ICD: İntrakardiyak defibrilatör, YBÜ: Yoğun bakım ünitesi

4. TARTIŞMA

Çalışmamızın sonucunda primer YBÜ kabul sebebi kardiyak nedenler olan ve ekstübe edilen hastaların bir kısmına girişimsel işlem planlandığı görülmüş olup özellikle ST eleve olmayan MI ve izole VA'lere girişimsel işlem uygulandığı görülmüştür. Bu bulgular, kardiyoloji kliniğinde yapılan kardiyolojik değerlendirme ve müdahalelerin anestezi YBÜ'leri sonrası hastaların yönetiminde kritik bir rol oynadığını ortaya koymaktadır.

Özellikle MV desteği ihtiyacı kalmayan bu hastalar YBÜ tedavileri tamamlandıktan sonra primer etiyolojinin araştırılması ve tedavi edilmesi amacıyla kardiyoloji bölümü tarafından değerlendirilmelidir.

Üçünü basamak YBÜ'ne kabul edilen hastaların tanıları değişkenlik göstermektedir. Üçüncü basamak YBÜ'lerinde çoğunlukla MV ihtiyacı olan hastalar tedavi altına alınırken primer etiyolojilerinde farklıklar görülmektedir. Ayvat 2019 yılında yaptığı çalışmada YBÜ'sine en çok yatış yapılan hasta grubu olarak postoperatif hasta grubu, ikinci sırada pulmoner hastalıklar, üçüncü sırada ise kardiyovasküler hastalıklar olduğunu bildirmiştir.[1] Simchen ve ark. ise yaptıkları geniş çaplı çalışmada YBÜ yatışlarında en sık neden olarak pulmoner nedenleri bulurken üçüncü en sık sebebin kardiyovasküler nedenler olduğunu göstermişlerdir.[2] Bizim YBÜ'de de yatış sebeplerinin önemli bir kısmını MV ihtiyacı olan kardiyak nedenli hastalar oluşturmaktadır.

KY hayatı tehdit eden bir hastalıktır ve büyüyen bir halk sağlığı sorunudur. KY, nefes darlığı, yorgunluk, azalmış egzersiz toleransı, ödem, artmış juguler venöz basınç (JVP), pulmoner konjesyon ve periferik ödem gibi tipik semptomlarla seyreden klinik bir sendromdur. Bunlar, metabolik talebe yanıt olarak kalp debisinin sürdürülememesine neden olan bozulmuş miyokard fonksiyonunun sonuçlarıdır. KY dünya genelinde insanların %1 ile %3'ünü etkilemektedir.[11] MV'nun uygun kullanımı, dekompanse KY ve akut solunum yetmezliği olan hastaların ilk stabilizasyonu ve tedavisinde önemli bir yardımcı tedavi olarak görülmelidir. Pozitif basınç kollabe alveollerin genişlemesiyle oksijenlenmenin arttırılması, alveollerden ve interstisyel alandan pulmoner dolaşıma sıvı geçişinin uyarılması, solunum kas yükünün ve solunum işinin azaltılması, kardiyak yükün boşaltılması yoluyla hemodinaminin stabil hale getirilmesini sağlar.[12] MV'a ihtiyaç duyan hastalar yüksek mortaliteye sahip önemli bir alt grubu oluşturmaktadır.[13,14] Miller ve ark. yüksek sayıda hastayla yaptıkları çalışmada KY hastalarının %2,5 oranında MV ihtiyacı olduğunu bildirmişlerdir. 30 günlük mortalitede ise MV uygulanan hastalarda MV uygulanmayalara oranla yaklaşık sekiz katlık artış olduğunu bildirmişlerdir. Taburculuk sonrası 30 gün içinde

tekrar yatış oranı ise MV tedavisi görenlerde iki kat oranda olduğu gösterilmiştir.[15] Bizim ekstübe ettiğimiz kardiyak nedenli hastalarımızın % 71'ni KY'ne bağlı dispne ve solunum yetmezliği hastaları oluşturmaktaydı. Bu hastaların %22'sine yeni KY tanısı konulmasına rağmen MV ihtiyacı oluşmuştu. Servis bakımı sırasında eksitus olan 7 hastanın 3'ü ise KY hastası idi. 99 hastaya ilaç tedavisi düzenlenerek taburculuk gerçekleştirilirken 1 hastaya ise ileri aort darlığı nedeniyle TAVI önerilmişti.

AKA kardiyak mekanik aktivitenin durması sonucunda dolaşım belirtilerinin olmamasıdır.[16] AKA, Amerika Birleşik Devletleri ve Batı Avrupa'daki tüm yetişkin doğal ölümlerinin %15-20'sinden ve tüm kardiyovasküler ölümlerin %50'si kadarından sorumludur.[17] AKA'lerin %80'inden fazlası KAH'nın içinde bulunduğu yapısal kalp hastalığından kaynaklanmaktadır.[18] Daha az yaygın olan diğer etiyolojiler arasında kanalopatiler (%5-15) ve idiyopatik VA (%5) yer almaktadır.[19] Bizim hastalarımızın % 22,1'ini PRS hastalar oluşturduğu görüldü. Bu 32 PRS hastanın 2sinde ST eleve MI, 6 hastada ST eleve MI ile birlikte VA var iken, 8 hastada izole VA geliştiği görülmektedir. AKA görülme sıklığı yaş ilerledikçe artmaktadır ve 75 yaşta zirveye ulaşmaktadır.[18] AKA'lerin hayatta kalması aynı zamanda acil müdahale sistemlerine erken erişim, erken kardiyopulmoner resüsitasyon, erken defibrilasyon ve ileri kalp bakımı da birçok faktöre bağlıdır. Gerekirse perkütan koroner müdahaleyi de içeren erken reperfüzyon, AKA'lerde sağkalımı iyileştirmede esastır.[20] Lazzeri ve ark. yaptıkları çalışmada ST eleve MI hastalarında MV ihtiyacı oranını %7,6 olarak göstermişlerdir. MV ihtiyacı olan hastaların %51,8'i hastane gelişi öncesi, %16,9'u kateter labaratuvarında, %22,6'sına ise acil serviste MV uygulanmaya başlandığını bildirmişlerdir.[21] ESC 2020 kılavuzu ST segment yükselmesi olmayan hemodinamik olarak stabil olmayan hastalarda gecikmiş anjiografi uygulanabileceğini bildirmişlerdir.[22] Desch ve ark yaptıkları geniş çaplı çalışmada ST eleve olmayan hastane dışı AKA hastalarında erken anjiografi ve geç anjiografi karşılaştırıldığında mortalite, hastane yatış süresi, yoğun bakım yatış süresi, inme riski, böbrek yetmezliği riskinde anlamlı fark

olmadığını bildirilmiştir. Bu çalışmada geç anjiografi uygulanan hastaların anjiyoya alınma süresi ise yaklaşık 46 saatti.[23] Bizim hastalarımızdan 16 hastaya perkutan koroner girişim uygulanırken, 3 hastaya CABG uygulanmıştır. 13 hastaya yatış öncesi ST elevasyonu nedeniyle primer perkutan koroner girişim uygulanırken, 16 hastaya extübe edildikten sonra koroner anjiografi yapılmıştır. Öncesinde perkütan koroner girişim uygulanan hastaların ortalama 9,23 gün YBÜ yatışı olurken ekstübasyon sonrasında anjio uygulanan hastaların ise ort 5,23 gün YBÜ yatışı olmuştur. Bizim hastalarımızın literatüre göre daha geç anjiyoya alınmasının sebebi hastaların tamamının MV hastalarından oluşmasıydı.

Defibrilatörler aritmik ölümü durdurmaya çalışarak hayat kurtarır. Her ne kadar ICD bu aritmilerde hayat kurtarıcı olsa da ne yazık ki VA nedeniyle ICD'ye yanıt vermeyen AKA oranının %5 ile %17 arasında olduğu görülmektedir.[24] Decsh ve ark. hastaların %55,5'inde şoklanabilir ritmler geliştiği görülmüştür.[23] Bizimde 32 PRS hastasının %46,9'unda VA geliştiği görüldü. 4 hastada ise PRS olmadan izole VA şikayeti ile yoğun bakım yatışı yapılmıştı. Bizim hastalarımızdan 8 hastaya VA'den dolayı ICD uygulanmıştır. ICD takılan hastalardan %13'ünde eksitus gerçekleşirken %87 hasta sağlıklı bir şekilde taburcu olmuştur.

5. SONUÇ

Kardiyak kaynaklı takip edilen hastalar ekstübe edildikten sonra taburcu edilirken eve taburcu etmeden önce primer etiyolojinin araştırılması açısından kardiyoloji kliniğine danışılması ve özellikle malign VA ve KY hastalarının ICD implantasyonu ve ilaç tedavilerinin düzenlenmesi, ST eleve olmayan MI hastalarının anjiolarının planlanması ve ilaç tedavilerinin düzenlenmesi açısından değerlendirilmesinin oldukça önemli olduğunu unutmamak gereklidir.

Limitasyon

Bu çalışmanın bazı limitasyonları vardır. Öncelikli olarak bu çalışma retrospektif olarak planlanmıştır ve sadece anestezi YBÜ'de yatan kardiyak sebepli MV uygulanan hastalar ve bu hastalardan ekstübasyon sonrasında kardiyoloji

bölümüne devredilen hastalar incelendiğinden dolayı tüm hastalara ulaşamamak en önemli limitasyonumuzdu.

Makale Bilgi Formu

Finansman

Yazarlar bu çalışmanın araştırması, yazarlığı veya yayını için herhangi bir mali destek almamıştır.

Çıkar Çatışması / Ortak Çıkar Beyanı

Yazarlar tarafından herhangi bir çıkar çatışması veya ortak çıkar beyan edilmemiştir.

Telif Hakkı Beyanı

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Research Article

Factors Affecting Mortality in Chronic Obstructive Lung Disease

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Objective: Chronic obstructive pulmonary disease (COPD) is a progressive lung disease causing inflammation and airflow limitation. COPD is a major cause of death worldwide. In Türkiye, COPD represents a significant health concern, ranking as the third leading cause of mortality. This study investigates factors predicting mortality in stable COPD patients. We aim to identify factors beyond respiratory function tests that can guide prognosis in these patients.

Materials and Methods: We analyzed data from 75 deceased COPD patients and 98 age-matched living patients with COPD. Pulmonary function tests and blood tests were reviewed. Statistical analysis identified potential relationships between lung function, co-morbidities, and mortality in COPD.

Results: While no significant differences in demographics (gender, age, smoking history, BMI) were found, lung function (%FEV1, %FVC, PEF, MEF25-75) was significantly associated with mortality in deceased patients. Deceased patients also had lower hemoglobin, hematocrit, and higher sedimentation/CRP levels. Eosinophil levels were significantly higher in living patients. Multivariate logistic regression analysis revealed heart failure and lung cancer as significant factors for COPD mortality.

Discussion and Conclusion: This study investigated the factors predicting mortality in COPD. Elevated inflammatory markers in stable COPD patients suggested persistent inflammation. Our findings indicate that Pulmonary Function Tests, eosinophil count, hemoglobin, hematocrit, CRP, and sedimentation rate may be valuable predictors of mortality in these patients. These markers offer advantages due to their affordability, rapid accessibility, and practicality for follow-up.

Keywords: Chronic obstructive pulmonary disease, Mortality, Pulmonary function test

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable chronic disease in which harmful gases and particles cause inflammation in the lungs and airways, leading to progressive air restriction. It is responsible for most of the deaths caused by the respiratory system diseases. COPD is a serious airway disease that causes the death of 3 million people every year in the world. It is thought that this number will be 4.5 million in 2030[1]. According to the World Health Organization, COPD is predicted to be the third leading cause of death in 2030. The prevalence of COPD in Türkiye is 19.1%. It is the 4th most common disease causing mortality in the world and the 3rd cause in Türkiye[2].

The disease progresses with exacerbations. Exacerbations cause the disease to progress. In COPD, where there is a chronic inflammatory response to harmful gases and particles, inflammation is not only limited to the lung but also shows systemic features. The disease is common in smokers and its frequency increases with age. Comorbidities accompanying COPD contribute to the progression of the disease, make the management of the disease difficult, and contribute to the severity and mortality of COPD. These include diseases such as cardiovascular diseases, osteoporosis, muscle weakness, endocrinological and metabolic diseases, and cancer3. Mortality is a diagram that shows the death rate for a target population over a specific period of time. Accurate prediction of mortality is important, thus helping to identify patients for

whom therapeutic measures will improve outcomes. The following factors are important in showing mortality in COPD: respiratory function tests, patient age, gender, body mass index, six-minute walk test, arterial hypoxemia, hypercapnia values, exacerbation frequency and comorbid diseases[4].

Studies on biomarkers indicating mortality in stable COPD patients are limited. Our aim is to examine the factors that predict mortality in patients who come to the regular outpatient clinic for routine check-ups other than COPD attacks.

2. MATERIAL AND METHODS

886 patients diagnosed with COPD who applied to Kahramanmaraş Sütçü İmam University Chest Diseases Polyclinic and came for routine control were analysed retrospectively. A total of 75 deceased COPD patients who came to our hospital within the last 6 months and had Pulmonary function test (PFT) and blood tests performed were included in the study. Among the living COPD patients, 98 age-matched COPD patients were added to the study. The medical records of deceased patients were retrospectively reviewed. The blood parameters of the patients included in the study were evaluated in the stable period, not during the acute attack period. Patients were excluded from the study if they did not have PFT or if their PFT results did not meet the international GOLD criteria for COPD, had chronic kidney failure, hematological diseases, cirrhosis, or non-COPD lung pathologies (interstitial lung diseases, bronchiectasis). However, patients admitted during an acute exacerbation were not included in the study. Causes of death in COPD patients were also not considered. Pulmonary function testing was performed in COPD patients using the ZAN 500 spirometer. In accordance with the GOLD criteria, a forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ratio of <70% was used as the diagnostic threshold for COPD. COPD severity was categorized into four stages based on FEV1 values (≥80% predicted, mild; 50% ≤ FEV1 <80% predicted, moderate; 30% ≤ FEV1 <50% predicted, severe; FEV1 <30% predicted, very severe).

Data analysis was performed using the SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) 22 software package. Descriptive statistics were presented as n (%) for categorical variables and mean ± standard deviation (Mean ± SD) for continuous variables. Between-group comparisons of categorical variables were conducted using the Pearson Chi-square test, while comparisons of parametric continuous variables were performed using Student's t-test. Multiple logistic regression analysis adjusted for gender and age was carried out to identify risk factors for mortality in COPD patients. The level of statistical significance was set at $p<0.05$ for the analysis.

The study was approved by the Kahramanmaras Sütçü İmam University Ethics Committee (Decision Date: 06.06.2013, Decision No: 79) to ensure ethical compliance. Written institutional permission was obtained from the hospital where the study was conducted.

3. FINDINGS

The study involved 173 patients with chronic obstructive pulmonary disease (COPD), including 75 deceased patients and 98 living patients. Among the deceased patients, 65 (86.7%) were male and 10 (13.3%) were female. In the living patients, 82 (83.7%) were male and 16 (16.3%) were female. The mean age of the deceased patients was 74±9.9 years, while the mean age of the living patients was 71.6±9.8 years. There were no statistically significant differences in mortality based on gender, age, smoking history, or body mass index (BMI) (Table 1).

Table 1.

Demographic findings

	Deceased COPD(n=75)	Living COPD(n=98)	P value
Sex (Male/Female)	65/10(%86.7/13.3)	82/16(%83,7/16.3)	p=0.59
Age	74±9.9	71.6±9.8	p=0.11
Height	166.7±7.1	166±8.9	p=0.6
Weight	71.9±16.4	73.1±14.3	p=0.61
BMI	25.8±5.5	26.5±5.1	p=0.39
Cigarette pack year	41.3±24.4	36.5±26.8	p=0.41

Abbreviations: BMI: Body Mass Index, COPD: Chronic Obstructive Pulmonary Disease

FEV1 as a percentage of predicted was 51.8 ± 19.4 in deceased COPD patients and 59.5 ± 19.4 in living COPD patients. Our study found a significant association between mortality and FEV1%, FVC%, peak expiratory flow (PEF), and maximal expiratory midflow (MEF25-75)% values ($p < 0.05$) (Table 2).

Table 2.

Respiratory function test and blood results

	Deceased COPD(n=75)	Living COPD(n=98)	P Value
FEV1	51.8±19.4	59.5±19.4	p=0.011
FVC	67.1±19.8	81.6 ± 21.6	p=0.000
FEV1/FVC	58.8±9.9	57.3±10	p=0.34
PEF	36.8±19.3	44.9±18.7	p=0.007
MEF25-75	38.5±18.7	29.8±14.9	p=0.001
Hemoglobin	13.1±2	14.4±1.2	p=0.000
Hematocrit	39.8±6.3	43.3±3.4	p=0.000
MCV	87.3±7.1	86.8±7.9	p=0.7
Platelet	266.4±111,5	265.5±69.4	p=0.95
MTV	8.3±1.1	8.2±0.9	p=0.3
Sedimentation	38.8±26.1	22,4±15.7	p=0.001
CRP	31.8±33.1	10,6±15.4	p=0.000
Leukocyte	8.9±3.1	8.7±2.1	p=0.74
Neutrophil	6.1±2.9	5.7±1,8	p=0.31
Lymphocyte	1,7±1.1	1.9±0.7	p=0.06
Monosit	1.1±2.1	0.7±0.9	p=0.22
Eosinophil	0.16±0.19	0.27±0.33	p=0.02
Basophil	0.68±0.09	0.08±0.11	p=0.48
Lymphocyte/neutrophil	6.1±8.1	4.1±5.9	p=0.69

Abbreviations: **FEV1**: Forced Expired Volume in 1 Second, **FVC**: Forced Vital Capacity, **PEF**: Peak Expiratory Flow, **MEF25-75**: Maximum Expiratory Flow 25-75% of FVC, **MCV**: Mean Corpuscular Volume, **MTV**: Mean Thrombocyte Volume, **CRP**: C-Reactive Prote

Hemoglobin levels were significantly higher in living patients (14.4 ± 1.2 g/dL) compared to deceased patients (13.1 ± 2.0 g/dL). Similarly, hematocrit levels were also significantly higher in living patients (43.3 ± 3.4%) compared to deceased patients (39.8 ± 6.3%). These findings were statistically significant.

Sedimentation was 38.8±26.1 in deceased patients and 22.4±15.7 in living patients (p<0.01). CRP was 31.8±33.1 in deceased patients and 10.6±15.4 in living patients (p<0.01). Sedimentation and CRP values were significantly lower in living patients.

Eosinophil level was 0.16±0.19 in deceased patients and 0.27±0.33 in living patients, and this finding was significantly higher in living patients (p:0.02). Lymphocyte/neutrophil count was 6.1±8.1 in deceased patients and 4.1±5.9 in living patients. Leukocyte, monocyte, lymphocyte/neutrophil ratio, basophil, platelet and neutrophil ratio were higher in deceased COPD patients but the difference was not statistically significant. Table 2 summarizes the respiratory function test and hemogram results of the study participants.

In multiple logistic regression analysis, heart failure [OR 95%CI: 2.734 (1.097 to 6.818)] and lung cancer [OR 95%CI: 8.116 (1.433 to 45.963)] were identified as significant risk factors for COPD mortality, independent of age and gender (p<0.05). (Table 3)

Tablo 3.

Multiple logistic regression analysis adjusted for gender, age and comorbidities to identify risk factors for mortality in COPD patients.

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.	
					P Value	OR value	Lower	Upper
Diabetes Mellitus	.048	.693	.005	1	0.945	1.049	.269	4.083
Heart Failure	1.006	.466	4.656	1	0.031	2.734	1.097	6.818
Hypertension	-.869	.473	3.367	1	0.067	.419	.166	1.061
Gastrointestinal diseases	1.073	.630	2.901	1	0.089	2.924	.851	10.054
Lung Cancer	2.094	.885	5.601	1	0.018	8.116	1.433	45.963

Entered variables: Diabetes mellitus, heart failure, Hypertension, Stomach diseases, lung cancer.

4. DISCUSSION

COPD is a prevalent disease with a significant impact on mortality. Several factors contribute to COPD mortality, among which smoking stands out as a primary determinant. Smokers exhibit a steeper decline in FEV1, a key lung function measure, and experience higher mortality rates compared to non-smokers[5]. In our study, the cigarette pack-year rate was higher in deceased patients compared to living patients; however, this difference did not reach statistical significance.

COPD is more common in men and increases in frequency with age. This may be due to the fact that men smoke more and are more exposed to dust and particles in their professions. In our study, 65 of the 75 COPD patients who died were men, and although not significant, the death rate was higher.

PFT play a crucial role in the diagnosis of COPD and are also necessary for staging the disease. In patients diagnosed with COPD, there is a decrease in FEV1, FVC, MEF25-75, PEF and FEV1/FVC depending on the severity of airway obstruction.

The decrease in FEV1 is more pronounced than the decrease in FVC. FEV1 is a measure of the severity of airflow obstruction and is among the determinants of mortality. It is the most commonly used parameter to predict mortality[6]. In our study, we found that spirometric parameters FEV1 and FVC were significantly associated with mortality. FEV1 and FVC were significantly lower in COPD patients who died (p<0.05). PEF is the maximum airflow rate obtained during forced vital capacity (FVC) maneuver. It is used to assess obstruction in the large airways and is correlated with FEV1. A study by Jithoo et al. found that pre-bronchodilator PEF measurement was effective in identifying patients with moderate to severe COPD[7]. In our study, PEF was found to be significantly lower in patients who died (p=0.007). MEF25-75 reflects airflow in small airways and is reduced in COPD patients[8]. COPD leads to small airway disease. One study mentioned that MEF25-75 may be falsely high in patients with severe obstruction because the expiration time is shortened[9]. In our study, MEF25-75 was significantly higher in deceased COPD patients (p=0.001), and this finding may be due to shortened of expiration time.

Age-related changes in the lungs are similar to those in COPD. As people age, lung function deteriorates, and the incidence of disease and mortality increases[10]. In our study, the age of the deceased patients was not significantly different, but was found to be higher.

Low hemoglobin levels lead to reduced exercise tolerance, increased dyspnea, and impaired quality of life. A study has shown that low hemoglobin is associated with increased mortality[11]. In our study, hemoglobin and hematocrit values were found to be significantly higher in living COPD patients, which is consistent with the literature (p<0.01). Higher hemoglobin and hematocrit levels observed in surviving patients highlight the importance of managing anemia to improve patient survival.

Sedimentation and CRP are used as clinical markers of acute inflammation. In chronic diseases such as COPD, elevated CRP levels can be observed due to chronic inflammation. Inflammatory markers are important for monitoring COPD prognosis and predicting exacerbations. CRP is an acute phase reactant that increases in inflammation. It has been shown to be elevated in COPD patients in both stable and exacerbation phases[12]. A study found a slight to moderate increase in plasma concentration to be associated with mortality in patients with stable COPD[13]. Some studies in COPD patients have found increased CRP to be associated with mortality and decreased lung function[14]. In our study, CRP and sedimentation rate were significantly higher in patients who died (p<0.01).

A study found that eosinophil levels were twice as high in outpatient COPD patients compared to hospitalized patients[15]. Another study reported that COPD patients with eosinophilia had higher lung function and fewer exacerbations[16]. In our study, eosinophil levels were significantly higher in living COPD patients (p = 0.02). In early stages of COPD, lung cancer and heart failure are the most significant causes of mortality, while in later stages respiratory failure is the leading cause of death[17]. In our study, the presence of heart failure and lung cancer was found to be significantly associated with increased mortality (p<0.05). Presence of comorbidities such as heart failure and lung cancer significantly worsened the prognosis of patients with COPD. These comorbidities are frequently found in conjunction with COPD and can increase disease severity and mortality risk.

Our findings highlight the complex interplay of factors such as age, sex, lung function parameters, hematologic indices, inflammatory markers, and comorbidities significantly influence mortality. The higher hemoglobin and hematocrit levels observed in surviving patients highlight the importance of managing anemia to improve patient survival. By addressing modifiable risk factors, optimizing medical management, and implementing early intervention strategies, we can improve the prognosis of COPD patients and reduce mortality rates.

Although our study offers valuable information regarding factors associated with COPD mortality, several limitations should be considered. The retrospective nature of the study and its relatively small sample size may restrict the generalizability

of our results. Moreover, the absence of detailed data on specific variables, including environmental exposures and medication adherence, could have affected the outcomes.

5. CONCLUSION

Chronic inflammation plays a crucial role in the pathogenesis of COPD. In our study, elevated levels of inflammatory markers such as CRP and sedimentation rate in stable COPD patients indicate the persistence of inflammation. Our data suggests that SFT, eosinophil count, hemoglobin, hematocrit, CRP, sedimentation and comorbidities such as heart failure are valuable predictors of mortality in the follow-up of stable COPD patients. The affordability, rapid accessibility, and practicality of these tests during follow-up constitute an advantage.

Article Information Form

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Authors' Contribution
Idea and design in our researches H.Ş and H.K; Supervision; H.Ş and H.K, Collection and Processing of Data; H.Ş and H.K, Analysis and Interpretation of Data; H.Ş and H.K, Writing of the Manuscript; All authors agreed to be responsible for the accuracy and completeness of the study

The Declaration of Conflict of Interest/ Common Interest
No conflict of interest or common interest has been declared by authors.

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Evaluation of Acute Enteritis Cases in Adults Presenting to the Emergency Department: A Single Tertiary Care Hospital Experience

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Introduction: Acute enteritis can occur due to numerous bacterial, viral, and parasitic infections. This clinical condition can have various spectra in vulnerable patient groups with immunodeficiency and inflammatory bowel disease. This study aimed to examine cases of acute enteritis in the emergency unit of a tertiary-care hospital.

Material and Methods: This cohort study was conducted with consecutive patients between September 2022 and November 2023. The clinical, laboratory, and microbiological data of the 194 patients were retrospectively examined. Patients with immunocompromised (IC) or inflammatory bowel disease (IBD) were analyzed in a healthy population.

Results: The mean age of patients was 47 ± 19 (19 - 91). One-third of the patients had IC, and in the stool analysis, leukocytes and blood were positive in one-third and one-twentieth of the patients, respectively. Only one-tenth of patients had positive stool culture results. IC patients presented with metabolic acidosis, increased creatinine levels, and acute-phase reactant levels. Despite the lower prevalence of leukocytes and blood in stool samples, culture positivity was higher in IC patients.

Conclusion: Stool culture positivity was low for the diagnosis of acute enteritis. Culture examination is important in IC patients, even in the absence of direct microscopic findings. Because patients with IC are more susceptible to complications, clinical assessment is important.

Keywords: Enteritis, Diarrhea, Culture, Immunocompromised

1. INTRODUCTION

Due to improvements in sanitation and medical management of diseases worldwide, diarrheal diseases are not as devastating and as feared as it was in the previous centuries.[1] However, they still remain an important cause of morbidity and mortality globally; in 2016 it was estimated to have caused more than 1.5 million deaths in the world, among which a third was children aged less than 5 years.[2] In terms of worldwide disability-adjusted life years (DALYs) lost, diarrhea was third in 2016, responsible for 74·4 million DALYs, more than half of which occurred among children younger than 5 years.[2] In 2019 the number of diarrheal cases worldwide was estimated to be near seven billion.[3]

In developing nations, watery small intestinal or bloody diarrhea (dysentery) can be caused by diverse bacteria, viruses, or parasites. In such countries, diarrheal diseases occur all year round at a certain rate and are overlaid with spikes of increased cases due to epidemics.[4] Diarrhea may also occur during other viral and parasitic infections. Non-infectious etiologies of diarrhea, such as inflammatory bowel disease, drug side effects, endocrine diseases, and malabsorption, should also be considered in patients with repeated episodes of acute diarrhea.

Because diarrheal symptoms are mostly mild, self-limiting patients do not seek medical assistance. Even if they do, unless there is persistent fever, severe abdominal pain, bloody diarrhea, severe dehydration, immune suppression, inflammatory bowel disease, or significant cardiovascular disease, laboratory testing or imaging studies are not generally warranted.[4,5] This is because the yield of stool microscopy and cultures for the culprit pathogens is low (12.6%), even lower in

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diarrhea patients hospitalized for more than 72 hours (1.4%).[6] For most cases, the results reported are too late to be used in this self-limited disease. Therefore, this study aimed to examine the clinical characteristics of acute enteritis in the emergency unit of a tertiary care hospital.

2. MATERIAL AND METHODS
2.1. Methods of the study

This retrospective cohort study was conducted on 194 consecutive patients treated at a single tertiary care hospital between September 2022 and November 2023 with a diagnosis of acute enteritis. Demographic and clinical data of the patients were collected from the archives of paper patient files. Laboratory and microbiological data were collected by using an automated laboratory reporting system. The main etiologies of patients were classified as immunocompromised (IC), inflammatory bowel disease (IBD), or healthy. Patients with malignancy, immune deficiency, autoimmune disease, chronic renal and hepatic disease, or diseases requiring immunosuppressive drugs were considered IC. The presence of stool leukocytes and blood positive for stool culture was examined in the patient groups. Acute kidney injury, metabolic acidosis, liver enzyme elevation, and systemic inflammation markers were evaluated in the cohort.

The institutional and/or national research committee's ethical guidelines were followed for all methods used in this study, including people. The study adhered to the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. Ethical approval for this study was obtained from the local research committee of the Istanbul University, Istanbul Faculty of Medicine [Approval No:2023-306]. Informed consent was obtained by opt-out from all patients or members of their families. Patient records and information were anonymized and de-identified before analysis.

2.2. Statistical analysis

Patient data were analyzed using IBM SPSS for Windows version 28.0 0.0(190) (Armonk, New York, U.S.A.). Numerical data are presented as mean ± standard deviation and categorical data as frequency and percentage. Two-group comparisons of numerical data with normal distribution were carried out using the independent samples Student's t-test. If the numerical data had a non-normal distribution, the Mann-Whitney U test was used. Categorical data comparisons were performed using the χ^2 test. If the expected frequencies in cells were lower than five, groups were joined where appropriate until the expected cell count exceeded five. For 2 × 2 contingency tables, Yates correction was performed. If the assumptions were violated for 2 × 2 tables, Fisher's exact test was used.

3. RESULTS
3.1. Patient characteristics

Patient demographic data are presented in Table 1. The patients' ages ranged from 19 to 90 years old. IC patients were older (52 ± 17 vs. 45 ± 19 years, p=0.018), and IBD patients were younger (49 ± 18 vs. 40 ± 17, p=0.006) than the remaining patients. In the acute enteritis patient cohort, there was a slight predominance of female patients (47% vs %53), which was not apparent in IBD patients (49% vs. 51%), but was slightly more pronounced in IC patients (44% vs. 56%), but the difference was not statistically significant. Half of the patients were previously healthy before their index disease; one-sixth of the patients had IBD and malignancy. Clinical and biochemical data at admission are presented in Table 1. One-third of the patients were IC, and leukocytes and blood were positive in one-third and one-twentieth of patients, respectively. Only one-tenth of patients tested positive for stool culture. Stool culture results and antibiotic sensitivities of the isolates are shown in Table 2. The majority of the isolates were Salmonella spp. or Campylobacter spp. The only noteworthy observation of antibiotic resistance patterns was that Campylobacter spp. isolates were resistant to both ciprofloxacin and tetracycline, but sensitive to macrolides.

Table 1.

Demographic and biochemical data of the enteritis patients (n=194)

Parameters	n(%) or Mean ±SD*(Minimum – Maximum)
Age (years)	47 ± 19 (19 - 91)
IC	52 ± 17 *(p=0.018)**
IBD	49 ± 18 *(p=0.006)**
Gender	
Male	92 (47%)
Female	102 (53%)
Accompanying diseases	
None	96 (50%)
Inflammatory Bowel Disease	35 (18%)
Malignancy	35 (18%)
Hematologic	10 (5%)
Gastrointestinal	14 (7%)
Other	11 (6%)
Immune deficiency states	3 (1.5%)
Renal diseases	16 (8%)
Hepatic diseases	3 (1.5%)
Other chronic diseases	6 (3%)
Clinical parameters	
Immunocompromised	66 (34.0%)
Blood positive in stool	11 (5.7%)
Leukocytes present in stool	57 (29.4%)
Stool culture positive	20 (10.3%)
Blood chemistry	
Creatinine (mg/dl)	1.4 ± 1.4 (0.5-12.1)
Lactate (mmol/l)	1.6 ± 1.1 (0.4-8.1)
Ionized Ca^{+2}(mmol/l)	1.2 ± 0.1 (0.8-1.5)
CRP (mg/dl)	52 ± 73 (1-395)
ALT (IU/l)	23 ± 20 (2-123)
AST (IU/l)	25 ± 23 (6-225)
Blood gases	
pH	7.37 ± 0.07 (7.02-7.53)
Na^+ (meq/l)	137 ± 5 (118-148)
K^+ (meq/l)	4.0 ± 0.6 (1.1-6.4)
Cl^- (meq/l)	107 ± 10 (88-122)
$HCO3^-$ (meq/l)	22.2 ± 3.6 (11.2-36.0)
Anion gap (meq)	9 ± 5 (0 -25)
Blood count	
Hemoglobin (gr/dl)	12.2 ± 2.2 (6.2-16.2)
WBC (10^3 cells/ml)	9.1 ± 4.5 (0.3-28.3)
Neutrophils (10^3 cells/ml)	6.8 ± 4.1 (0.1-22.1)
Lymphocytes (10^3 cells/ml)	1.5 ± 0.9 (0.1-6.7)
Platelets (10^3 count/ml)	265 ± 123 (18-717)

* Abbreviations: SD; Standard deviation, n (%) or Mean ±SD*(Minimum – Maximum), CRP: C-reactive protein, ALT: Alanine transaminase, AST: Aspartate transaminase, WBC: White blood cell, * Mann-Whitney u test

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Table 2.

Stool culture and antibiotic sensitivity of isolates

Pathogen	Count	Antibiotic resistance n (%)				
	n (%)	Ampicillin	Ciprofloxacin	Trimethoprim	Macrolides	Tetracycline
Aeromonas spp.	1(5%)	-	0 (0%)§	0 (0%)	-	-
Salmonella spp.+	8(40%)	0 (0%)	0 (0%)	0 (0%)	-	-
Campylobacter spp.*	8(40%)	-	8 (100%)	-	0 (0%)	8 (100%)
Shigella spp.†	1(5%)	0 (0%)	0 (0%)	1 (100%)	-	-
Vibrio spp.‡	2(10%)	2 (100%)€	0 (0%)	0 (0%)	-	-

+; *C type Salmonella 2, S.enteritidis 5, S.typhimurium 1,*,*; C.jejuni 7, other 1,†;Sh. sonnei 1,‡;V. vulnificus 1, V. parahemolyticus 1,* §; Levofloxacin sensitive, €; Ampicillin-clavulanate sensitive

3.2. Clinical and laboratory characteristics of acute enteritis with immunocompromised patients

The frequency of positive stool leukocyte and blood in stool was lower in IC patients (40% vs. 19%, p=0.005, OR: 0.36 (95% CI 0.17-0.75)) and (36% vs. 0%, p=0.017, OR: 0.64 (95% CI 0.57-0.71)) respectively. However, there was no significant difference between culture positivity in immunocompetent and IC patients (10% vs. 11%).

On total blood count, IC patients had lower hemoglobin (12.5 ± 2.1 vs. 11.7 ± 2.3 g/dl, p=0.029) and platelet levels (298 ± 120 vs. 210 ± 109 *103/ml, p<0.001). On biochemical data, serum creatinine (1.1 ± 1.0 vs. 1.8 ± 1.9 mg/dl, p=0.012), CRP (42 ± 54 vs. 69 ± 95 mg/dl, p=0.05) and lactate (1.4 ± 0.7 vs. 1.9 ± 1.4 mmol/l, p=0.016) levels were higher and HCO3- levels (23.0 ± 3.3 vs 20.8 ± 3.6 mmol/l, p<0.001) lower in IC patients. (Table 3)

Table 3.

Clinical and laboratory characteristics of acute enteritis with immunocompromised patients

	Immunocompromised Patients	Immunocompotent Patients	P-*value*
Stool leukocyte (%)	19	40	**0.005**
Stool blood (%)	0	36	**0.017**
Culture positivity (%)	11	10	0.785
Hemoglobin (g/dL)	11.7 ± 2.3	12.5 ± 2.1	**0.029**
PLT (10³/mL)	210 ± 109	298 ± 120	**<0.001**
Creatinine (mg/dL)	1.8 ± 1.9	1.1 ± 1.0	**0.012**
CRP (mg/dL)	69 ± 95	42 ± 54	**0.05**
Lactate (mmol/l)	1.9 ± 1.4	1.4 ± 0.7	**0.016**
HCO3 (mmol/l)	20.8 ± 3.6	23.0 ± 3.3	**<0.001**

Abbreviations: PLT: Platelet count, CRP: C-reactive protein, HCO3: Bicarbonate,
*Mann-Whitney u test, Student's t-test, χ2 test

3.3. Clinical and laboratory characteristics of acute enteritis with inflammatory bowel disease patients

The frequency of detection of blood and leukocytes in stool was significantly higher in IBD patients than in other members of the cohort (20% vs. 2.5 %, p<0.001, OR: 9.7 (95% CI 2.7-35.3) for blood and 63% vs. 22 %, p = 0.005, OR: 6.0 (95% CI 2.7-13.1) for leukocytes, respectively). There was no significant difference in stool culture positivity between patients with and without IBD (3% vs. 12%, p=0.134). On comparison of biochemistry parameters of patients with or without IBD, serum creatinine (0.8 ± 0.2 mg/dl vs. 1.6 ± 1.6 mg/dl, p<0.001), AST (18 ± 5 IU/l vs. 28 ± 26 IU/l, p=0.031) and ALT (16 ± 13 IU/l vs. 25 ± 22 IU/l, p=0.008) levels were lower, and serum bicarbonate levels (24.6 ± 2.0 mmol/l vs. 21.7 ± 3.6 mmol/l, p<0.001) were higher in IBD group. On blood count parameters white blood cell count (10.5 ± 4.5 *1000 cells/ml vs. 8.7 ± 4.4 *1000 cells/ml, p=0.021), lymphocyte count (1.9 ± 0.7 *1000 cells/ml vs. 1.3 ± 1.0 *1000 cells/ml, p=0.004) and platelet counts (364 ± 136 *1000 cells/ml vs. 236 ± 103 *1000 cells/ml, p<0.001) were higher in the IBD group. (Table 4)

Table 4.

Clinical and laboratory characteristics of acute enteritis with inflammatory bowel disease patients

	IBD Patients	Immunocompotent Patients	*P-value*
Stool leukocyte (%)	63	22	**0.005**
Stool blood (%)	20	2.5	**<0.001**
Culture positivity (%)	3	12	0.134
Creatinine (mg/dL)	0.8 ± 0.2	1.6 ± 1.6	**<0.001**
AST (IU/L)	18 ± 5	28 ± 26	**0.031**
ALT (IU/L)	16 ± 13	25 ± 22	**0.008**
HCO3 (mmol/L)	24.6 ± 2.0	21.7 ± 3.6	**<0.001**
WBC (10³/mL)	10.5 ± 4.5	8.7 ± 4.4	**0.021**
LYMPH (10³/mL)	1.9 ± 0.7	1.3 ± 1.0	**0.004**
PLT (10³/mL)	364 ± 136	236 ± 103	**<0.001**

Abbreviations: IBD: Inflammatory bowel disease, AST: Aspartate transaminase, ALT: Alanin transaminase, HCO3: Bicarbonate, WBC: White blood cell, LYMPH: lymphocyte, PLT: Platelet count,
*Mann-Whitney u test, Student's t-test, χ2 test

3.4. Laboratory characteristics of patients with positive stool leukocytes

Stool culture positivity and blood in stool were higher in patients with positive stool leukocytes (6% vs. 21%, p=0.003, OR: 4.3 (95% CI 1.65-11.19)) and (3% vs. 12%, p=0.016, OR: 4.66 (95% CI 1.31-16.59)), respectively. In terms of biochemistry and blood counts, only a significant difference was observed in the platelet count, which was higher in the positive stool leukocyte group (248 ± 116 vs. 306 ± 131, p=0.009). (Table 5)

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Table 5.

Laboratory characteristics of patients with positive stool leukocytes

	Positive Stool Leukocyte	P-value
Stool culture positivity (%)	21/16	0.003
Stool blood (%)	12/3	0.016
PLT (10^3/mL)	306 ± 131/248 ± 116	0.009

Abbreviations: PLT: Platelet count
*Mann-Whitney u test, Student's t-test, χ2 test

4. DISCUSSION

In this study, half of the patients in the cohort were previously healthy, one-sixth had IBD, and one-third were IC. Only one-tenth of patients had positive stool culture results. Stool culture positivity and etiologic agents were similar to a hospital-based retrospective study reported previously.[6] The most noteworthy finding was the stool culture yield; the presence of stool leukocytes or blood increased the positivity of stool cultures fourfold. However, positive leukocyte or blood in stool was significantly lower in IC patients, but no significant difference in culture positivity was observed compared to immunocompetent patients. Detection of blood and leukocytes in stool was significantly higher in IBD patients with lower stool culture positivity without reaching significance compared to patients without IBD.

It should also be noted that stool culture positivity was unchanged in IC (10% vs. 11%), although stool leukocyte positivity was low, reflecting the fact that the leukocyte count was low in these patients. In IBD patients, blood and leukocyte positivity in stool was high, reflecting IBD disease activity rather than dysentery, and stool culture yields were very low without statistical significance (3% vs. 12%, p=0.134). In contrast, cases of IBD in which stool blood and leukocyte positivity reflected IBD disease activity and the yields of stool cultures were low.

White blood cell, lymphocyte, and platelet counts were higher in the IBD group than in the non-IBD group. The findings in patients were as expected and reflected the characteristics of this disease, such as higher rates of leukocytes and blood in stool, which were caused by IBD disease activation rather than infection. Higher white blood cell count and platelet counts may also reflect increased inflammation in this group of patients.[7]

IC patients had lower hemoglobin and platelet levels and higher serum creatinine, CRP, and lactate levels. Significant findings in IC patients compared to immunocompetent patients include lower hemoglobin and platelet levels, reflecting the suppression of erythroid and megakaryocytic series. Innate and adaptive immunity play distinct roles in host defense. Owing to the presence of malignancy, chronic kidney disease, or immune deficiency disorders, IC patients are more likely to develop opportunistic infections that could cause acute enteritis.[8] Both immune deficiency and infection caused bone marrow suppression in this patient group. Higher CRP levels reflect greater circulatory compromise and inflammation in IC patients.

Acute enteritis is characterized by vomiting and nausea, with dehydration mostly developing in the mild-to-moderate range. Severe dehydration may result in acute kidney injury via pre-renal hypoperfusion. Because of impaired compensation for acute enteritis and excessive fluid loss with diarrhea, these patient groups presented with higher lactate and creatinine levels. In addition, metabolic acidosis was increased in patients with IC. In addition to contributing to kidney disease, bicarbonate loss in the gastrointestinal tract along with diarrhea also plays a role in the development of metabolic acidosis. Adequately restored fluid loss is essential for controlling the kidney injury and acid-base balance.[9]

This study has some limitations. The number of patients was relatively small, and only Turkish patients were included in the study. Despite this limitation, the patient cohort revealed significant findings, including an adequate number of patients in special groups.

In conclusion, gastroenteritis was found to be numerically less frequent in stool culture positivity. However, the caveat was in IC cases, in which the positivity of stool leukocytes and blood decreased without a change in stool culture positivity. Early diagnosis and management of enteritis in IC patients are important to prevent the development of systemic complications.

Article Information Form

The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

The Declaration of Research and Publication Ethics

The research followed the ethical guidelines established by the Helsinki Declaration and its later revisions, or those of an equivalent kind. The study was approved by the local research committee at Istanbul University, Istanbul Faculty of Medicine. (Acceptance No. 2023-306.)

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Empathetic Attitudes and Violence Management Skills in Nursing Students: Relationships and Outcomes

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Objective: The study aimed to examine the relationship between empathic tendency and violence management competence in clinical practice among nursing students.

Materials and Method: This correlational study was conducted among nursing students enrolled in the spring semester of the 2024-2025 academic year at a university in the eastern region of Türkiye between March 2024 and June 2024. The study population consisted of nursing students (N=812) enrolled in the spring semester in academic year. The sample size was determined to be 287 students using OpenEpi version 3 "Sample Size Calculation for a Known Population" with an effect size of 80% and a confidence interval of 95%. Data were collected using a personal information form, the Empathic Tendency Scale and the Violence Management Competence Scale for Nursing Students in Clinical Practice.

Results: The study found that the mean score of nursing students on the Clinical Violence Management Skills Scale was 93.72 ± 27.03 (28, 140), while the mean score on the Empathic Tendency Scale was 65.12 ± 8.52 (41, 91). A weak but statistically significant positive correlation was observed between the mean score on the Empathic Tendency Scale and both the overall mean score and the sub-dimensions of the Violence Management Competence Scale (P<0.001, P<0.05).

Conclusion: The study concluded that nursing students have above-average levels of empathic tendency and violence management competence in clinical practice. It was observed that as students' empathic tendencies increased, their competence in managing violence in clinical settings also improved.

Keywords: Clinical practice, Empathetic tendency, Nursing stundent, Violence management

1. INTRODUCTION

Empathy is a critical component of effective patient care, supporting trust and communication between healthcare professionals and patients.[1,2,3] In nursing, empathy is defined as the ability to understand and share a patient's feelings, which promotes compassionate care and improves patient outcomes. Higher levels of empathy in nurses are associated with better patient care and increased job satisfaction.[4] The promotion of empathy in nursing education is essential to equip students with the skills necessary to deal with patients with complex interactions and emotional challenges.[5]

Workplace violence is a significant issue in nursing, with incidents ranging from verbal abuse to physical assault. Nursing students are particularly at risk as they are often in vulnerable situations. A survey of nursing students found that they were exposed to various forms of violence, including verbal, physical, psychological and sexual abuse, mainly from patients and their family members. Such experiences can have emotional and psychological consequences, damaging students' self-confidence and affecting their professional identity and self-esteem.[5,6,7] Therefore, effective management of violence is an important skill that nursing students need to develop. The ability to calmly and effectively manage violent situations can prevent escalation and ensure the safety of both healthcare workers and patients.[8,9]

Empathic attitudes can influence how nursing students perceive and respond to violent situations. Empathy can help nurses understand the underlying emotions and causes of aggression in patients, thereby de-escalating stressful situations.[10,11] In addition, an empathic approach may reduce the likelihood of violence by providing a safer and more supportive environment. Structural equation modelling suggests that higher levels of empathy in nurses are associated with greater moral sensitivity and better management of ethical dilemmas.[12] Studies have reported that greater empathy in nursing students leads to better care and higher patient satisfaction.[10,12]

Empathy, a critical component of nursing, has a significant impact on the quality of patient care and the overall nursing environment. In recent years, there has been a growing emphasis on the empathic attitudes of nursing students, particularly in relation to their ability to manage situations involving violence. Understanding how empathy influences violence management is particularly important given the prevalence of workplace violence among nurses. Given the complex and often stressful environments in which nurses work, empathy and the ability to manage violence are fundamental skills. Therefore, this study aims to examine the relationship between empathic tendencies and violence management competence in clinical practice among nursing students.

2. MATERIAL AND METHODS
2.1. Type of study

This study was conducted as a descriptive and correlational study to determine the relationship between the level of empathic tendency and violence management competence in clinical practice among nursing students.

2.2. Place and time of the study

The study was conducted between March 2024 and June 2024 with nursing students who were studying in the spring semester of 2024-2025 in the nursing department of a university in the east of Türkiye.

2.3. Study population and sample

The population of the study consisted of nursing students (N=812) studying in the spring semester of 2024-2025 in the nursing department of a university in eastern Türkiye. As all students were involved in clinical practice during this period, all students were accepted as the population. In the power analysis using OpenEpi Version-3 "Sample Selection with Known Universe", the sample was determined to be 287 students with an effect size of 80% and a confidence interval of 95%. Inclusion criteria: Nursing students aged 18 years or older, studying in the Faculty of Nursing, and without communication problems were included. Exclusion criteria: not volunteering for the study, missing data.

2.4. Data collection

The data of the study were collected using the Personal Information Form, the Empathic Tendency Scale and the Violence Management Competence Scale for Nursing Students in Practice Areas, which included the socio-demographic characteristics of the students and their exposure to violence. These forms were prepared by the researchers using Google Form and sent online to the students, who were contacted via their official email addresses. The questionnaires took approximately 10-15 minutes to complete.

Personal Information Form: This form was designed by the researchers to inquire about the socio-demographic information of the students and their exposure to violence. The form contains a total of 5 questions asking about age, gender, marital status, whether they had ever experienced violence while providing care and the type of violence they had experienced.

Empathic Tendency Scale (ETS): Developed by Dökmen (1988) to measure an individual's emotional sensitivity. The scale contains 20 items related to empathic tendency and is scored on a 5-point Likert scale. Positive empathic sentences are scored between 1 and 5, while negative empathic sentences are scored by reverse coding (reverse items are added). In Dökmen's (1988) validity and reliability study, the reliability coefficient was found to be 0.91. In the present study, the internal consistency coefficient (Cronbach's alpha) of the

empathic tendency scale was calculated to be 0.85. The highest score that can be obtained from the scale is 100 and the lowest score is 20. High scores on the scale indicate that individuals have positive empathic abilities.[13]

Violence Management Competence Scale for Nursing Students: The scale was developed by Lu and colleagues in 2021.[14] The Turkish validity and reliability study of the scale was conducted by Karabey et al. in 2022 and the Cronbach alpha value was found to be 0.88. This scale was developed to help students understand their competencies in experiencing and managing violence in clinical practice and to identify and assess their educational needs. The five-point Likert scale consists of 28 items and four sub-dimensions: "post-incident recovery" (1-10), "violence information management" (11-19), "violence intervention and interaction" (20-25) and "violence intervention" (26-28). The lowest score that can be obtained from the scale is 28 and the highest score is 140. An increase in the total score indicates an increase in the level of violence management competence of nursing students.[15] In this study, the Cronbach alpha value of the scale was found to be 0.97.

2.5. Data analysis

The data for this research is based on the statistical analysis of the survey results collected through Google Forms. Descriptive statistics (frequency, percentage, mean and standard deviation), independent samples t-test, ANOVA, Mann-Whitney U test, Kruskal-Wallis test, correlation analysis and Cronbach's alpha coefficient were used to evaluate the data.

Statistical analyses were performed using the SPSS 23.0 software package, with a significance level of $p < 0.05$.

2.6. Ethical considerations of the study

Prior to the commencement of the research, the necessary approvals were obtained from the Ethics Committee for Scientific Research and Publication of X University, Health Sciences (E-33117789-044-163245), as well as from the university where the research was conducted. In addition, students participating in the study were given detailed information about the purpose and procedures of the study, and those who agreed to participate were asked to sign an informed consent form. Students were informed of their right to withdraw from the study at any time. All of these procedures were carefully followed during the online implementation of the research, and the confidentiality of participants was assured.

3. RESULTS

The study found that the mean age of the nursing students was 20.54±2.92 years, 72.1% were female, 96.5% were single, and 10.5% had experienced violence in nursing, of which 6.3% was psychological violence (Table 1). The mean score of the students on the Empathic Tendency Scale (ETS) was 65.12±8.52, and their mean score on the Violence Management Competence Scale in Clinical Practice was 93.72±27.03. It was observed that the nursing students' empathic tendency and violence management competence in clinical practice were above the moderate level (Table 1).

Table 1.

Sociodemographic characteristics of nursing students and mean scores on the MWVCS and ETS

Sociodemographic Characteristics	N (%)	X±SD (min, max)
Age	287	20.54±2.92 (18, 39)
Gender		
Female	207 (72.1)	
Male	80 (27.9)	
Marital Status		
Single	277 (96.5)	
Married	10 (3.5)	

Table 1. (Continued)

Previous Experience of Violence While Providing Care	
Yes	30 (10.5)
No	257 (89.5)
Type of Violence Encountered	
Physical	9 (3.1)
Verbal	3 (1)
Psychological	18 (6.3)
ETS*	65.12±8.52 (41, 91)
MWVCS**	93.72±27.03 (28, 140)
Post-Incident Recovery	34.7±10.56 (10, 50)
Violence Knowledge Management	28.62±8.7 (9, 45)
Violence Response and Interaction	20.79±6.35 (6, 30)
Violence Intervention	9.6±3.21 (3, 15)

*ETS: Empathic Tendency Scale   **MWVCS: Violence Management Competence Scale for Nursing Students

The study found that female nursing students' mean scores for the sub-dimensions of competence in managing violence in practice, post-incident recovery, managing information about violence, responding to violence and communication were significantly higher than those of male students (Table 2).

Table 2.

Comparison of MWVCS, sub-dimensions and ETS mean scores of nursing students with socio-demographic characteristics

Socio-Demographic Characteristics	**MWVCS∞**	**Post-Incident Recovery**	**Violence Information Management**	**Violence Response and Communication**	**Violence Intervention**	**ETSβ**
Gender						
Female	97.33±24.34	36.32±9.42	29.68±8.15	21.57±5.72	9.75±3.04	65.94±8.84
Male	84.38±31.25	30.52±12.15	25.87±9.48	18.78±7.44	9.2±3.6	63.01±7.29
t*/p	3.719/**0.000**	3.843/**0.000**	3.165/**0.002**	3.017/**0.003**	1.321/0.188	2.636/0.009
Marital Status						
Single	93.74±26.64	34.73±10.46	28.59±8.58	20.78±6.28	9.62±3.16	64.94±8.42
Married	93.3±38.04	33.9±13.56	29.4±12.13	21±8.69	9±4.47	70.2±10.26
U/p**	0.093/0.761	0.002/0.964	0.4/0.527	0.398/0.528	0.316/0.574	1.959/0.162
Previous experience of violence in care						
Yes	88.26±33.86	31.86±12.29	27.43±11.04	20.1±8.33	8.86±4.04	65.63±9.98
No	94.36±26.12	35.03±10.31	28.75±8.4	20.87±6.1	9.68±3.1	65.06±8.36
t*/p	-0.953/0.347	-1.358/0.183	-0.636/0.529	-0.494/0.624	-1.076/0.29	0.299/0.767
Type of violence experienced						
Physical	81.55±44.94	28.55±17.37	25.88±14.57	19.66±10.13	7.44±5.05	64.88±8.56
Verbal	82.33±49.86	30.66±18.87	25.33±15.17	18±10.81	8.33±5.03	63.66±5.13
Psychological	96.44/24.95	34.61±8.11	29.94±8.34	21.88±7.02	10±3.25	67.27±11.06
KW***/p	0.442/0.802	0.101/0.951	0.354/0.838	0.483/0.785	2.061/0.357	0.58/0.748

*Independet t test, **Man Whitney U, ***Kruskal Wallis, ∞ Nursing Students' Competence in Managing Violence in Practice Scale, β Empathy Tendency Scale

The study found a positive but weakly significant relationship between the mean scores of the Empathy Tendency Scale and the total scores and sub-dimension scores of the Competence in Managing Violence in Practice Scale among nursing students (Table 3).

Table 3.

Relationship between nursing students' Empathic Tendency Scale (ETS) and mean scores on the Competence in Managing Violence in Practice Scale (MWVCS) and its sub-dimensions

	MWVCS*	Post-Incident Recovery	Violence Information Management	Violence Response and Communication	Violence Intervention
ETS **r***/p**	0.153/0.01	0.187/0.001	0.125/0.035	0.145/0.014	0.045/0.45

*Nursing Students' Competence in Managing Violence in Practice Scale, **Empathy Tendency Scale, ***Correlation Analysis

4. DISCUSSION

The study found that 10.5% of nursing students had been exposed to violence, and more than half of this was psychological violence. Özdemir et al. reported that a quarter of nursing students were exposed to violence in clinical practice and the most common types of violence were verbal and psychological violence.[16]

The study found that nursing students had above-average empathic tendencies and competence in managing violence in practice settings. Studies conducted with Turkish students showed that the empathic tendencies of nursing students were at a medium level, in parallel with our findings.[17,18,19] Özdemir et al. found that the mean of the violence management competence scale of nursing students in the practice area was 94.0±27.5 (above average).[16] Similar results were reported by Aksoy et al. and Karabey et al.[15,20]

The study found that female nursing students had better practice violence management skills than male students. In contrast to our findings, Özdemir et al. and Karabey et al. found that the violence management competence of nursing students in the field of practice did not vary according to gender.[15,16] If women generally have a calmer structure than men, it can be assumed that they have a more positive attitude to violence management. In the study, it was found that the empathic tendency and violence management competence of nursing students in the area of empathic tendency and practice did not change according to marital status, previous experience of violence and the type of violence encountered. In İster and Altınbaş's study, it was found that empathic tendency did not change according to

marital status.[21] To date, no studies have been found that examined empathic tendencies in nursing students according to the type of violence they encountered and the type of violence they encountered. Aksoy et al. and Karabey et al. reported in their research with nursing students that violence management competence in the field of practice did not change according to the status of previous violence and the type of violence encountered.[15,20]

The study found that as the empathic tendency of nursing students increased, so did their competence in managing violence in practice. Structural equation modelling by Du et al. showed that higher levels of empathy in nurses were associated with greater moral sensitivity and better management of ethical dilemmas, which may include effective management of violence.[12] Our finding is important because it demonstrates the impact of empathy in managing an important situation such as violence, which can have destructive consequences.

5. IMPLICATIONS FOR NURSING PRACTICE AND RESEARCH

The findings of this study highlight the importance of incorporating empathy development and violence management training into nursing education curricula. Given that nursing students with higher empathic tendencies demonstrated better competence in managing violence, educational programs should emphasize the development of empathic skills alongside traditional clinical competencies. Simulation-based training sessions and reflective practices could be utilized to enhance students' empathic abilities and prepare them for real-life scenarios

involving violence in clinical settings. Additionally, tailored interventions that consider gender differences in violence management may be beneficial, as female students exhibited higher competence in this area.

Healthcare institutions should also provide ongoing support and training for nursing students during their clinical placements. This support could include mentorship programs where experienced nurses model empathetic and effective violence management behaviors. By fostering a supportive environment, nursing students can develop the confidence and skills needed to manage violent situations effectively, thereby improving patient care and safety.

This study opens several avenues for further research. Future studies could explore the underlying mechanisms that link empathic tendency to violence management competence. Investigating how different educational strategies, such as role-playing, simulation, and reflective practices, impact these competencies could provide valuable insights for curriculum development.

6. CONCLUSIONS AND RECOMMENDATIONS

The study found that nursing students had above average levels of empathy and violence management competence in practice settings, and as students' empathy increased, so did their violence management competence in practice settings. The relationship between empathy and violence management competence in nursing students is an important area of research with important implications for nursing education and practice. Empathy not only improves patient care, but also provides nursing students with the necessary tools to effectively manage violence in the workplace. It may be recommended to include empathic tendencies in nursing education and violence management competencies in practice settings, to raise awareness of this issue, and to conduct research on a wider and diverse range of topics.

Limitations

This study has some limitations. The data were collected from a single university and through self-reported surveys, which is a limitation of the research.

Article Information Form

Authors' Contribution
Seher Çevik Aktura: Conceptualization, Methodology, Software, Supervision Reviewing and Editing.

Hanife Çelik: Conceptualization, Data curation, Writing- Original draft preparation, Investigation.

Declaration of Competing Interest
Authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The Ethical Aspect of the Study
Prior to the commencement of the research, the necessary approvals were obtained from the Ethics Committee for Scientific Research and Publication of Bingol University, Health Sciences (E-33117789-044-163245), as well as from the university where the research was conducted. In addition, students participating in the study were given detailed information about the purpose and procedures of the study, and those who agreed to participate were asked to sign an informed consent form. Students were informed of their right to withdraw from the study at any time. All of these procedures were carefully followed during the online implementation of the research, and the confidentiality of participants was assured.

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Research Article

The Predictive Role of Strain Parameters in Predicting All-Cause Mortality in Diabetic Hypertensive Patients with Normal Left Ventricular Systolic Function in Long-Term Follow-up

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Objective: To demonstrate the relationship of all-cause mortality in the long term and speckle-tracking echocardiography parameters in a cohort of diabetic hypertensive cases that had preserved left ventricle ejection fraction (LV-EF).

Methods: The study included 141 diabetic hypertensive cases with preserved LV-EF were retrospectively analyzed. After applying exclusion criteria, 121 patients were included. Two groups were formed according to out-of-hospital mortality status. Laboratory and echocardiography data were analyzed.

Results: The mean age of the 121 patients was 58.4±8.04 years, and the median follow-up duration was 10.08 years. Echocardiographic left atrial strain parameters, namely left atrium reservoir phase strain (35.7±8.7 vs 29.8±7.3, p-value: 0.047), left atrium conduit phase strain (LAScd%) (17.6±5.8 vs 13.3±4.1, p-value: 0.028), and left atrium reservoir phase peak strain (1.5±0.4 vs 1.22±0.3, p-value: 0.037), were worse in the mortality group. In right ventricular strain evaluation, four-chamber right ventricular strain (RV4CSL%) (26.1±5.4 vs. 20.8±6.2, p-value: 0.005) was also worse in the mortality group. Multivariate analysis revealed that the mean daytime systolic blood pressure (odds ratio [OR]: 1.769, p-value: 0.028), LAScd% (OR: 0.820, p-value: 0.015), RV4CSL% (OR: 0.078, p-value: 0.043) independently predicted mortality. Kaplan-Meier analysis showed that LAScd%≤15.3 and RV4CSL%≤24.8 were predictive of mortality (p-values: 0.023 and 0.016, respectively).

Conclusion: Strain parameters, assessed via echocardiography, can be useful diagnostic and follow-up tools for determining prognosis and guiding early risk factor management in diabetic hypertensive patients, especially in comparison to traditional volumetric parameters.

Keywords: Hypertension, Diabetes mellitus, Strain parameters, Preserved ejection fraction, Mortality

1. INTRODUCTION

The rising prevalence of type 2 diabetes mellitus is concerning.[1] Diabetes mellitus places a significant burden on society due to high healthcare costs and poor patient outcomes.[2] Cardiac dysfunction in diabetes mellitus is often clinically silent, with many patients remaining asymptomatic until later stages of the disease. Even among asymptomatic, normotensive, and well-controlled diabetic cases, it is estimated that around 50% have some degree of cardiac dysfunction.[3] Another well-known risk factor for adverse cardiovascular events is hypertension, which has a high global prevalence. Over time, hypertension results in structural cardiac alterations, including left ventricular

hypertrophy, myocardial fibrosis, and ventricular dysfunction. Echocardiography is a valuable diagnostic and follow-up tool in diagnosing and monitoring the end-organ damage caused by diabetes mellitus and hypertension.[4]

Speckle-tracking echocardiography is a sensitive modality for non-invasively detecting early regional and global myocardial dysfunction that cannot be identified using conventional 2D echocardiographic imaging.[5]

In the current study, we sought to explore the predictive role of myocardial strain values in determining all-cause long-term mortality in

diabetic hypertensive cases that had preserved systolic function of the left ventricle.

2. MATERIAL AND METHODS

The study was approved by the Ethics Committee of SBÜ Trabzon Faculty of Medicine (31.05.2023/10496660-27) in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients'.

This retrospectively designed, single-center, cohort study included a patient population derived from a previous study.[6] Mortality data were obtained from the Medula system, and the relationship between speckle-tracking echocardiography data and mortality was analyzed. The study included diabetic hypertensive patients who consecutively underwent strain evaluation between August 2012 and July 2013.

2.1. Study population

Patients who had been receiving treatment for hypertension and diabetes for at least one year were selected. After excluding patients with secondary hypertension, those with a systolic/diastolic blood pressure of >130/80 mmHg were evaluated. Further excluded from the study were patients with echocardiographic wall motion abnormalities (regional or global), left ventricular ejection fraction (LV-EF) < 50%, coronary artery disease causing significant stenosis, ongoing anginal complaints or positive stress tests, chronic liver and kidney disease, malignant arrhythmia, atrial fibrillation, high-grade heart block, valve disease (moderate and above), history of ischemic or hemorrhagic stroke, or sleep apnea. Lastly, 20 patients who were non-compliant with ambulatory blood pressure monitoring (ABPM) readings and/or had poor echocardiographic images were excluded. As a result, the sample consisted of 121 patients.

Demographic and clinical information of the patients were obtained when they first applied to the hospital. We examined fasting glucose, lipid markers, creatinine, and HbA1c levels. The calculation of the glomerular filtration rate was undertaken using the Modification of Diet in Renal Disease formula. Body mass index was determined by dividing weight in kg by height in square meters, and body surface area was obtained as follows: (weight$^{0.425}$ x height$^{0.725}$) x 0.007184. All patients underwent 24-hour ABPM and echocardiography.

2.2. ABPM

We used the Agilis-CDABPM (ELA Medical, France, 2002) device for 24-hour ABPM. We recorded blood pressure at 15-minute intervals during the day and at 30-minute intervals at night. Readings were considered valid if ≥80% of measurements were recorded. In addition, at least 14 daytime measurements and at least seven nighttime measurements were required for analysis. The patients' reported wake and sleep times were individually corrected.

2.3. Echocardiography

The echocardiographic examination did perform with the Philips IE33 system (Philips Medical Systems, Andover, MA, USA). Data acquisition completed by a 5-1 MHz sector transducer. Strain imaging was undertaken using EchoPAC™ software, version 108.1.12 (GE Medical Systems, Horten, Norway). Four-chamber right ventricular strain analysis (RV4CSL) was performed by manually adjusting boundaries of the right ventricle using the four-chamber apical view, with the software automatically detecting and adjusting the contour. Measurements were averaged from six segments (three from the septum and three from the free wall). Right ventricular strain measurements were taken during maximum ventricular contraction (right ventricular peak systolic strain). Left atrial strain was similarly analyzed using automated contours in the apical four-chamber view, with manual adjustments made to optimize the imaging. Six automatically separated segments were evaluated. The wall thickness was adjusted to 2–3 mm. The imaging was optimized with manual adjustments, starting from the mitral valve annulus and progressing along the endocardial border of the left atrium lateral wall, the left atrium roof, and the left atrium septum wall, and ending at the opposite tricuspid annulus to avoid including the pericardium. Segments that did not

allow for visualization of atrial wall motion were excluded from the analysis through manual manipulations. End diastole was defined as the beginning of the cardiac cycle for left atrial strain, marked by the R wave on the electrocardiogram. Strain parameters were measured across different cardiac phases (LASr: reservoir phase strain, LAScd: conduit phase strain, LASct: contraction phase strain, pLASRr: reservoir phase peak strain rate, pLASRcd: conduit phase peak strain rate, and pLASRct: contraction peak strain rate). All echocardiograms were measured and evaluated by a cardiologist blinded to the patients' conditions, according to the guidelines set out by the American Society of Echocardiography and the European Association of Cardiovascular Imaging[7].

2.4. Statistical analysis

Data were analyzed using SPSS software (Version 23.0, SPSS, Inc., Chicago, IL). The normality of the data distribution was assessed using visual and analytical (Kolmogorov-Smirnov) methods. Levene's test was used to test homogeneity of variances. Continuous variables were presented as mean ± standard deviation, and categorical variables as percentages. The chi-square or Fisher's exact test (when the chi-square test did not meet assumptions due to expected low cell counts) was used to compare categorical groups. Normally distributed parameters were assessed using a two-tailed Student's t-test, while the Mann-Whitney U test was used for continuous variables that were not normally distributed. A p-value of <0.05 was considered statistically significant.

Parameters showing statistically significant differences between the mortality and non-mortality groups (Table 1) were first evaluated using univariate Cox regression analysis. Parameters that remained significant in univariate Cox regression were further examined using multivariate Cox regression analysis. Sensitivity and specificity of parameters independently associated with cardiovascular mortality were evaluated using receiver operator curve (ROC) analysis. After ROC analysis, Kaplan-Maier plots were created using the cross-sectional values of variables with the highest sensitivity and specificity.

3. RESULTS

The mean age of the 121 patients was 58.4 ± 8.04 years, and the median follow-up duration was 10.08 years. Concerning demographic characteristics, the mortality group had statistically higher values for age (57.2 ± 7.7 vs. 64.2 ± 6.9 years, p-value: 0.001), diabetes mellitus duration (6.4 ± 5.1 vs. 9.2 ± 7.2 years, p-value: 0.041), and hypertension duration (6.48 ± 5.1 vs. 10.5 ± 9.1 years, p-value: 0.003). All systolic blood pressure (SBP) parameters showed significantly elevated values in the mortality group, while the remaining baseline characteristics did not statistically significantly differ (Table 1). A higher rate of patients in the mortality group used calcium channel blockers [26 (26%) vs. 12 (57%), p-value: 0.005]. Laboratory parameters were not significantly different between the mortality and non-mortality groups (Table 2).

Table 1.

Demographic characteristics

	Mortality (-) (n = 100)	Mortality (+) (n = 21)	p value
Gender (male), n (%)	42 (42)	7 (33.3)	0.315
Age (years)	57.2 ± 7.7	64.2 ± 6.9	<0.001
Hyperlipidemia, n (%)	53 (53)	10 (47.6)	0.417
Current smoking, n (%)	89(89)	17 (81)	0.246
Previous MI, n (%)	5 (5)	2 (9.5)	0.350
Prior CAD, n (%)	25 (25)	7 (33.3)	0.296
Previous PCI, n (%)	18(18)	7 (33.3)	0.103
BMI kg/m^2	32.7 ± 5.1	33.2 ± 5.1	0.705

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Table 1. (Continued)

DM duration (years)	6.4 ± 5.1	9.2 ± 7.2	0.041
HT duration (years)	6.48 ± 4.6	10.5 ± 9.1	0.003
Average SBP (mmHg) (Dt)	138.2 ± 17.2	155.5 ± 8.6	<0.001
Average DBP (mmHg) (Dt)	78.4 ± 9.7	82.6 ± 5.5	0.115
Average SBP (mmHg) (Nt)	134.1 ± 19.1	151.5 ± 17.4	0.001
Average DBP (mmHg) (Nt)	72.7 ± 10.4	78.2 ± 10.1	0.060
Office SBP (mmHg)	147.1 ± 14.4	156.4 ±1 2.6	0.031
Office DBP (mmHg)	89.6 ± 11.8	93 ± 10.5	0.278
Overall SBP (mmHg)	137 ± 16.1	153.2 ± 8.5	<0.001
Overall DBP (mmHg)	76.5 ± 9.6	80.5 ± 5.1	0.137

MI: Myocardial infarction, CAD: Coronary artery disease, PCI: Percutaneous coronary intervention, BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Dt: Daytime, Nt: Nighttime

Table 2.

Medical treatments and laboratory data

	Mortality (-) (n = 100)	Mortality (+) (n = 21)	p value
ARB, n (%)	41 (41)	5 (23.8)	0.108
ACEI, n(%)	47 (47)	10 (47.6)	0.573
Beta-blocker, n (%)	39 (39)	9 (42)	0.463
Diuretic n (%)	49 (49)	8 (38.1)	0.252
CaCB, n (%)	26 (26)	12 (57)	0.005
Oral anti-diabetic, n (%)	94 (94)	18 (85.7)	0.188
SGLTi, n (%)	16 (16)	4 (19)	0.492
Insulin, n (%)	14 (14)	5 (23.2)	0.208
Fibrate, n (%)	6 (6)	3 (14.3)	0.191
Statin, n (%)	42 (42)	10 (47.6)	0.636
Blood glucose (mg/dL)	149.6 ± 60	164.5 ± 57.2	0.302
Creatinine (mg/dL)	0.79 ± 0.18	0.81 ± 0.19	0.575
Hemoglobin (g/dL)	13.2 ± 1.2	12.7 ± 1.6	0.094
C-reactive protein (mg/dL)	0.22 (0.09-1.09)	0.2 (0.12-0.29)	0.248
HbA1c (%)	7.9 ± 1.5	8.2 ± 1.7	0.443
eGFR	88.8 ± 18.5	79.8 ± 16.1	0.050

ARB: Angiotensin II receptor blockers, ACEI: Angiotensin-converting enzyme inhibitor, CaCB: Calcium channel blocker, eGFR: Estimated glomerular filtration rate, SGLTi: Sodium-glucose transport protein 2 inhibitor.

Echocardiographic left atrial strain parameters, namely LASr% (35.7 ± 8.7 vs. 29.8 ± 7.3, p-value: 0.047), LAScd% (17.6 ± 5.8 vs. 13.3 ± 4.1, p-value: 0.028), and pLASRr (1.5 ± 0.4 vs. 1.22 ± 0.3, p-value: 0.037), were worse in the mortality group. In the right ventricular strain evaluation, RV4CSL% (-26.1 ± 5.4 vs. -20.8 ± 6.2, p-value: 0.005) was also worse in the mortality group. The groups did not significantly differ in relation to the remaining echocardiographic parameters (Table 3).

Table 3.

Echocardiographic data

	Mortality (-) (n = 100)	Mortality (+) (n = 21)	p value
LVEF	58.5 ± 6.5	58.1 ± 9.6	0.837
Sm	0.09 ± 0.02	0.08 ± 0.01	0.266
Em	0.11 ± 0.03	0.09 ± 0.02	0.085
Am	0.13 ± 0.03	0.12 ± 0.04	0.757
E/Em	7.5 ± 2.8	8.8 ± 3.6	0.189
E/A	0.94 ± 0.29	0.78 ± 0.22	0.101
LAVI	33.5 ± 11	34.8 ± 12.1	0.326
LAEI	1.15 ± 0.53	1.25 ± 0.56	0.600
GLSs LALASr, %	35.7 ± 8.7	29.8 ± 7.3	0.047
GLSe LALAScd, %	17.6 ± 5.8	13.3 ± 4.1	0.028
GLSa LA LASct, %	18.1 ± 4.5	16.8 ± 4.6	0.387
GLSRs LApLASRr	1.5 ± 0.4	1.22 ± 0.3	0.037
GLSRe LA pLASRcd	1.8 ± 0.4	1.5 ± 0.3	0.485
GLSRa LApLASRct	2.3 ± 0.5	2.2 ± 0.6	0.355
GLS LVGLSLV, %	-18.7 ± 2.7	-18.9 ± 4.1	0.823
GLS RVRV4CSL, %	-26.1 ± 5.4	-20.8 ± 6.2	0.005
AASI	0.49 ± 0.13	0.56 ± 0.17	0.058

LVEF: Left ventricular ejection fraction, Em: Early diastolic tissue velocity, Sm: Systolic tissue velocity, Am: Late diastolic tissue velocity, LAVI: Left atrium volume index, LAEI: Left atrium expansion index, LASr: Strain during reservoir phase, LAScd: Strain during conduit phase, LASct: Strain during contraction phase, pLASRr: Peak strain rate during reservoir phase, pLASRcd: Peak strain rate during conduit phase, pLASRct: Peak strain rate during contraction phase, GLSLV: Left ventricular global longitudinal strain, RV4CSL: right ventricular four-chamber strain, AASI: Ambulatory artery stiffness index

Univariate and multivariate logistic regression analyses were conducted to ascertain independent predictors of mortality. In univariate logistic regression analysis, mean daytime SBP (odds ratio [OR]: 1.769 p-value: 0.028), LAScd% (OR: 0.820 p: 0.015), and RV4CSL% (OR: 0.078 p-value: 0.043) were determined to independently predict mortality (Table 4).

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Table 4.

Independent predictors of mortality

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Age	1.127	1.055-1.204	<0.001			
DM duration	1.075	1.009-1.146	0.025			
HT duration	1.094	1.040-1.150	0.001			
Average SBP (Dt)	1.054	1.024-1.085	<0.001	1.769	1.005-2.943	0.028
Average SBP (Nt)	1.037	1.013-1.061	0.003			
Office SBP	1.058	1.004-1.115	0.036			
Overall SBP	1.048	1.020-1.078	0.001			
eGFR	0.974	0.950-0.999	0.044			
CaCB	3.226	1.375-7.758	0.007			
LASr, %	0.914	0.837-0.997	0.043			
LAScd, %	0.852	0.739-0.982	0.027	0.820	0.698-0.963	0.015
pLASRr	0.130	0.020-0.828	0.031			
RV4CSL, %	1.179	1.046-1.330	0.007	0.078	0.007-0.924	0.043

DM: Diabetes mellitus, HT: Hypertension, SBP: Systolic blood pressure, Dt: Daytime, Nt: Nighttime, eGFR: Estimated glomerular filtration rate, CaCB: Calcium channel blocker, LASr: Strain during reservoir phase, LAScd: Strain during conduit phase, pLASRr: Peak strain rate during reservoir phase, RV4CSL: Right ventricular four-chamber stra

Mean SBP (mmHg) (Dt) ≥ 148.5 mmHg was identified as having 80% sensitivity and 76% specificity in predicting mortality, with positive and negative predictive values (PPV and NPV) of 38.2% and 96.2%, respectively. LAScd ≤ 15.3 had 80% sensitivity and 24% specificity in predicting mortality, with a PPV of 10% and an NPV of 94.5% (Table 5). Kaplan-Meier analysis revealed that LAScd deterioration was associated with mortality (p-value: 0.023) (Figure 1). RV4CSL ≤ 24.8 had 80% sensitivity and 24% specificity in predicting mortality, with a PPV of 23.6% and an NPV of 95.4% (Table 5). According to Kaplan-Meier analysis, RV4CSL deterioration was related to mortality (p-value: 0.016) (Figure 2).

Figure 1.

Kaplan–Meier survival analysis. The Kaplan–Meier curve shows the survival curves according to LAScd
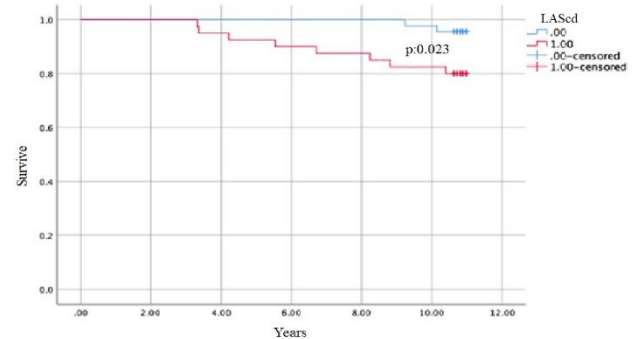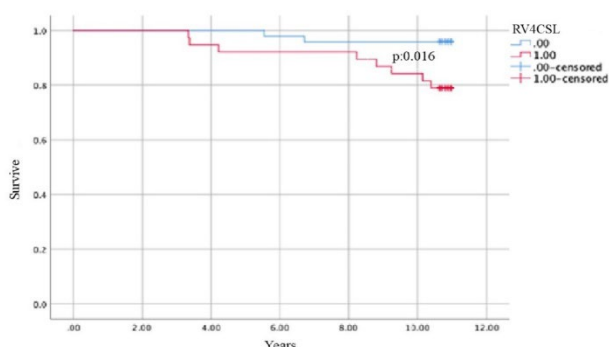
Figure 2.

Kaplan–Meier survival analysis. The Kaplan–Meier curve shows the survival curves according to RV4CSL

4. DISCUSSION

This study showed that right ventricular and left atrial strain parameters, independent of other factors, were correlated with mortality from all causes in diabetic and hypertensive cases. In addition, mean daytime SBP was found to independently predict all-cause death, apart from the strain parameters.

Hypertension-induced cardiac remodeling impairs the balance between collagen types (1 and 3), which are major components of the extracellular matrix.[8] Increased stress, particularly in the subendocardial zone, contributes to heterogeneous myocardial fibrosis. This irregular collagen synthesis and cardiac fibrosis in hypertension patients have been linked to reduced global longitudinal strain and early systolic dysfunction.[9] Hypertension's effect on cardiovascular and mortality from all causes and morbidity has been well-documented in many studies. Consistently, our study revealed that all SBP values were elevated in the mortality group, and mean daytime SBP independently predicted all-cause mortality in multivariate logistic regression analysis. Therefore, detection and control of hypertension should be a priority.

The higher mean BP in the mortality group results in an increase in the use and number of medications. While the use of Angiotensin Converting Enzyme Inhibitors (ACEI)/ Angiotensin receptor blockers (ARB), Diuretic, Beta-blocker was similar in our patient population, this difference naturally emerged in

the use of calcium channel blockers (CaCB). As the authors, we do not think that the use of CaCB is directly related to mortality. However, we included CaCB in the statistical analysis in order to provide objective support for other data that will emerge in subsequent studies.

Hypertension also affects left atrial morphology and function. Increased left atrial size and changes in left atrial strain are frequently observed in the tissue Doppler imaging of hypertensive patients.[10] The increasing focus on atrial dimensions and functionality has improved our understanding of how the atria contribute to cardiovascular performance in both healthy and diseased states.[11] Several population-based studies have shown that left atrial analyses can predict outcomes in the long term.[12] Hypertensive and diabetic cases, even with normal left atrial size, often exhibit impaired left atrial deformation mechanics, and the coexistence of both diseases worsens this impairment in an additive manner.[13] Compared to conventional left atrial function parameters, strain parameters are less load-dependent and relatively independent of coupling effects.[14] Reduced left atrial strain is linked to older age, an increased prevalence of atrial fibrillation, hypertrophy of the left ventricle, reduced systolic performance in the left and right ventricles, and impaired left ventricular diastolic functioning.[15]

In a study by Cameli et al., 312 patients were monitored for an average duration of 3.1 years and evaluated in two groups according to the presence of cardiovascular events. Significant deterioration in left atrial parameters was observed in the group with cardiovascular events. The association between worsening left atrial PLAS as categorized by Kaplan-Meier analysis and cardiovascular events was clearly demonstrated. A key finding in that study was that the left atrial strain parameter was more valuable than volumetric parameters for assessing left atrial dysfunction and prognosis.[11] Modin et al. evaluated 385 patients without atrial fibrillation, ischemic heart disease, or heart failure, investigating the relationship between left atrial strain parameters and a composite endpoint of heart failure, cardiovascular mortality, and ischemic heart disease. Although there was no

difference in left atrial enlargement between the groups, a deterioration in LASr values was found in the combined endpoint group.[16] This finding suggests that volumetric parameters are affected later than strain parameters and highlights the importance of strain values in determining prognosis. Similarly, in our study, LAScd, LASr, and pLASRr values were adversely affected in the mortality group, while the groups did not significantly differ in volumetric parameters. LAScd was identified as a parameter that independently predicted mortality, maintaining its significance in multivariate analysis. Both our findings and the literature demonstrate that traditional left atrial assessment parameters may be late in predicting adverse events. Therefore, early intervention, especially in patients with risk factors, can be performed by incorporating functional parameters and strain assessment.

For many years, the significance of right ventricular function was largely overlooked. However, with accumulating evidence from both healthy and diseased populations, the understanding of the significance of the right ventricle has advanced. Assessing right ventricular function using conventional echocardiographic techniques is challenging due to its complex geometry, leading to inconsistent results.[17] Speckle-tracking echocardiography is an advanced modality with the potential of addressing some of these limitations.[18] Lejeune et al. investigated the RV4CSL parameter in the long term in cases of heart failure with preserved EF. RV4CSL was identified as an independent predictor of mortality from all causes. In the same study, evaluation of the patients were in two groups according to RV4CSL revealed that the impaired RV4CSL group had lower left-right ventricular EF and tricuspid annular plane systolic excursion and higher N-terminus pro-B-type natriuretic peptide values.[19] In the current study, while systolic and diastolic function were not significantly different between the mortality and non-mortality groups, RV4CSL was impaired in the mortality group, and this parameter was an independent predictor of all-cause mortality in multivariate logistic regression analysis. Deterioration in RV4CSL without corresponding

impairment in traditional parameters may allow time for early intervention in controlling and treating risk factors. In addition, this finding shows the importance of evaluating the heart as a whole rather than focusing solely on the left side in echocardiographic evaluation.

5. CONCLUSION

Hypertension and diabetes mellitus are recognized risk factors for cardiovascular events, and their importance is well-established within the healthcare community. As with any disease, early intervention and preventive measures are crucial for preventing cardiovascular events. Traditional follow-up methods may delay early intervention. Echocardiography is the most commonly used tool for monitoring and detecting the effects of diabetes mellitus and hypertension on the cardiovascular system. Both our study and the literature show that traditional volumetric echocardiography parameters are late predictors of adverse events. Therefore, it is essential to evaluate high-risk patients using functional echocardiographic parameters, even if volumetric echocardiography parameters are normal. Early detection of potential deterioration in functional parameters may allow for tighter control of risk factors and reduced mortality and morbidity. Strain parameters, which provide functional evaluation through echocardiography, should be utilized as diagnostic and follow-up tools for determining prognosis and facilitating early control of risk factors, especially in comparison to volumetric parameters.

Limitations

This study is limited by its single-centered nature and the small sample size. In addition, patient selection was not randomized. The reliability of the results could be enhanced through a multicenter study involving a larger sample. Since the EchoPAC™ program used for strain analysis did not have a specific interface for RV, it was modified with operator support on the modified RV using the LV interface.

Article Information Form

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Galectin-3 Level in Carotid Artery Stenosis

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Objective: Carotid atherosclerosis is an important cause of cerebral ischaemic events and asymptomatic diagnosis of patients with advanced carotid artery stenosis is important in preventing stroke-related mortality and morbidity. Galectin-3 is known to increase inflammation by inducing the expression of a number of proinflammatory molecules in plaque pathophysiology. In this study, we aimed to evaluate the utility of serum galectin-3 level as a potential assessment tool for the severity of carotid artery disease.

Material and Methods: This prospective cross-sectional study was conducted between 06.12.2024 and 26.12.2024 in the stroke outpatient clinic of the department of neurology, Health Sciences University Adana City Training and Research Hospital. A total of 109 patients were included in the study, including 69 consecutive patients admitted with advanced (70-99% stenosis) carotid artery stenosis (CAS) and 40 patients without CAS in carotid imaging were included in the control group. An interventional neurologist and an additional neurologist determined the degree of CAS by examining carotid computed tomography angiography or carotid magnetic resonance angiography. The lipid profile (total cholesterol, high molecular weight lipoprotein, low molecular weight lipoprotein, triglycerides, apolipoprotein A1, apolipoprotein B), CRP and albumin levels were recorded. Galectin-3 levels were analysed in serum centrifuged blood.

Results: Age, hypertension incidence rate, triglycerides and Gal-3 values were found to be statistically significantly higher in the advanced CAS group compared to controls. For advanced CAS in ROC analysis; Gal-3 value was found to have a moderate discrimination ability (70-80%).

Conclusion: Our study suggests that Gal-3 levels may be used as a potential marker for the severity of carotid artery disease in CAS patients. Since advanced CAS patients are associated with a high stroke risk in follow-up, it is important that this condition is diagnosed early and treatment is directed.

Keywords: Carotid artery stenosis, Galectin-3, CRP, Albumin, Stroke

1. INTRODUCTION

Stroke is one of the leading causes of mortality and morbidity worldwide. Carotid atherosclerosis contributes significantly to cerebral ischaemic events and increasing evidence suggests that it is associated with the stability of carotid plaque tissue. Rupture of atherosclerotic plaque can lead to thrombus formation and embolisation of the thrombus to distantly located intracranial arteries.[1,2,3]

Galectin-3 (Gal-3), a member of the galectins, a family of b-galactoside-specific lectins, is predominantly found in the cytoplasm, migrates to the nucleus and is secreted to the cell surface and biological fluids such as serum and urine. It plays important functions in numerous biological activities including cell growth, apoptosis, pre-mRNA splicing, differentiation, transformation, angiogenesis, inflammation, fibrosis and host defence. Different studies have shown that Gal-3 can be used as a diagnostic or prognostic biomarker for heart disease, kidney disease and types of cancer. Gal-3 has been recognised to be extremely useful in the detection of many of these diseases, especially at an early stage.[4]

The mechanisms by which Galectin-3 may increase the risk of atherosclerotic events are not fully understood. In the literature, Gal-3 has been reported to increase inflammation by inducing the expression of a number of proinflammatory molecules well known in plaque pathophysiology and has been found to be abundant not only in advanced lesions but also at both mRNA and

protein levels. Gal-3 has been shown to be involved in experimental animal models of atherosclerosis, possibly mediated by the proinflammatory effects of galectin-3, suggesting that Gal-3 levels could potentially be used as a novel biomarker of advanced plaques. In studies further implicating galectin-3 in atherosclerosis, galectin-3 inhibition in experimental mouse models of atherosclerosis reduced atherosclerotic plaque progression and inflammation. [5,6] Two studies by Zhuang et al. and Han et al. showed that higher serum Gal-3 levels were associated with stroke severity at hospitalisation and stroke prognosis at discharge.[7,8]

C-Reactive Protein (CRP) is a proinflammatory protein produced by the liver under proinflammatory cytokine induction in the acute phase response. Elevated levels of highly sensitive CRP have been associated with both increased risk of ischaemic stroke and poor functional outcome and recurrent stroke prediction in patients with minor stroke or transient ischaemic attack (TIA).[9] It has been reported in the literature that the combination of ultrasound-detected intraplaque neovascularisation and CRP levels may allow more accurate assessment of plaque stability.[10] However, carotid artery stenosis (CAS) resulting from atherosclerosis of the carotid artery is associated with ischaemic stroke, and in patients undergoing carotid angiography the ratio of CRP to albumin ratio (CAR) has been shown to be an independent risk factor for severe CAS in relation to increased severity of carotid stenosis.[11]

There is a lack of strong clinically relevant biomarkers that can predict adverse outcomes in the CAS population. CAS is often asymptomatic and difficult to detect before adverse outcomes occur; therefore, having the ability to predict patients at higher risk of an adverse event is vital in developing targeted and effective preventive strategies. In this study, we aimed to investigate the association of serum galectin-3, an inflammatory protein, and CAR with CAS and their ability to predict adverse outcomes including TIA, cerebrovascular accident (CVA) and death, suggesting that the association of Gal-3 and CAR may be considered as a potential index of the severity of carotid artery disease.

2. MATERIALS AND METHODS

2.1. The population and sample of the research

This prospective cross-sectional study was conducted between 06.12.2024 and 26.12.2024 in the stroke outpatient clinic of the Department of Neurology, Health Sciences University Adana Şehir Training and Research Hospital. A total of 109 patients were included in the study, including 69 consecutive patients admitted with asymptomatic advanced CAS (70-99% stenosis) and as a control group, 40 patients who presented to the outpatient clinic with dizziness, vertigo and no CAS was detected on carotid imaging. An interventional neurologist and an additional neurologist determined the grade of CAS by carotid computed tomography angiography or carotid magnetic resonance angiography. Patients with a history of total carotid stenosis, myocardial infarction within the last six months, TIASVO were excluded. Patients with severe hepatic or renal insufficiency, heart failure, atrial fibrillation and valvular abnormalities commonly associated with possible sources of cardioembolism were excluded. Also excluded were patients with concurrent diseases affecting the expression of inflammatory mediators, such as those with a history of major surgery in the past month, a history of malignancy, chronic inflammatory autoimmune diseases, and patients with acute infection.

2.2. Data collection tools

Past medical history including hypertension, hypercholesterolaemia, diabetes mellitus (DM), history of stroke, coronary artery disease, obesity, smoking, alcohol habits and medications were collected.

Patients with systolic blood pressure of 140 mmHg and/or diastolic blood pressure of 90 mmHg were considered hypertensive. Patients with a diagnosis of DM were recorded. A body mass index above 30 kg/m² was considered obesity. Patients receiving lipid-lowering therapy or patients with total cholesterol (TC) levels higher than 200 mg/dL, low molecular weight lipoprotein (LMWL) cholesterol or triglyceride (TG) levels higher than 150 mg/dL were considered hyperlipidaemic. Routine lipid profile

(total cholesterol, high molecular weight lipoprotein, LDL, triglyceride, apolipoprotein A1, apolipoprotein B, CRP and albumin levels were in patients and control group. Gal-3 levels were analysed in serum centrifuged blood

2.3. Enzyme-linked immunosorbent assay (ELISA)

Blood samples from the patient and control groups were collected in a serum separator tube. After coagulation for 2 hours at room temperature, they were centrifuged at 1000 x g for 20 minutes. Test samples were aliquoted and stored at -80°C for later use.

Galectin-3 concentration in serum samples was determined by Human GAL3 (galectin-3) ELK2790 ELISA Kit (ELK biotechnology, USA). All kit contents were stored at -20°C, and the kit was placed at 4°C one day before the study day. Serum samples were also placed at 4°C one day before the study day. The test procedure was applied to DS2 (DYNEX, USA) Enzyme-Linked Immunosorbent Assay (ELISA) Automated Processing System according to the manufacturer's instructions and galectin-3 levels in serum samples were measured. Measurement range: 0.16-10 ng/mL. Absorbance was read at 450 ± 10 nm.

2.4. Statistical method

Patient data collected within the scope of the study were analysed with IBM Statistical Package for the Social Sciences (SPSS) for Macos 29.0 (IBM Corp., Armonk, NY). Frequency and percentage for categorical data, mean, standard deviation, median, minimum and maximum for continuous data were given as descriptive values. Normality test of the variables was evaluated by Kolmogorov Smirnov test. "Mann Whitney U-Test" was used for comparisons between groups and "Chi-Square or Fisher's Exact Test" was used for comparisons of categorical variables. ROC analysis was performed for serum galectin C value, which was thought to have a discriminative effect for being sick, and the ROC curve was drawn. The results were considered statistically significant when the p value was less than 0.05.

3. FINDINGS

A total of 109 participants (69 patients and 40 controls) were included in the study. The ages of the participants ranged between 26-83 years with a median age of 65 years, 36.7% (n=40) were female and 63.3% (n=69) were male. The distribution of demographic and clinical findings of the patient and control groups is shown in Table 1. The age and the rate of HT in the advanced CAS group were found to be statistically significantly higher than in the control group (p=0.008, p=0.010).

Table 1.

Distribution of demographic and clinical findings

Variables (N=109)	Total	Advanced CAS (n=69)	Control (n=40)	p-value
	n (%) or Median (Min-Max)	n (%) or Median (Min-Max)	n (%) or Median (Min-Max)	
Age	65 (26-83)	**68 (44-83)**	**63 (26-81)**	**0.008[a]**
Gender				1.000[b]
Woman	40 (36.7)	25 (36.2)	15 (37.5)	
Male	69 (63.3)	44 (63.8)	25 (62.5)	
Comorbidities				
HT	75 (68.8)	**54 (78.3)**	**21 (52.5)**	**0.010[b]**
DM	44 (40.4)	32 (46.4)	12 (30)	0.140[b]
KAH	52 (47.7)	35 (50.7)	17 (42.5)	0.529[b]
SVO	16 (14.7)	10 (14.5)	6 (15)	1.000[b]
Migraine	4 (3.7)	2 (2.9)	2 (5)	0.623[b]

Table 1. (Continued)

Hyperlipidaemia	41 (37.6)	27 (39.1)	14 (35)	0.823[b]
Obesity	16 (14.7)	7 (10.1)	9 (22.5)	0.140[b]
Smoking	52 (47.7)	35 (50.7)	17 (42.5)	0.529[b]
Alcohol use	6 (5.5)	3 (4.3)	3 (7.5)	0.667[b]

* Patient group only. [a]Mann Whitney U-Test [b]Chi-square or Fisher's Exact Test.
CAS: Carotid artery stenosis, HT: Hypertension, DM: Diabetes Mellitus, CAD: Coronary Artery Disease, CVO: Cerebrovascular event

In the advanced CAS group, TG and Gal-3 values were statistically significantly higher than controls (p= 0.012, p=< 0.001) (Table 2).

Table 2.

Distribution of laboratory measurements

Laboratory (N=109)	Total	Advanced CAS (n=69)	Control (n=40)	p-value
	Median (Min-Max)	Median (Min-Max)	Median (Min-Max)	
Total cholesterol	171 (77-344)	166 (80-344)	171 (77-302)	0.910[a]
HDL	46 (23-96)	46 (23-96)	47.5 (31-68)	0.242[a]
LDL	105 (32-234)	105 (32-234)	109.5 (44-202)	0.338[a]
Triglyceride	128 (35-844)	**134 (53-844)**	**105.5 (35-352)**	**0.012[a]**
Apolipoprotein-b	89 (35-155)	87 (47-155)	90 (35-151)	0.456[a]
Apolipoprotein-a1	136 (49-225)	135 (49-225)	139 (105-179)	0.591[a]
Albumin	41 (32-52)	40 (32-52)	42 (32-46)	0.111[a]
CRP	3 (0.1-15.1)	2.8 (0.1-15.1)	3.8 (0.7-9.1)	0.358[a]
CRP/Albumin ratio	0.1 (0-0.4)	0.1 (0-0.4)	0.1 (0-0.2)	0.540[a]
Gal-3	0.5 (0-2.9)	**0.5 (0.3-2.9)**	**0.2 (0-1.5)**	**<0.001[a]**

[a]Mann Whitney U-Test.
CAS: Carotid artery stenosis, HDL: High density lipoprotein, LDL: Low density lipoprotein, CRP: C-Reactive protein, Gal-3: Galectin-3

In the ROC analysis, the area under the curve for alpha was 75.6% and the cut-off value was 0.37. The area under the curve shows the statistical significance of the discrimination ability of the diagnostic test. The diagnostic test evaluated in our study determined that the Gal-3 value had a moderate discrimination ability (70-80%) for advanced CAS (Table 3) (Figure 1).

Table 3.

ROC analysis result for serum Gal-3 measurement parameter in advanced CAS patients

Risk Factor	AUC (95% CI)	Border	p-value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Gal-3	0.756 (0.647-0.865)	>0.37	<0.001	91.3	70.3	85.1	81.2

AUC: Area Under Curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value.
CAS Carotid artery stenosis Gal-3: Galectin

Figure 1.

Serum Gal-3 ROC Curve
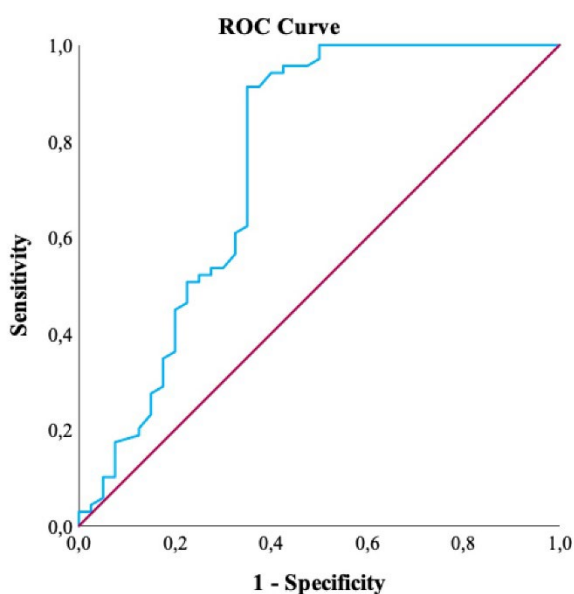
Gal-3: Galectin-3

4. DISCUSSION

In our study, Gal-3 value was found to be statistically significantly higher for advanced CAS and it was determined that this value had a moderate discrimination ability (70-80%). The hypothesis that atherosclerosis-related agents such as Gal-3 may enter the circulation and reflect the ongoing activity within atherosclerotic plaques is still a matter of debate.[12] In the literature, there are studies indicating that Gal-3 may be a marker of advanced plaques and may indicate stroke prognosis.[4,5,6,7] Similarly, another study found that intra-plaque Gal-3 expression levels increased proportionally as plaque width and degree of inflammation increased.[13] In another study, serum Gal-3 levels did not correlate with Gal-3 concentration in carotid plaques, suggesting that circulating Gal-3 may not be a marker of carotid plaque vulnerability. In a study, Gal-3 was found to be a predictive marker for cerebrovascular events in female patients undergoing CEA for atherosclerotic carotid stenosis. Thus, it was thought that Gal-3 could be used to select patients at high risk for the development of atherothrombotic cerebrovascular events and to prevent the occurrence of ischaemic events by intensifying their medical treatment.[14]

Studies describing the role and mechanism of Gal-3 in vascular calcification under different pathological conditions, including atherosclerosis, DM and chronic kidney disease, are summarised in the literature.[15]

However, limited data have previously documented the relationship between coronary plaque destabilisation and plasma Gal-3 levels.[16] In another study, Gal-3 levels were found to be a marker of inflammatory and metabolic distress, reflecting coronary atherosclerotic plaque instability and has been shown to be associated with long-term mortality.[17] In our study, Gal-3 levels increased in patients with advanced CAS compared to the healthy group, and we think that Gal-3 levels can be monitored in patients with CAS and used in CAS grade follow-up. However, long-term follow-up was not performed in our patient group, the relationship between Gal-3 levels and the frequency of cerebrovascular disease development in patients with advanced CAS may be revealed in future studies.

Gal-3 is a stable biomarker that is not associated with age, BMI org ender and does not exhibit circadien variation.[18]

TG elevation, whose exact role in atherosclerosis and potential benefits as a therapeutic target are still a matter of debate, was found to be statistically significantly higher than other lipid values in our study. Studies have shown that hypertriglyceridemia is common and is a significant contributor to the risk of atherosclerosis. Certain hypertriglyceridemia treatments have shown variable success in reducing the risk of atherosclerosis. [19,20]

Unlike the literature, CRP/ albumin (CAR) ratio was not found to be associated with the severity of carotid stenosis in our study. In contrast, elevated CAR was found to be an effective marker for the assessment of adverse outcomes in stroke patients and those who underwent mechanical thrombectomy.[21,22]

5. CONCLUSION

Our study suggests that Gal-3 levels may be used as a potential marker for the severity of carotid artery disease in CAS patients. Since advanced CAS

patients are associated with a high risk of stroke in follow-up, it is important that this condition is diagnosed early and treatment is directed.

Limitations

Our study has some limitations. Firstly, our sample size is relatively small and confirmatory studies in larger and diverse populations are required. Second, because our study has a cross-sectional design, we cannot assess the dynamics of changes in galectin-3 levels over time. Finally, our study did not examine the effects of genetic variations on galectin-3 levels, which may lead to deficiencies in understanding individual differences and genetic predisposition. More extensive studies are needed in the future to address these limitations.

Article Information Form

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The Declaration of Conflict of Interest/ Common Interest
No conflict of interest or common interest has been declared by authors.

Ethical Statement
In our cross-sectional study, which was conducted in strict adherence to the Declaration of Helsinki, the study protocol was approved by the local ethics committee, at its meeting on 05.12.2024 (decision no:247) and written informed consent was provided by all participants.

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Evaluation of Osteoporosis and Associated Factors in Patients with Type 1 Diabetes Mellitus

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Objective: This paper aims to assess the prevalence of osteoporosis in patients with T1DM by studying the influence of the main risk factors: BMI, calcium intake, vitamin D, lactose intolerance, and BMD, along with the risk of fractures.

Material and Methods: Cross-sectional study in 30 patients with T1DM and 30 normal controls. BMD was measured using DEXA, further calculating BMI, daily calcium intake, and vitamin D levels. Osteoporosis and fracture risk were evaluated by statistical analysis using the data obtained.

Results: Patients with T1DM had lower BMI ($p < 0.001$), lower daily calcium intake ($p < 0.001$), and lower L1-L4 Z scores ($p = 0.002$) compared to controls. High HbA1c was significantly associated with an increased risk of hip fracture ($OR = 1.58$, $p = 0.022$), and low BMI was also a crucial predictor of increased risk of fracture ($OR = 1.49$, $p = 0.012$) and osteoporosis ($OR = 1.29$, $p = 0.018$). It could be seen that lactose intolerance and calcium deficiency considerably increased the risk of osteoporosis and fractures.

Conclusion: Our study underlines the pivotal role of BMI, calcium intake, and lactose intolerance in determining osteoporosis and fracture risk in T1DM patients. Our findings emphasize once more how managing these risk factors by specific interventions may play a key role in preventing osteoporosis and fractures.

Keywords: Type 1 diabetes mellitus, Osteoporosis, Bone mineral density, Fracture risk, Calcium intake, Lactose intolerance, Vitamin D

1. INTRODUCTION

Osteoporosis is an important disease for public health, being characterized by a progressive reduction in bone mass, increasing the risk and incidence of fractures.[1] Both osteoporosis and diabetes mellitus are rising worldwide, contributing to high morbidity and mortality. [2] It is, therefore, crucial to follow up with such patients and their treatment. While T1DM accounts for only a small fraction of all diabetic patients, they are notably affected by diabetes-related complications at a higher prevalence rate.

T1DM is a form of the autoimmune disease characterized by the destruction of pancreatic beta cells.[3] Treatment of T1DM by insulin is needed for successful glycemic control to minimize or evade the complications related to diabetes.[4, 5] In inadequately controlled individuals with T1DM, neuropathy, retinopathy, nephropathy, and cardiovascular complications can occur.[6, 7] Although T1DM is a known secondary cause of osteoporosis, it is under-screened compared to other complications in clinical practice.[8] This will, unfortunately, lead to the patient being seen with osteoporosis only after the disease has progressed to a point beyond which prevention is possible. It mostly results in deterioration in the quality of life and permanent disability secondary to hip and vertebral fractures. This altogether harmed the social lives of people and the economies of countries.[8] Besides, because T1DM patients are younger and diagnosed early, more harm will be felt.

Salari et al. [9] extensively reviewed 86 studies that included about one hundred million participants. The mean prevalence of osteoporosis was 18.3%. In the breakdown of 70 reports, the prevalence of osteoporosis was 23.1% in women and 11.7% in men.

T1DM in both genders promotes deterioration in the microarchitecture of bone, leading to osteoporosis, characterized by a reduction of bone mineral density.[10] Indeed, anabolic activity is reduced due to the absolute insulin deficiency in T1DM patients. Most patients with T1DM develop the disease when young and usually cannot attain optimal peak bone mass. In addition, hyperglycemia enhances glycosylation of tissues, adversely affecting bone tissue quality.[11] As such, there are higher bone loss and fracture risks in patients with diabetes complications.[11, 12] In fact, T1DM patients in the study by Valerio G. et al. [12] presented with bone mineral density lows, a feature associated with poor glycemic control. As such, this population of patients should be kept under good glycemic control.

Very few studies have been exclusively conducted on T1DM regarding bone mineral densities, though many are present regarding diabetes. Since osteoporosis is considered a disease of advanced age, it can be overlooked in young patients with Type 1 DM. However, many complications, such as osteoporosis, can begin in the early stages in patients with Type 1 DM. Fractures and permanent damage that may occur at an early age both disrupt the patient's comfort of life and cause high costs. This research aims to find the rate of osteoporosis in patients diagnosed with T1DM and assess the role of important factors such as overall calcium intake, vitamin D levels, lactose intolerance, and the risk of fracture.

2. METHODS

This hospital-based cross-sectional study was conducted following approval from the Local Non-Invasive Clinical Research Ethics Committee (Decision No: 2019/02, Date: 30.01.2019). Patients were consecutively selected from our internal medicine and endocrinology outpatient clinics between January 2019 and January 2020. Our study included patients between 18 and 50 with type 1 DM. When selecting patients for the study, patients who did not have other secondary osteoporosis-causing diseases were included. Secondary osteoporosis-causing causes were evaluated in the exclusion criteria. Exclusion criteria included patients with malignancy, chronic renal failure (GFR < 60 ml/min), systemic

steroid use, Cushing's disease, hyperthyroidism, a diagnosis of celiac disease, and pregnancy. Patients with a history of bone surgery were not included in the study. Vitamin D levels, in accordance with the literature, were considered sufficient if they were above 20 ng/ml, insufficient if they were between 10 and 20 ng/ml, and deficient if they were below 10 ng/ml. Since vitamin D deficiency is among the causes of secondary osteoporosis, patients with vitamin D insufficiency were not included in our study. The control group consisted of 30 healthy individuals aged between 18 and 50.

The diagnosis of diabetes was made using the American Diabetes Association (ADA) criteria[13]. Antibody-positive patients were included in the study, with results confirmed by repeat testing[14]. Written informed consent was obtained from each participant. Patients were questioned regarding smoking and alcohol consumption, as well as their histories of fractures and lactose intolerance. Daily calcium intake was assessed using the IOF Bone Health Calcium Calculator. Bone mineral density (BMD) was measured at three anatomical sites—total lumbar spine, total hip, and femoral neck—using dual-energy X-ray absorptiometry (DEXA) with a Hologic-Discovery scanner (USA). In our study, the Z score was used for diagnosis in premenopausal women and men under 50 years of age in accordance with the World Health Organization Osteoporosis diagnostic criteria[15]. The FRAX score, which estimates the 10-year probability of fractures, was calculated for each patient. Vitamin D levels were measured using the Beckman Coulter DxI 800 immunoassay, and additional laboratory analyses were performed with a Beckman Coulter AU5800 analyzer.

2.1. Statistical analysis

The data from the study were analyzed using the SPSS 25.0 statistical software. Descriptive statistics were presented as frequencies, percentages, means, and standard deviations. The Pearson chi-square test was employed to compare categorical variables, while the Mann-Whitney U test was used for comparing groups with continuous variables that did not follow a normal distribution. Initially, a univariate analysis was

conducted, followed by a multivariate analysis to account for potential confounding factors. A p-value of less than 0.05 was considered statistically significant.

3. RESULTS

The study included 30 patients with T1DM and 30 healthy controls. Gender distribution was similar between the groups (53.3% male vs. 46.7% female in T1DM; 40.0% male vs. 60.0% female in controls, p = 0.438). The mean age was comparable (32.2 ± 9.5 years vs. 32.7 ± 8.1 years, p = 0.739). Height did not differ significantly between the groups (166.6 ± 10.9 cm vs. 164 ± 9 cm, p = 0.711). However, the T1DM group had a considerably lower mean weight (69.43 ± 11.5 kg vs. 79 ± 11 kg, p = 0.002) and BMI (25.09 ± 4.2 kg/m^2 vs. 28.9 ± 3.3 kg/m^2, p < 0.001). The mean duration of diabetes in the T1DM group was 15.3 ± 12.0 years. Smoking (30.0% vs. 23.3%, p = 0.770) and exercise habits (43.3% vs. 23.3%, p = 0.171) were similar between the groups (Table 1).

Table 1.

Sociodemographic characteristics of the study groups

		Type 1 DM (n=30) Mean (±SD)	Control (n=30) Mean (±SD)	p
Gender, n (%)				
	Male	16 (53.3)	12 (40.0)	0.438[a]
	Female	14 (46.7)	18 (60.0)	
Age (years)		32.2 ±9.5	32.7±8.1	0.739[b]
Height (cm)		166.6 ±10.9	164 ±9	0.711[b]
Weight (kg)		69.43 ±11.5	79 ±11	0.002[b]
BMI (kg/m²)		25.09 ±4.2	28.9 ±3.3	<0.001[b]
DM duration (years)		15.3 ±12.0	-	-
Smoke, n(%)				
	Yes	9 (30.0)	7 (23.3)	0.770[a]
	No	21 (70.0)	23 (76.7)	
Exercise, n(%)				
	Yes	13 (43.3)	7 (23.3)	0.171[a]
	No	17 (56.7)	23 (76.7)	

BMI: body mass index, DM: diabetes mellitus
[a]Chi-square test, [b]Mann Whitney U test

Figure 1 illustrates the distribution of complications among patients with T1DM. The most common complication was neuropathy, affecting 16 patients, followed by retinopathy in 6 patients and nephropathy in 3 patients. Cardiovascular disease was observed in 2 patients. Overall, 18 patients experienced at least one complication (Figure 1).

Figure 1.

Distribution of complications in patients with type 1 DM
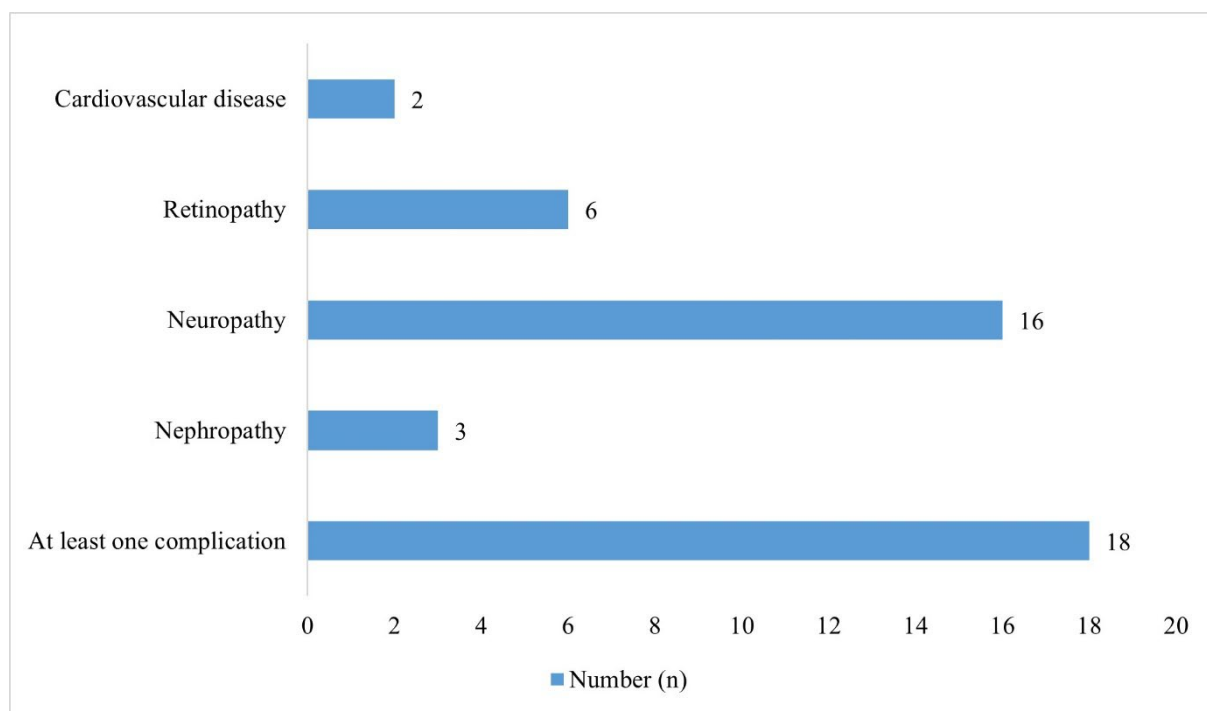
The T1DM patients had significantly higher creatinine levels (0.89 ± 0.15 mg/dL vs. 0.77 ± 0.09 mg/dL, p = 0.002) and fasting plasma glucose (FPG) levels (189.8 ± 79.7 mg/dL vs. 79.7 ± 7.0 mg/dL, p < 0.001) compared to the control group. HbA1c was also significantly higher in the T1DM group (8.6 ± 1.8% vs. 5.7 ± 0.2%, p < 0.001). The T1DM group had lower low-density lipoprotein (LDL) levels (108.9 ± 40.4 mg/dL vs. 119.9 ± 12.8 mg/dL, p = 0.005) and triglycerides (TG) (103.3 ± 73.1 mg/dL vs. 127.1 ± 28.5 mg/dL, p < 0.001) compared to controls. No significant differences were found in glomerular filtration rate (GFR) (115.8 ± 25.3 mL/min vs. 110.8 ± 13.8 mL/min, p = 0.156) or hemoglobin (Hgb) levels (14.3 ± 1.7 g/dL vs. 14.0 ± 1.2 g/dL, p = 0.391) (Table 2).

Vitamin D levels were similar between groups (38.5 ± 8.7 mg/dL vs. 34.9 ± 4.6 mg/dL, p = 0.131), but daily calcium intake was significantly lower in the T1DM group (903.23 ± 288.4 mg/dL vs. 1162.7 ± 253.9 mg/dL, p < 0.001). Calcium intake was insufficient in a more significant proportion of T1DM patients (73.3% vs. 30.0%, p = 0.002), and lactose intolerance was more prevalent in the T1DM group (36.7% vs. 10.0%, p = 0.033). Bone mineral density, as assessed by DEXA, showed significantly lower L1-L4 Z scores in the T1DM group (-0.83 ± 1.3 vs. 0.16 ± 0.79, p = 0.002), although femur neck Z scores did not differ significantly (-0.237 ± 1.34 vs. -0.013 ± 0.96, p = 0.283). The T1DM group also had higher FRAX major osteoporosis risk (5.1 ± 2.4% vs. 2.8 ± 1.0%, p < 0.001) and femur fracture risk (1.05 ± 1.4% vs. 0.17 ± 0.2%, p = 0.003) (Table 2).

Table 2.

DEXA results, FRAX risk, and biochemical properties of the study groups

	Type 1 DM (n=30) Mean (±SD)	Control (n=30) Mean (±SD)	p*
Creatinine (mg/dL)	0.89 ±0.15	0.77 ±0.09	0.002
GFR (ml/dk)	115.8 ±25.3	110.8 ±13.8	0.156
LDL (mg/dL)	108.9 ±40.4	119.9 ±12.8	0.005
TG (mg/dL)	103.3 ±73.1	127.1 ±28.5	<0.001
Hgb (g/dL)	14.3 ±1.7	14.0 ±1.2	0.391
FPG (mg/dL)	189.8 ±79.7	79.7 ±7.0	<0.001
HbA1c (%)	8.6 ±1.8	5.7 ±0.2	<0.001
D vitamin (mg/dL)	38.5±8.7	34.9±4.6	0.131
Daily Ca intake(mg/dL)	903.23±288.4	1162.7±253.9	<0.001
FRAX major osteoporosis risk (%)	5.1±2.4	2.8±1.0	<0.001
FRAX femur fracture risk (%)	1.05±1.4	0.17±0.2	0.003
L1-L4 Z score	-0.83±1.3	0.16±0.79	0.002
Femur neck Z score	-0.237±1.34	-0.013±0.96	0.283
Calcium Intake, n(%)			
Sufficient	8(26.7)	21(70.0)	0.002[a]
Insufficient	22(73.3)	9(30.0)	
Lactose intolerance, n(%)			
Yes	11(36.7)	3(10.0)	0.033[a]
No	19(63.3)	27(90.0)	

LDL: Low-density lipoprotein, Ca: Calcium Hgb: hemoglobin FPG: fasting plasma glucose FRAX: Fracture Risk Assessment Tool, D vitamin: 25-hydroxyvitamin D GFR: Glomerular filtration rate DEXA: Dual-energy X-ray absorptiometry, DM: Diabetes mellitus FRAX: Fracture Risk Assessment Tool
*Mann Whitney U test, [a]Chi-square test

3.1. L1-L4 Z score and related factors in patients with T1DM

In patients with T1DM, L1-L4 Z scores greater than -2 were compared to those with Z scores less than or equal to -2 to identify related factors. The mean BMI was significantly higher in patients with Z scores > -2 (27.5 ± 4.0 kg/m^2 vs. 23.4 ± 3.8 kg/m^2, p = 0.009). The duration of diabetes was shorter in patients with Z scores > -2 (7.2 ± 11.8 years vs. 10.2 ± 7.8 years, p = 0.032). Fasting plasma glucose (FPG) levels were lower in patients with Z scores > -2 (134.8 ± 68.4 mg/dL vs. 190.5 ± 93.5 mg/dL, p = 0.044), as were HbA1c levels (6.9 ± 1.9% vs. 8.4 ± 1.9%, p = 0.019). Patients with Z scores > -2 also had higher LDL levels (118.3 ± 29.4 mg/dL vs. 89.0 ± 24.0 mg/dL, p = 0.004) and higher triglyceride levels (121.0 ± 58.0 mg/dL vs. 77.3 ± 18.2 mg/dL, p = 0.004).

Although age, height, weight, hemoglobin, and GFR were not significantly different between the groups, patients with Z scores > -2 had higher vitamin D levels (37.4 ± 7.4 mg/dL vs. 32.0 ± 0.93 mg/dL, p = 0.050) and greater daily calcium intake (1066.7 ± 293.2 mg vs. 813.3 ± 256.7 mg, p = 0.018) (Table 3).

Table 3.

L1-L4 Z Score and related factors in patients with type 1 DM

	L1-L4 Z score > -2 (n=22)	L1-L4 Z score ≤ -2 (n=8)	p*
	Mean (±SD)	Mean (±SD)	
Age (years)	32.5±8.7	32.6±9.6	0.948
Height (cm)	165.4±9.7	170.6±11.5	0.210
Weight (kg)	75.2±11.5	68.8±16.1	0.322
BMI (kg/m²)	27.5±4	23.4±3.8	0.009
DM time (years)	7.2±11.8	10.2±7.8	0.032
FPG (mg/dL)	134.8±68.4	190.5±93.5	0.044
HbA1c (%)	6.9±1.9	8.4±1.9	0.019
Hemoglobin (g/dL)	14.2±1.5	13.9±1.44	0.550
LDL (mg/dL)	118.3±29.4	89.0±24.0	0.004
Triglycerides (mg(dL)	121.0±58.0	77.3±18.2	0.004
GFR (ml/dk)	113.2±20.4	113.7±24.6	0.965
D vitamin (mg/dL)	37.4±7.4	32.0±0.93	0.050
Ca intake (mg)	1066.7±293.2	813.3±256.7	0.018

Ca: Calcium, DM: Diabetes Mellitus FPG: fasting plasma glucose, D vitamin: 25-hydroxyvitamin D, GFR: glomerular filtration rate
*Mann Whitney U test

3.2. Factors associated with the FRAX femoral neck fracture risk

Factors associated with the FRAX femoral neck fracture risk were analyzed in patients with T1DM. Gender, smoking status, and exercise habits did not show significant differences in fracture risk scores (male: 0.90 ± 1.53 vs. female: 0.36 ± 0.57, p = 0.769; non-smokers: 0.45 ± 0.85 vs. smokers: 1.06 ± 1.67, p = 0.114; no exercise: 0.61 ± 1.11 vs. exercise: 0.61 ± 1.24, p = 0.714). However, the presence of diabetes-related complications was associated with a significantly higher fracture risk (1.40 ± 1.73 vs. 0.27 ± 0.51, p = 0.001). Similarly, patients with insufficient calcium intake had a higher fracture risk (1.03 ± 1.46 vs. 0.16 ± 0.27, p < 0.001), as did those with lactose intolerance (1.89 ± 1.84 vs. 0.22 ± 0.29, p = 0.001). The duration of diabetes did not significantly affect the fracture risk (1-10 years: 1.2 ± 1.74 vs. 11-60 years: 0.95 ± 1.34, p = 0.851) (Table 4).

Table 4.

Factors associated with the risk of FRAX femoral neck fracture risk in patients with type 1 DM

		FRAX femoral neck fracture risk score	p*
		Mean (±SD)	
Gender	Male	0.90±1.53	0.769
	Female	0.36±0.57	
Smoke	No	0.45±0.85	0.114
	Yes	1.06±1.67	
Exercise	No	0.61±1.11	0.714
	Yes	0.61±1.24	
DM Duration (years)	1-10	1.2±1.74	0.851
	11-60	0.95±1.34	
Complication	No	0.27±0.51	0.001
	Yes	1.40±1.73	

Table 4. (Continued)

Calcium Sufficiency	No	1.03±1.46	<0.001
	Yes	0.16±0.27	
Lactose Intolerance	No	0.22±0.29	0.001
	Yes	1.89±1.84	

DM: Diabetes Mellitus
*Mann Whitney U test

3.3. The logistic regression analysis for an increased risk of femoral neck fracture

In Model 1, higher body weight was associated with an increased fracture risk (OR = 1.09, 95% CI: 1.00–1.18, p = 0.048). A higher BMI was also a significant predictor of increased fracture risk (OR = 1.49, 95% CI: 1.09–2.04, p = 0.012). Elevated HbA1c levels were significantly associated with a higher fracture risk (OR = 1.58, 95% CI: 1.06–2.33, p = 0.022), as was insufficient calcium intake (OR = 1.007, 95% CI: 1.009–1.014, p = 0.015). The presence of diabetes-related complications dramatically increased the risk of femoral neck fractures (OR = 15.76, 95% CI: 1.68–147.50, p = 0.016). In Model 2, BMI remained a significant predictor of fracture risk (OR = 1.49, 95% CI: 1.09–2.04, p = 0.012), as did calcium intake (OR = 1.01, 95% CI: 1.00–1.02, p = 0.03). Age, height, smoking, exercise, vitamin D levels, and GFR did not significantly correlate with fracture risk in either model (Table 5).

Table 5.

Logistic regression analysis for femoral neck fracture risk and affecting factors

	Model 1				Model 2			
	OR	95% GA		p	OR	95% GA		p
Age	1.03	0.93	1.13	0.52				
Height	1.05	0.97	1.15	0.19				
Weight	1.09	1.00	1.18	**0.048***				
BMI	1.49	1.09	2.04	**0.012***	1.49	1.09	2.04	**0.012***
Smoke	3.15	0.56	17.57	0.19				
Exercise	1.00	0.16	5.98	1.00				
HbA1c	1.58	1.06	2.33	**0.022***				
D vitamin	1.21	0.92	1.59	0.16				
Ca intake	1.007	1.009	1.014	**0.015***	1.01	1.00	1.02	**0.03***
Complication	15.76	1.68	147.50	**0.016***				
GFR	1.02	0.98	1.06	0.308				

BMI: Body mass index, Ca: Calcium, GFR: Glomerular filtration rate

3.4. The logistic regression analysis for the risk of osteoporosis

In Model 1, higher BMI was significantly associated with an increased risk of osteoporosis (OR = 1.29, 95% CI: 1.04–1.59, p = 0.018). Additionally, insufficient calcium intake was found to be a significant risk factor (OR = 1.004, 95% CI: 1.00–1.007, p = 0.037), and lactose intolerance was strongly associated with an increased risk of osteoporosis (OR = 7.96, 95% CI: 1.60–39.50, p = 0.011).

In Model 2, BMI remained a significant predictor of osteoporosis (OR = 1.24, 95% CI: 1.00–1.54, p = 0.048), as did lactose intolerance (OR = 7.96, 95% CI: 1.60–39.50, p = 0.011). Age, height, weight, smoking, exercise, HbA1c, vitamin D levels, and diabetes-related complications did not significantly correlate with osteoporosis risk in either model (Table 6).

Table 6.

Logistic regression analysis for osteoporosis and affecting factors

	Model 1			Model 2		
	OR	95% GA		P	OR	95% GA		p
Age	1.00	0.92	1.09	0.97			
Height	1.05	0.97	1.13	0.18			
Weight	0.95	0.89	1.02	0.17			
BMI	1.29	1.04	1.59	**0.018***	- 1.24	1.00	1.54	**0.048***
Smoke	0.30	0.06	1.38	0.12			
Exercise	0.81	0.17	3.7	0.78			
HbA1c	1.38	0.98	1.94	0.06			
D vitamin	0.75	0.56	1.02	0.07			
Ca intake	1.004	1.00	1.007	**0.037***			
Lactose intolerance	7.96	1.60	39.50	**0.011***	- 7.96	1.60	39.50	**0.011***
Complication	2.7	0.59	12.35	0.19			
GFR	1.00	0.96	1.03	0.95			

BMI: Body mass index, Ca: Calcium, GFR: Glomerular filtration rate

4. DISCUSSION

The present study explained several important factors related to the development of femoral neck fractures and osteoporosis in T1DM patients: increased BMI was a strong predictor of heightened risk concerning femoral neck fracture and osteoporosis throughout, underlining the multifaceted effect of adiposity on bone health in this population. In addition, dietary calcium intake and lactose intolerance were strongly associated with an increased risk of osteoporosis. Indeed, poor glycemic control, as manifested by high levels of HbA1c, further complicated by the presence of diabetes-related complications, was associated with an increased risk of fractures of the femoral neck. These findings emphasize the need for targeted interventions on BMI management, adequate intake of calcium, and lactose intolerance to reduce the risk of osteoporosis and subsequent fractures in patients with T1DM. Further discussion will be conducted on the wider clinical implications of such associations, which may inform potential preventative strategies. T1DM is a rapidly rising incidence condition where insulin deficiency is at the core and is associated with many complications, including osteoporosis.

Since impaired bone formation and failure to achieve optimal peak bone mass are major factors, reduced bone strength and increased risk for osteoporosis later in life are typical for T1DM patients.[16] It exerts a negative effect on bone development through several mechanisms: suppression of the expression of genes critical for osteoblast maturation [17], a direct inhibiting effect on bone formation, increasing the expression of proinflammatory cytokines that impede osteoblast differentiation, and increased osteoblastic apoptosis.[18] Moreover, hyperglycemia increases osteoclast activity through the production of free oxygen radicals.[19] The consequence of chronic hyperglycemia is the development of microvascular complications: neuropathy, retinopathy, and nephropathy.[20] Additionally, it can aggravate the condition of osteoporosis by encouraging increased protein loss.[21]

T1DM is related to poor bone quality and an increased risk of fractures. While most studies report lower BMD in patients with T1DM, some studies did not find any significant effect on the measurements of BMD. According to the results of DEXA in 30 patients with T1DM, our study showed that the L1-L4 Z score was below -1 in 15 patients (50%) and below -2 in 8 patients (26.7%). Our results also demonstrate that, compared with controls, L1-L4 Z scores were significantly lower in our T1DM patients. Similar to this study, Gunczler et al. [22] found reduced BMD in T1DM

patients, with 45% of L2-L4 Z scores below -1. Similarly, Valerio et al. [12] showed that 37% of L1-L4 Z scores were below -1, and 11% were below -2 in T1DM patients. Our results of DEXA are in concordance with the literature, corroborating that BMD is decreased in patients with T1DM.

Both cross-sectional and longitudinal studies have shown that poor glycemic control in T1DM patients is significantly associated with an increased risk of the development of osteoporosis and fractures.[23, 24] For example, Heilman et al. [25] reported that poor glycemic control, linked with higher levels of HbA1c, was significantly associated with increased risk for osteoporosis in patients with T1DM. Our regression analysis surprisingly did show that those subjects presenting with higher levels of HbA1c had a significantly higher risk for hip fractures. In the study conducted by Brandao et al., they found that bone mineral density was worse in type 1 Diabetes patients with poor metabolic control, and BMD was inversely correlated with HbA1c[26].

Another critical factor affecting BMD is BMI. It has been found that a lower BMI is associated with an increased risk of osteoporosis because adipose tissue exerts its action by providing mechanical loading and adipocytokines, which increase BMD. As patients with T1DM usually have a lower BMI, their likelihood of developing osteoporosis and fractures is thereby increased[27]. This is supported by the study of Bridges MJ et al. [28], which found a significant relationship with increased BMI and increased BMD. In the study conducted by Tuominenin et al. [29], lower BMD was found in patients with type 1 DM. When the factors associated with lower BMD were evaluated, BMI was lower in patients with type 1 DM, and it has been associated with low BMI and low BMD in the literature. In our study, BMI was indeed lower in patients with T1DM, and this was associated with an increased risk of hip fractures and lower BMD.

Prolonged hyperglycemia can cause microvascular complications that may contribute to bone density loss through many mechanisms. Conditions like retinopathy and neuropathy could also predispose the patients to a great chance of

falling and, consequently, increase the risk of fractures.[30, 31] Eller-Vainicher et al. [32] demonstrated a lower BMD in patients with chronic complications, consistent with our findings.

Lower BMD was also associated with lower vitamin D levels in our study. However, in terms of the risk for hip fracture, our regression analysis did not find any significant relationship with the level of vitamin D. This finding is in partial agreement with that of Wierzbicka et al. [33], who reported a positive association of vitamin D level with muscle mass. While the need for vitamin D supplementation to prevent complications of diseases has been emphasized, how T1DM affects vitamin D metabolism has been underexamined in the literature, and more investigation is needed.

Although a few studies have been conducted linking low daily calcium intake with osteoporosis, there are not enough studies performed on patients with T1DM.[34] Maggio et al. [35] demonstrated that the daily calcium intake was insufficient in patients with T1DM and underlined the importance of adequate calcium intake. In the current study, the daily calcium intake was also significantly lower in T1DM patients compared to the control group. Moreover, the subjects with low calcium intake had lower BMD and increased risk of femoral hip fractures, which places our study among the first studies in this field.

Another determinant of osteoporosis in patients with T1DM is lactose intolerance. While the association between lactose intolerance and osteoporosis is well-established in the general population, there is a lack of studies in patients with T1DM. Honkanen et al. [36] observed a lower BMD in lactose-intolerant subjects, which was explained by their lower calcium intake. This is further supported by our results, in that we have found increased osteoporosis and hip fracture risk among the T1DM patients with lactose intolerance, with great importance given to ensuring that enough calcium intake protects against such risks.

5. CONCLUSION

In summary, our study shows the multifactorial nature of bone health in patients with T1DM. It

underscores the critical role of glycemic control, BMI, calcium intake, and lactose intolerance in determining bone mineral density and fracture risk. While much of the previous work has centered primarily on the general diabetic population, our results strongly emphasize the peculiar susceptibilities of patients with T1DM concerning osteoporosis development and femoral neck fractures. Identifying low BMI, insufficient calcium intake, and lactose intolerance as major risk factors underline the requirement for focused interventions to prevent bone loss in this population. It is finally noted that vitamin D metabolism has not been well studied in T1DM patients and its role in bone health points toward areas for future investigation. Our study contributes to the growing body of evidence that calls for comprehensive management strategies in T1DM to mitigate the long-term complications associated with compromised bone health.

Limitations

Our sample size is relatively small due to the lower prevalence of T1DM in the general population, which inherently limits the availability of eligible participants for the study.

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The Declaration of Conflict of Interest/ Common Interest
No conflict of interest or common interest has been declared by authors.

Copyright Statement

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İş Sağlığı Okuryazarlığı Ölçeğinin Türkçe Geçerlilik ve Güvenilirliğinin Değerlendirilmesi

Evaluation of the Turkish Validity and Reliability of the Occupational Health Literacy Scale

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Amaç: Bu çalışmanın amacı İş Sağlığı Okuryazarlığı Ölçeğini Türkçeye uyarlamaktır.

Metod: Metodolojik tipte olan bu çalışma Ocak-Temmuz 2024 tarihleri arasında farklı sektörlerde çalışan 631 kişinin katılımıyla gerçekleştirilmiştir. Veri toplamak için kişisel bilgi formu ve İş sağlığı okuryazarlığı ölçeği kullanılmıştır. Ölçeğin geçerliliği kapsam geçerliliği, yapı geçerliliği ve yakınsak-ıraksak geçerlilik ile değerlendirilmiştir. Ölçüm değişmezliğini belirlemek için cinsiyetler arasında çoklu gruplarda doğrulayıcı faktör analizi yapılmıştır. Güvenilirlik için cronbach alpha, düzeltilmiş madde toplam korelasyonu ve bileşik güvenilirlik analiz edilmiştir.

Bulgular: Kapsam geçerlilik indeksi tüm maddelerde 0.78'in üzerinde olduğu bulunmuştur. Doğrulayıcı faktör analizi orijinal iki faktörlü yapıyı doğrulamıştır. Uyum iyiliği indeks değerleri kabul edilebilir ve mükemmel aralıkta bulunmuştur. Cinsiyetler arası ölçüm değişmezliği sonuçları tatmin edicidir. Ölçeğin cronbach alpha katsayısı 0.87 olarak bulunmuştur.

Sonuç: İş sağlığı okuryazarlığı ölçeğinin Türkçe versiyonu geçerli ve güvenilir bir ölçüm aracı olarak bulunmuştur.

Anahtar Kelimeler: İş sağlığı, Sağlık okuryazarlığı, Geçerlilik, Güvenilirlik

Objectives: The aim of this study was to adapt the Occupational Health Literacy Scale into Turkish.

Method: This methodological cross-sectional study was conducted with the participation of 631 people working in different sectors between January and July 2024. Personal information form and Occupational health literacy scale were used to collect data. The validity of the scale was evaluated with content validity, construct validity and convergent-divergent validity. Confirmatory factor analysis was performed in multiple groups between genders to determine measurement invariance. For reliability, cronbach alpha, corrected item-total correlation and composite reliability were analysed.

Results: The content validity index was found to be above 0.78 for all items. Confirmatory factor analysis confirmed the original two-factor structure. Goodness-of-fit index values were found to be in the acceptable and excellent range. Cross-gender measurement invariance results were satisfactory. The cronbach alpha coefficient of the scale was found to be 0.87.

Conclusion: The Turkish version of the occupational health literacy scale was found to be a valid and reliable measurement tool.

Keywords: Occupational health, Health literacy, Validity, Reliability

EXTENDED ABSTRACT

Introduction

Work life is an important part of individuals' lives. There are many factors affecting individuals' work life. One of these factors is health literacy. Health literacy is defined as the ability of individuals to understand and apply health-related information and concepts. It is stated that individuals with high health literacy have high levels of skills and welfare in their work life and also have a high quality of life. In business life, occupational health literacy should be taken as a basis rather than individual health literacy. Occupational health literacy is more valuable in the assessment of health literacy in work life because it includes

field-specific procedures and practices. There are instruments that measure occupational health literacy and many of them have been adapted to the Turkish population. However, there are some shortcomings in these tools. These include lack of domain specificity, lack of conceptual frameworks, lack of important concepts such as willingness, responsibility and skills. Based on these shortcomings, Friedrich et al. developed the occupational health literacy scale. The occupational health literacy scale stands out with its conceptual structure and inclusive aspect.

The purpose of this study is to evaluate the Turkish validity and reliability of the Occupational Health Literacy Scale developed by Friedrich et al.

Method

This research was conducted between January and July 2024 in methodological type. Within the scope of the research, it was aimed to collect data 5-10 times the number of scale items. Although 120 participants were sufficient for the twelve items in the scale, data were collected from 631 employees to reveal the factor structure more strongly. Data were collected through face-to-face interviews. Personal information form and Occupational Health Literacy Scale were used to collect the data. The personal information form included questions such as age, gender, marital status, place of employment, and education level of the employees.

Occupational health literacy scale is a field-specific measurement tool developed by Friedrich et al. The scale consists of two sub-dimensions and 12 items. The scale is prepared in 4-point Likert type. These sub-dimensions are knowledge and skill-based approach to health (8 items) and willingness and responsibility for health (4 items). The cronbach alpha coefficient of the knowledge and skills-based approach to health subscale is 0.88 and the cronbach alpha coefficient of the willingness and responsibility for health subscale is 0.74. For the language validity of the scale, the steps in the good practices guide were followed. Expert opinion was consulted to evaluate the content validity of the scale. SPSS 25 and AMOS 21 programs were used to analyze the data. In the evaluation of the validity of the Occupational

Health Literacy Scale, confirmatory factor analysis was used for construct validity and average variance extracted, composite reliability, average shared variance and heterotrait monotrait values were used for convergent-divergent validity. Confirmatory factor analysis was used to evaluate the measurement invariance of the scale in multiple groups across genders. In this context, the statistical significance level of $\Delta\chi2$ difference, ΔCFI, ΔRMSEA and ΔSRMR values were examined in structural, scalar and metric invariance. The reliability of the scale was evaluated with cronbach alpha internal consistency coefficient and item-total correlation.

Results

The participants were 67.5% male, 67.5% married, 43.3% high school graduates, 48.5% factory workers and the average age of the participants was 35.73±8.61. Confirmatory factor analysis was conducted to confirm the two-factor structure of the occupational health literacy scale. The standardized factor loads of the knowledge and skill-based approach to health sub-dimension were calculated between 0.83-0.86, and the standardized factor loads of the willingness and responsibility for health sub-dimension were calculated between 0.80-0.84. As a result of confirmatory factor analysis, Cmin/df= 3.978, CFI= 0.973, GFI= 0.948, NFI= 0.964, TLI= 0.966 and RMSEA= 0.068 were calculated as goodness of fit indices for the Turkish version of the Occupational Health Literacy Scale. In determining the measurement invariance between genders, first, structural invariance between genders was tested. According to the results of the analysis ($\chi2$= 377.606, RMSEA=0.064 (90% [CI], 0.057-0.071), CFI=0.956, SRMR=0.023) fit index values were calculated. Second, metric invariance was tested by restricting the factor loadings to be the same across genders. Goodness of fit indices for metric invariance ($\chi2$=386.170, RMSEA=0.061 (90% [CI], 0.054-0.068), CFI=0.956, SRMR=0.024) were calculated. On the other hand, compared to structural invariance, the p value for $\Delta\chi2$ was > 0.05, ΔRMSEA=0.003, ΔCFI=0.000, and ΔSRMR=0.001. Third, the scalar invariance of the Turkish version of the Occupational Health

Literacy Scale was tested. For this purpose, factor loadings and item intercepts were constrained equally for both genders. Model goodness-of-fit indices (χ2=396.073, RMSEA=0.061 (90% [CI], 0.054-0.068), CFI=0.955, SRMR=0.032) were calculated for scalar invariance. When compared according to metric invariance, the p value for $\Delta\chi$2 was > 0.05, ΔRMSEA= 0.000, ΔCFI = -0.001, and ΔSRMR= 0.008. Composite reliability and average variance extracted values were analyzed to determine the convergent validity of the Turkish version of the occupational health literacy scale. According to the results of the analysis; composite reliability = 0.95 and average variance extracted = 0.74 for the knowledge and skill-based approach to health sub-dimension; composite reliability = 0.92 and average variance extracted = 0.75 for the willingness and responsibility for health sub-dimension. The divergent validity of the scale was evaluated with heterotrait monotrait and average shared variance. For the Turkish version of the occupational health literacy scale, heterotrait monotrait = 0.023 and average shared variance = 0.001. Cronbach's alpha internal consistency coefficient, corrected item-total correlation and composite reliability were used to assess the reliability of the scale. According to the results of the analysis; cronbach alpha for the Turkish version of the occupational health literacy scale was found to be 0.875, 0.95 for the knowledge and skill-based approach to health sub-dimension and 0.89 for the willingness and responsibility for health sub-dimension.

Conclusion

This study revealed that the Turkish adaptation of the occupational health literacy scale is a valid and reliable measurement tool for assessing occupational health literacy in employees. Since the occupational health literacy scale determines individual-specific health literacy in the workplace, it can be used in situation assessment, health promotion and preparation of future intervention programs.

1. GİRİŞ

Çalışma hayatı, bireylerin yaşam döngüsü içerisinde sağlık ve esenliklerini etkileyen bir faktördür[1]. Bireysel düzeyde sağlık okuryazarlığı

yüksek olan çalışanların sağlıklarından daha fazla sorumlu oldukları, iş becerilerinin ve refahlarının yüksek olduğu ve iyi bir yaşam kalitesine sahip oldukları belirtilmektedir[2-4]. İş hayatında bireysel sağlık okuryazarlığı ele alınsa da örgütsel boyutun da göz ardı edilmemesi gerektiği belirtilmektedir. Sağlıkla ilgili prosedürler, örgütsel misyon ve işyeri iklimi gibi sosyal ve kültürel koşulların bireysel sağlık okuryazarlığı üzerinde etkisi olduğu belirtilmektedir[5]. Mesleki sağlık okuryazarlığı, bireysel sağlık okuryazarlığının alana özgü bir şekilde değerlendirilmesini içerir[6]. Mesleki sağlık okuryazarlığı, kişilerin çalışma hayatı koşullarında sağlıkla ilgili bilgilere erişme, bu bilgileri işleme ve uygulama konusundaki bilgi, beceri ve istekliliklerini kapsamaktadır. İş sağlığı bilgilerinin uygun bir sağlık yaklaşımı ile birlikte işlenmesinin, işyerinde sağlığı, sürdürülebilir çalışma becerisini ve refahı olumlu yönde etkilemenin temelini oluşturacağı belirtilmektedir[6,7]. Alana özgü iş sağlığı okuryazarlığını ölçmek için daha önce hazırlanmış üç nicel ölçek bulunmaktadır. Bunlardan ilki Shannon ve Parker (2020) tarafından geliştirilen Sağlık İletişimi Anketi, ikincisi Suthakorn ve ark. (2020) tarafından geliştirilen Tayland Kayıt Dışı Çalışanlar için Mesleki Sağlık Okuryazarlığı Ölçeği ve üçüncüsü Azizi ve ark. (2019) tarafından geliştirilen Çalışanlar için Sağlık Okuryazarlığı Ölçeğidir[8-10]. Tayland Kayıt Dışı Çalışanlar için İş Sağlığı Okuryazarlığı Ölçeği[10], çalışanların sağlığa aktif olarak katılma istekliliğini ve sağlık konusunda sorumluluk alma motivasyonunu içermemekte ve kayıtlı çalışanlar göz ardı edildiği için çalışan nüfusun tamamına genellenemediği görülmektedir. Ayrıca ölçekte yer alan madde sayısının fazla olması yanıtlama süresini etkilemektedir. Çalışanlar için Sağlık Okuryazarlığı Ölçeği'nin[8] kavramsal yapı ve spesifik odaktan yoksun olmasına rağmen karar verme ve öz yeterliliği içerdiği bildirilmektedir. Sağlık İletişimi Anketi[9] tek bir sektör için tasarlanmıştır ve sağlık okuryazarlığının kritik boyutunu vurgulamaktadır. Tayland Kayıt Dışı Çalışanlar için Mesleki Sağlık Okuryazarlığı Ölçeği'nin Türkçe uyarlama çalışması Uskun ve arkadaşları (2022) tarafından yapılmıştır[11]. İşçiler için Sağlık Okuryazarlığı Ölçeği'nin Türkçe uyarlaması Ezirmik tarafından yapılmıştır[12].

Çalışanların iş sağlığı okuryazarlığını ölçen bir diğer ölçüm aracı ise Friedrich ve ark (2023) tarafından geliştirilen İş Sağlığı Okuryazarlığı Ölçeği (İSOÖ)'dür. İSOÖ diğer ölçeklerden ayıran farklılıklara bakıldığında; kapsayıcı olması, kavramsal yapıya sahip olması ve çalışanların iş sağlığı okuryazarlığı faaliyetlerine olan istek ve sorumluluk durumlarını da değerlendirmesidir. İSOÖ 'nün kavramsal yapısına bakıldığında; bilgi ve beceriler temelinde istek ve sorumlulukla güçlendirilmiş, iş sağlığı bilgilerini işleyen ve mesleki ortamlara uygun sağlık yaklaşımını benimseyen, iş sağlığı okuryazarlığı modelinin sonucunda sürdürülebilir çalışma becerisi ve refah anlayışı yer almaktadır.

Bu çalışmanın amacı Friedrich ve arkadaşları (2023) tarafından geliştirilen İş Sağlığı Okuryazarlığı Ölçeği'nin Türkçe (İSOÖ-TR) uyarlamasını yapmaktır.

1.1. Araştırma hipotezleri

H1: İSOÖ-TR geçerli bir ölçüm aracıdır.

H2: İSOÖ-TR güvenilir bir ölçüm aracıdır.

H3: İSOÖ-TR ölçme değişmezliğine sahip bir ölçüm aracıdır.

2. MATERYAL VE METOD
2.1. Çalışma tasarımı ve katılımcılar

Bu çalışma metodolojik tipte yürütülmüştür. İş sağlığı okuryazarlığı ölçeğinin Türkçeye uyarlandığı bu çalışmada, ölçme aracı geliştirmeye ilişkin iyi uygulama rehberleri dikkate alınmıştır[13-15].

Friedrich ve diğerleri (2023) tarafından geliştirilen İSOÖ'nin hedef kitlesi farklı sektörlerde çalışanlar olarak belirlenmiştir. Mevcut çalışma kapsamında farklı sektörlerde çalışan bireyler çalışmaya dahil edilmiştir. Ruhsal sorunları olan bireyler çalışmaya dahil edilmemiştir. Bu çalışmanın örneklemini Türkiye'nin doğusunda yer alan bir ilde çeşitli sektörlerde çalışan bireyler oluşturmaktadır. Literatürde faktör analizi için 300 kişinin yeterli olacağı belirtilmektedir[16]. Katılımcı sayısı ile ilgili bir diğer yaygın görüş ise madde sayısının 5-10 katı kadar katılımcı olmasının yeterli olduğudur[13]. Bu çalışmada da literatürdeki minimum değerlerin altında kalmayacak şekilde 631 kişi ile gerçekleştirilmiştir.

2.2. Veri toplama

Araştırma verileri, Ocak ve Temmuz 2024 tarihleri arasında yüz yüze görüşme tekniği kullanılarak bir anket aracılığıyla toplanmıştır. Veri toplamak için kişisel bilgi formu ve İSOÖ kullanılmıştır.

2.3. Veri toplama araçları
2.3.1. Kişisel bilgi formu

Araştırmacılar tarafından hazırlanan kişisel bilgi formunda yaş, cinsiyet, eğitim düzeyi ve çalışma yeri ile ilgili bilgiler yer almıştır.

2.3.2. İş Sağlığı okuryazarlığı ölçeği

Friedrich ve arkadaşları (2023) tarafından çalışanların iş sağlığı okuryazarlık düzeyini belirlemek amacıyla geliştirilmiştir. Ölçek 12 madde ve iki alt boyuttan oluşmaktadır. Alt boyutlar, sağlığa bilgi ve beceri temelli yaklaşım (8 madde) ve sağlık için isteklilik ve sorumluluktur (4 madde). Sağlığa bilgi ve beceri temelli yaklaşım alt boyutunda maddeler 1: Çok zor-4: Çok kolay şeklinde puanlanmaktadır. Sağlık için isteklilik ve sorumluluk alt boyutunda maddeler 1: kesinlikle katılmıyorum-4: kesinlikle katılıyorum şeklinde puanlanmaktadır. Sağlığa bilgi ve beceri temelli yaklaşım alt ölçeğinin cronbach alpha katsayısı 0.88, sağlık için isteklilik ve sorumluluk alt ölçeğinin cronbach alpha katsayısı ise 0.74'tür. Ölçek puanının hesaplanmasında daha önceki genel sağlık okuryazarlığı ölçeklerinin hesaplama prosedürü izlenmiştir[17]. Bu bağlamda, ölçek geliştiricileri tarafından ortalama puanlar kullanılarak tam bilgi verisi ile tüm puanı hesaplamak için k-en yakın komşu algoritmasının (k=10) kullanıldığı ve tüm değerlerin 0 ile 50 arasında ortak bir metriğe dönüştürüldüğü bildirilmiştir. Her katılımcı için birinci faktörde yer alan 8 madde kullanılarak ortalama puan hesaplanmış ve ortalama puan kullanılarak metrik dönüşümü sağlanmıştır. Aynı işlemin ikinci faktörde yer alan maddeler için de tekrarlandığı bildirilmiştir. Ölçek puanının hesaplanabilmesi için bireylerin soruların en az %75'ine cevap vermesi gerekmektedir. İSOÖ puanı aşağıdaki formül ile hesaplanmaktadır: (M-1)X50/3[18].

2.4. İSOÖ-TR' nin dil ve kapsam geçerliliği

İSOÖ-TR' nin Türkçe dil ve kapsam geçerliliğinin değerlendirilmesinde Wild ve ark. (2005) iyi uygulamalar kılavuzu takip edilmiştir[19]. Bu kılavuz doğrultusunda, İSOÖ-TR hazırlık aşamasında araştırmacılar tarafından incelenmiş ve Türk toplumuna uyarlanması için ölçek sahibinden izin alınmıştır. İleri çeviri aşamasında, her iki dile de hâkim iki bağımsız çevirmen süreci yürütmüştür. Uzlaşma aşamasında ise uzman dilbilimcilerden gelen çeviriler her iki dile hâkim araştırmacılar tarafından incelenmiş ve tek bir Türkçe form üzerinde uzlaşmaya varılmıştır. Geri çeviri aşamasında ise araştırmacılar tarafından üzerinde uzlaşılan Türkçe form tekrar çeviriye gönderilmiştir. Geri çeviri, her iki dile de aşına olan ve orijinal ölçeğe aşına olmayan iki bağımsız uzman tarafından sağlanmıştır. Geri çeviri incelemesi araştırmacılar tarafından yapılmış ve çevrilen form incelenerek görüş birliğine varılmıştır. Uyumlaştırma aşamasında ise orijinal ölçek ile üzerinde görüş birliğine varılan geri çeviri formu karşılaştırılmış ve maddelerin anlamsal bütünlüğünün korunduğu görülmüştür.

Böylece İSOÖ-TR'nin dil geçerliliğini sağladığı kabul edilmiştir. Bilişsel bilgilendirme aşamasında, İSOÖ-TR'nin kapsam geçerliliği uzmanlar tarafından değerlendirilmiş ve maddelerin anlaşılabilirliği ve yanıtlama süreleri bir pilot çalışma ile değerlendirilmiştir.

İSOÖ-TR'nin kapsam geçerliliğinin değerlendirilmesinde doktora derecesine sahip, her iki dile hâkim ve ölçek geliştirme-uyarlama süreçlerini bilen 5 uzman (dört halk sağlığı hemşireliği akademisyeni, bir halk sağlığı hekimi) bir görev almıştır. Kapsam geçerliliğini değerlendirmek için madde kapsam geçerlilik indeksi (M-KGİ) ve ölçek kapsam geçerlilik indeksi (Ö-KGİ) kullanılmıştır. Polit ve ark. (2007) M-KGİ değerini 0,78 ve Ö-KGİ değerini 0,90 alt sınır olarak kabul etmiştir[20]. Uzmanlar 4'lü Likert ölçeği kullanmıştır (1: ilgili değil, 2: biraz ilgili, 3: ilgili, 4: çok ilgili). İSOÖ-TR'deki tüm maddelerin M-KGİ değerleri 0.78'den yüksektir ve Ö-KGİ değeri 0.95 olarak hesaplanmıştır. İSOÖ-TR'nin maddelerinin anlaşılabilirliğini ve yanıt sürelerini görmek için araştırmacı eşliğinde 20 işçi ile bir pilot çalışma gerçekleştirilmiştir. Pilot çalışmadaki çalışanlar ana çalışmaya dahil edilmemiştir.

İSOÖ-TR' nin Türkçe' ye uyarlama süreci Şekil 1'de özetlenmiştir.

Şekil 1.

İSOÖ' nün Türkçe adaptasyon süreci


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┌─────────────────────────────────────────────────────────────────┐
│        İş Sağlığı Okuryazarlığı Ölçeği Türkçe Versiyonu          │
└─────────────────────────────────────────────────────────────────┘
                              │
┌─────────────────────────────────────────────────────────────────┐
│     İş sağlığı okuryazarlığı ölçeğinin dil ve kapsam geçerliliği │
│                                                                   │
│  Hazırlık ➡ Çeviri ➡ geri çeviri ➡ geri çeviri incelemesi ➡     │
│  çeviri mutabakatı ➡ uyumlaştırma ➡ bilişsel değerlendirme      │
└─────────────────────────────────────────────────────────────────┘
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Geçerlilik

Yakınsak-ıraksak geçerlilik

Bulgular İSOÖ-TR'nin bu geçerliliği sağladığını desteklemektedir.

Kapsam geçerliliği

İSOÖ-TR'nin KGİ> 0.78

Yapı geçerliliği

Doğrulayıcı faktör analizi İSOÖ-TR'nin iki faktörlü yapısını doğrulamıştır.

Ölçüm değişmezliği

Bulgular İSOÖ-TR'nin bu geçerliliği sağladığını desteklemektedir.

Güvenilirlik

Cronbach alfa katsayısı

İSOÖ-TR'nin cronbach alfa: 0.87'dir. Alt boyutların cronbach alfa değerleri>0.7

Bileşik güvenilirlik

Alt boyutların bileşik güvenilirlik değerleri 0.92-0.95 arasındadır.

Madde toplam korelasyonu

Madde toplam korelasyonu değerleri >0.4

2.5. İstatistiksel analiz

Veri analizi için SPSS 25 ve AMOS 21 programları kullanılmıştır. Tanımlayıcı verileri analiz etmek için sayı, yüzde ve ortalama kullanılmıştır.

Yapı geçerliliğini belirlemek için doğrulayıcı faktör analizi (DFA) kullanılmıştır. DFA'da parametre tahminleri maksimum olabilirlik tahmin yöntemi kullanılarak gerçekleştirilmiştir. Maksimum olabilirlik tahmin yönteminin koşulu olan çok değişkenli normallik Mardia katsayısı ile değerlendirilmiştir[21]. Verinin çok değişkenli normalliği sağladığı görülmüştür. DFA kapsamında modelin uyum iyiliğini değerlendirmek için ki-kare istatistiğinin serbestlik derecesine bölünmesi (CMIN/DF), yaklaşık hataların ortalama karekökü (RMSEA), karşılaştırmalı uyum indeksi (CFI), normlaştırılmış uyum indeksi (NFI), Tucker Lewis indeksi (TLI) uyum indeksleri takip edilmiştir[16,22]. İSOÖ-TR'nin ölçüm değişmezliğinin belirlenmesinde DFA çoklu gruplarda gerçekleştirilmiştir. Bu kapsamda yapısal, skaler ve metrik değişmezlikte $\Delta\chi^2$ farkının istatistiksel anlamlılık düzeyi, ΔCFI, ΔRMSEA ve ΔSRMR değerleri incelenmiştir. Önceki çalışmaların önerilerine göre, İSOÖ için anlamlı olmayan $\Delta\chi^2$, ΔRMSEA < 0,050, ΔCFI < 0,004 ve ölçüm değişmezliği için ΔSRMR ≤ 0,01 kriterleri esas alınmıştır [23,24]. Ölçeğin yakınsak ve ıraksak geçerliliğini değerlendirmek için bileşik güvenilirlik (CR), ortalama açıklanan varyans (AVE), ortalama paylaşılan varyans (ASV) ve heterotrait-monotrait korelasyon oranı (HTMT) kullanılmıştır[15,25,26]. Güvenilirliği değerlendirmek için Cronbach alfa iç tutarlılık katsayısı, CR ve düzeltilmiş madde toplam korelasyonu kullanılmıştır.

2.6. Etik değerlendirme

İSOÖ' nün Türk toplumuna uyarlanması için öncelikle ölçeği geliştiren Friedrich'ten izin alınmıştır. Muş Alparslan Üniversitesi Bilimsel Araştırmalar ve Yayın Etiği Kurulundan etik kurul izni alınmıştır (Karar no: 1-49). Çalışmanın yürütülmesi için ilgili kurumlardan çalışma izni alınmıştır. Çalışmaya katılanlardan bilgilendirilmiş onam alınmıştır. Araştırma Helsinki Deklarasyonu standartlarına uygun olarak yürütülmüştür.

3. BULGULAR

Çalışmaya katılanların %67,5'i erkek, %67,5'i evli, %43,3'ü lise mezunu ve %48,5'i fabrika işçisiydi. Katılımcıların yaş ortalaması 35,73±8,61'dir (Tablo 1).

Tablo 1.

Katılımcıların kişisel özellikleri (n:631)

Özellikler	n	%
Cinsiyet		
Erkek	426	67.5
Kadın	205	32.5
Medeni durum		
Evli	426	67.5
Bekar	205	32.5
Eğitim durumu		
İlkokul	30	4.8
Ortaokul	192	30.4
Lise	273	43.3
Üniversite	136	21.6
Çalışma yeri/alanı		
Fabrika	306	48.5
Tekstil atölyesi	217	34.4
Oto sanayi	59	9.4
Medikal/laboratuvar	49	7.7
Yaş ort.	35.73±8.61 (20-63)	

Çalışmada İSOÖ' nün iki faktörlü yapısını doğrulamak için DFA yapılmıştır. Sağlığa bilgi ve beceri temelli yaklaşım alt boyutunun standardize edilmiş faktör yükleri 0,83-0,86 arasında, sağlık için isteklilik ve sorumluluk alt boyutunun standardize edilmiş faktör yükleri ise 0,80-0,84 arasında hesaplanmıştır. DFA sonucunda İSOÖ-TR'nin uyum iyiliği indeksleri olarak Cmin/df= 3,978, CFI= 0,973, GFI= 0,948, NFI= 0,964, TLI= 0,966 ve RMSEA= 0,068 hesaplanmıştır. Model için standardize edilmiş faktör yükleri Şekil 2'de yer alan yapısal eşitlik modelinde sunulmuştur.

Şekil 2.

İSOÖ-TR'ye ait yapısal eşitlik modeli
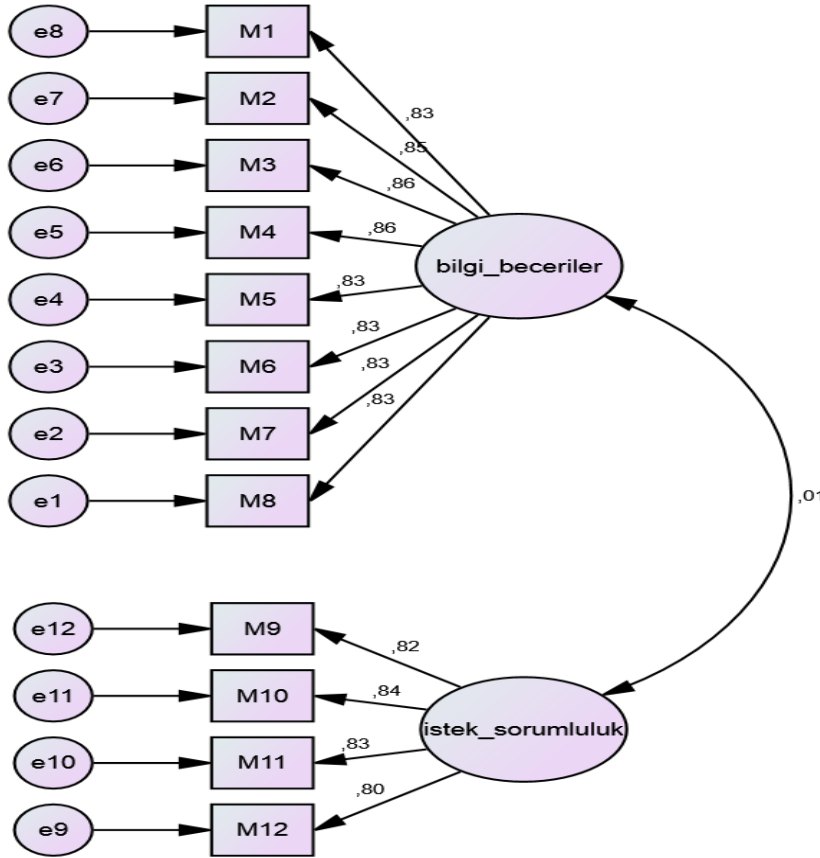
Çalışmada, İSOÖ-TR'nin farklı gruplarda aynı yapıyı gösterdiğini ortaya koymak amacıyla cinsiyetler arasında çoklu gruplarda DFA yapılmıştır. Bu kapsamda ölçüm değişmezliği üç aşamada (yapısal, metrik ve skaler) değerlendirilmiştir. Uyum iyiliği indeks değerleri ve modeller arasındaki farklar Tablo 2'de sunulmuştur.

Tablo 2.

İSOÖ-TR'nin cinsiyetler arası ölçüm değişmezliği

Model*	χ^2	RMSEA	RMSEA (%90 CI)	CFI	SRMR	Δ Model	Δ χ^2	ΔRMSEA	ΔCFI	ΔSRMR
			Model uyum indeksleri					**Model farkları**		
Yapısal	377,606	0.064	(0.057-0.071)	0.956	0.023	-	-	-	-	-
Metrik	386.170	0.061	(0.054-0.068)	0.956	0.024	Metrik-yapısal	8.564	-0.003	0.000	0.001
Skaler	396.073	0.061	(0.054-0.068)	0.955	0.032	Skaler-metrik	9.093	0.000	-0.001	0.008

*Tüm Δ χ2 için p değerleri > 0.05

İlk olarak, cinsiyetler arasında yapısal değişmezlik test edilmiştir. Analiz sonuçlarına göre ($\chi2=$ 377.606, RMSEA=0.064 (%90 [CI], 0.057-0.071), CFI=0.956, SRMR=0.023) uyum indeksi değerleri hesaplanmıştır. İkinci olarak, faktör yükleri cinsiyetler arasında aynı olacak şekilde kısıtlanarak metrik değişmezlik test edilmiştir. Metrik değişmezlik için uyum iyiliği indeksleri ($\chi2$=386.170, RMSEA=0.061 (%90 [CI], 0.054-0.068), CFI=0.956, SRMR=0.024) hesaplanmıştır. Öte yandan, yapısal değişmezlik ile karşılaştırıldığında, $\Delta\chi2$ için p değeri > 0.05, ΔRMSEA=0.003, ΔCFI=0.000 ve ΔSRMR=0.001 idi. Üçüncü olarak, İSOÖ-TR'nin skaler değişmezliği test edilmiştir. Bu amaçla, faktör yükleri ve madde kesişimleri her iki cinsiyet için eşit olarak kısıtlanmıştır. Skaler değişmezlik için model uyum iyiliği indeksleri ($\chi2$=396.073, RMSEA=0.061 (%90 [CI], 0.054-0.068), CFI=0.955, SRMR=0.032) hesaplanmıştır. Metrik değişmezliğe göre karşılaştırıldığında, $\Delta\chi2$ için p değeri > 0.05, ΔRMSEA= 0.000, ΔCFI = -0.001 ve ΔSRMR= 0.008'dir. İSOÖ-TR'nin yakınsak geçerliliğini belirlemek için CR ve AVE değerleri incelenmiştir.

Analiz sonuçlarına göre; sağlığa bilgi ve beceri temelli yaklaşım alt boyutu için CR= 0,95 ve AVE= 0,74; sağlık için isteklilik ve sorumluluk alt boyutu için CR= 0,92 ve AVE= 0,75 olarak bulunmuştur. Ölçeğin ıraksak geçerliliği HTMT ve ASV ile değerlendirilmiştir. İSOÖ-TR için HTMT= 0.023 ve ASV= 0.001 olarak hesaplanmıştır.

Ölçeğin güvenirliğini değerlendirmek için Cronbach alfa iç tutarlılık katsayısı, düzeltilmiş madde toplam korelasyonu ve CR kullanılmıştır. Analiz sonuçlarına göre; İSOÖ-TR için cronbach alpha 0,875, sağlığa bilgi ve beceri temelli yaklaşım alt boyutu için 0,95 ve sağlık için isteklilik ve sorumluluk alt boyutu için 0,89 olarak bulunmuştur. İSOÖ-TR'de yer alan maddelerin düzeltilmiş madde toplam korelasyon değerleri 0,40-0,73 arasında hesaplanmıştır. Sağlığa bilgi ve beceri temelli yaklaşım alt boyutu için CR= 0,92 ve sağlık için isteklilik ve sorumluluk alt boyutu için CR=0,95 olarak hesaplanmıştır. İSOÖ-TR'de yer alan maddelerin güvenilirlik bulguları Tablo 3'te gösterilmiştir

Tablo 3.

İSOÖ-TR'nin güvenilirlik bulguları

Maddeler	Madde toplam korelasyon	CR	Cronbach alfa
Sağlıkta Bilgi ve Beceri Temelli Yaklaşım Alt Boyutu		0.92	0.95
1- İşyerinde güvenlik ve sağlıkla ilgili bilgileri basit ve anlaşılır bir şekilde buluyorum	0.713		
2- İşimin sağlığım ve refahım üzerinde ne zaman kötü bir etkisi olduğunu değerlendirebilirim.	0.738		
3- İş sağlığı ve güvenliği hakkındaki bilgileri anlıyorum.	0.732		
4- Sağlığa zararlı iş durumlarına aktif olarak çözümler uygulayabilirim.	0.723		
5- Başkalarının sağlığı üzerinde olumlu bir etki yaratmak için onlarla birlikte çalışma koşullarını değiştirebilirim.	0.687		
6- İşyerinde sağlık ve esenliğe yönelik riskler hakkında başkalarıyla konuşabilirim	0.708		
7- Hangi iş sağlığını geliştirme hizmetlerinin benim için uygun olduğunu değerlendirebilirim.	0.701		
8- İşyerinde beni etkileyen sağlık riskleri hakkında kendi başıma bilgi bulabilirim	0.705		

Tablo 3. (Devamı)

Sağlık İçin İsteklilik ve Sorumluluk Alt Boyutu		0.95	0.89
9- İş sağlığı ve güvenliği kuralları hakkında kendimi bilgilendirmenin çok önemli olduğunu düşünüyorum	0.578		
10- İşyerinde sağlığım ve esenliğim için bilinçli olarak sorumluluk alırım.	0.402		
11- İşyerinde sağlık ve esenlikle ilgili bilgileri başkalarıyla paylaşırım	0.624		
12-Ben değişimin çok önemli olduğunu düşünüyorum	0.578		

4. TARTIŞMA

Geçmişten günümüze yapılan araştırmalar, sağlık okuryazarlığının bireysel özellikler ve ilgili faktörler arasındaki sonuçlarını incelemeye odaklanmıştır. Türk toplumunda alana özgü bir mesleki sağlık okuryazarlığı ölçüm aracının bulunmaması veya sınırlı olması, İSOÖ'nün Türkçeye uyarlanması ihtiyacını ortaya çıkarmıştır. Bu bölümde, mevcut çalışmanın sonuçları literatür ışığında tartışılmaktadır.

İSOÖ'nün Türk kültürüne uyarlanması sürecinde Wild ve ark. (2005) uluslararası kabul görmüş standartları kullanılmıştır[19]. Türkçeye çevrilen İSOÖ'nün uzmanlar tarafından yapılan kapsam geçerliliği değerlendirmesi sonucunda M-KGİ ve Ö-KGİ değerleri sınır değerlerin üzerinde bulunmuştur[20]. Maddelerin anlaşılabilirliğini ve yanıtlama süresini belirlemek amacıyla yapılan pilot çalışmada olumsuz bir geri bildirim alınmamıştır. Bu durum, İSOÖ-TR'nin başarılı bir çeviriye ve yeterli kapsam geçerliliğine sahip olduğu sonucunu desteklemektedir.

İSOÖ'nün orijinal 2 faktörlü yapısı Türkçe uyarlamada da doğrulanmıştır. İSOÖ-TR'nin DFA'sında tüm faktör yükleri 0,50'nin üzerinde hesaplanmıştır[22]. İSOÖ-TR'nin iki faktörlü yapısının model uyum iyiliği indeksleri orijinal çalışmaya benzer şekilde kabul edilebilir sınırlar içinde hesaplanmıştır[18,27-29].

İSOÖ'nün Türkçeye uyarlandığı bu çalışmanın sonuçları, İSOÖ-TR'nin iki faktörlü yapısının cinsiyete göre değişmez olduğunu ve ölçüm değişmezliğine ilişkin kanıtların (yapısal, metrik ve skaler dahil) bu aracın psikometrik özelliklerinin hem kadın hem de erkek gruplarında eşdeğer olduğunu göstermiştir[23,24]. Orijinal formda ölçüm değişmezliğine ilişkin bilgi görülmemiştir[18]. Bu sonuçlar kapsamında H₃ hipotezi kabul edilmiştir.

İSOÖ-TR'nin iki faktörlü modelinde aynı faktörde yer alan maddelerin yakınsamasını ve farklı faktörlerde yer alan maddelerin ıraksamasını değerlendirmek üzere yapılan analizde; sağlığa bilgi ve beceri temelli yaklaşım alt boyutu ile sağlık için isteklilik ve sorumluluk alt boyutunda CR değerlerinin 0,7'nin üzerinde, AVE değerlerinin ise 0,5'in üzerinde olduğu ve her iki alt boyutta da CR>AVE olduğu hesaplanmıştır[15,26,30]. Orijinal ölçeğin yakınsak geçerliliğinin belirlenmesinde faktör yüklerinin karesinin >0,5 olması ölçütü esas alınmış ve sonuç olarak yakınsak geçerliliği sağladığı tespit edilmiştir[18]. Iraksak geçerlik için yapılan analizde HTMT değeri 0,85'ten düşük çıkmış ve ASV>AVE olarak hesaplanmıştır[15,25]. Bu sonuçlar doğrultusunda H₁ hipotezi kabul edilmiştir.

İSOÖ-TR'nin cronbach alpha katsayısı 0,87'dir ve her bir alt boyutun cornbach alpha değerleri 0,70'in üzerindedir. Ayrıca tüm maddelerin düzeltilmiş madde toplam korelasyon değerleri 0,40'ın üzerinde hesaplanmıştır[30]. Benzer şekilde, orijinal ölçekte her bir alt boyutun cronbach alpha değerleri 0,7'den yüksek bulunmuş ancak düzeltilmiş madde toplam korelasyon değerleri rapor edilmemiştir (Friedrich vd., 2023). Ayrıca, alt boyutların CR değerleri 0,7'nin üzerindedir[22,28]. Bu sonuçlar İSOÖ-TR'nin yüksek güvenilirliğe sahip olduğunu desteklemektedir. H₂ hipotezi kabul edilmiştir.

Bu çalışma, İSOÖ'nün Türkçe uyarlamasının çalışanlarda iş sağlığı okuryazarlığını değerlendirmek için geçerli ve güvenilir bir ölçüm aracı olduğunu ortaya koymuştur. Bu ölçüm aracı, çalışma ortamında sağlığa uygun davranma konusunda bilgi, beceri ve istekliliği içermektedir.

İSOÖ-TR, işyerinde bireye özgü sağlık okuryazarlığını belirlediği için durum değerlendirmesinde, sağlığın geliştirilmesinde ve gelecekteki müdahale programlarının hazırlanmasında kullanılabilir.

Makale Bilgi Formu

Çıkar Çatışması / Ortak Çıkar Beyanı

Yazarlar tarafından herhangi bir çıkar çatışması veya ortak çıkar beyan edilmemiştir.

Etik Kurul Onay Beyanı

İSOÖ' nün Türk toplumuna uyarlanması için öncelikle ölçeği geliştiren Friedrich'ten e-posta aracılığıyla izin alınmıştır. Muş Alparslan Üniversitesi Bilimsel Araştırmalar ve Yayın Etiği Kurulundan etik kurul izni alınmıştır (Tarih/Karar no: 04.01.2024/1-49). Çalışmanın yürütülmesi için ilgili kurumlardan çalışma izni alınmıştır. Çalışmaya katılanlardan bilgilendirilmiş onam alınmıştır. Araştırma Helsinki Deklarasyonu standartlarına uygun olarak yürütülmüştür.

Telif Hakkı Beyanı

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Research Article

Evaluation of Metabolic Dysfunction-Associated Steatotic Liver Disease in Patients with Type 2 Diabetes Mellitus

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Aim: Diabetes mellitus (DM) is associated with the development and progression of metabolic dysfunction-associated steatotic liver disease (MASLD). In our study, we aimed to evaluate the findings of MASLD and fibrosis according to liver ultrasound (USG) imaging, FIB-4 score and fibroscan findings in patients with type 2 DM followed in our internal medicine clinic.

Methods: In our retrospective and cross-sectional study, 1282 patients diagnosed with type 2 DM whose anamnesis and previous examinations did not constitute an obstacle for inclusion in the study were included. The abdominal USG imaging of the patients were analysed from the system and the FIB-4 score was calculated. Liver stiffness (LS) measurements were performed with FibroScan® Mini 430 device (Echosens, France).

Results: USG imaging was performed in 474 (36.9%) of 1282 patients and MASLD was diagnosed in 341 (71.9%) of these patients. FIB-4 score$\geq$ was 1.3 in 45 of 341 patients diagnosed with MASLD. Fibroscan imaging was performed in 231 of 341 patients with MASLD. In 52 (22.5%) of 231 patients, LS measurements$\geq$ were 8 kPa

Conclusion: We recommend early screening of MASLD, which is associated with advanced fibrosis and increased cardiovascular mortality and morbidity in patients with DM, with liver USG, measurement of FIB-4 score and evaluation of LS with fibroscan in centres where possible.

Keywords: Diabetes mellitus, Fibroscan, FIB-4, MASLD, USG

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic, metabolic disease characterised by high blood glucose levels. According to data from the International Diabetes Federation, it is estimated that approximately 700 million people will suffer from type 2 DM in 2045[1]. DM may cause damage to the eyes, kidneys, blood vessels and nerves. The liver is also an organ associated with DM as it has an important role in glucose homeostasis. Non-alcoholic fatty liver disease (NAFLD), recently renamed as metabolic dysfunction-associated fatty liver disease (MAFLD) or metabolic dysfunction-associated steatotic liver disease (MASLD), is the most common chronic liver disease worldwide[2]. MASLD is defined by the presence of at least 1 of 3 criteria including DM, obesity or two or more evidence of metabolic dysfunction in addition to the presence of hepatic steatosis. Thus, unlike NAFLD, which is a diagnosis of exclusion, the diagnosis of MASLD does not require the exclusion of excessive alcohol consumption or other chronic liver diseases[3].

Recent datas indicate that nearly one-third of the general adult population is afflicted, rendering it one of the most prevalent non-communicable illnesses[4]. Its growth and progression are closely associated with metabolic disorders and insulin resistance. Consequently, its frequency is elevated, attaining 60-75% among individuals with type 2 diabetes mellitus[5]. Research indicates a robust bidirectional

association between MASLD and DM. MASLD elevates the risk of developing DM and the likelihood of micro- and macro-vascular complications in individuals with a history of DM; conversely, patients with diabetes often experience a more rapid progression to metabolic dysfunction-associated steatohepatitis (MASH), advanced liver fibrosis, cirrhosis, and hepatocellular carcinoma[6,7].

Biopsy is the most definitive diagnostic method for detecting and grading tissue damage in the liver. However, it is an invasive procedure with risks such as bleeding and infection. All DM patients with liver fat content >5% as determined by radiological imaging methods or biopsy are considered to have MASLD. Given the limitations of risk scoring and the invasive nature of liver biopsy, imaging is considered the main method for the diagnosis of MASLD. Due to its low cost, widespread availability and overall safety, liver ultrasound (USG) has become the guideline-recommended first-line modality for screening and diagnosis of MASLD. The fibrosis-4 (FIB-4) index, which is one of the simple scoring systems, is recommended to exclude significant or advanced liver fibrosis in patients with MASLD[8]. Considering the prevalence of the disease in the community, fibroscan has been developed as a noninvasive method for the detection of liver fibrosis and is one of the USG elastography methods. Studies have shown that fibroscan has a high performance in the diagnosis of fibrosis in patients with MASLD[9].

Despite the prevalence of MASLD in DM patients and its important extrahepatic complications, it is thought that it is often overlooked, under-recognised and under-screened in clinical practice. Increasing the awareness of clinicians about the risk and clinical significance of MASLD in patients with DM may lead to early diagnosis and timely intervention of MASLD, and the disease may be reversible. In our study, we aimed to evaluate the findings of MASLD and fibrosis according to USG imaging, FIB-4 score and fibroscan findings in patients with type 2 DM followed up in our internal medicine clinic.

2. MATERIAL AND METHOD
2.1. Study population and laboratory measurements

Our retrospective and cross-sectional study included 1282 patients with type 2 diabetes mellitus whose medical history and previous examinations did not constitute an obstacle to their inclusion in the study. Patients between 01.02.2024 and 31.12.2024 were included in the study. Diabetes mellitus was defined as fasting blood sugar level ≥126 mg/dL or HbA1c level ≥6.5% or treatment with antidiabetic medication[10]. In patients with acute-chronic liver diseases, malignancies, type 1 diabetes mellitus, pregnant women were excluded from the study. The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional ethics committee. Adana City Training and Research Hospital Ethics Committee approved the study with decision number 319 dated 02.01.2025. After 5 minutes of rest, in a dim and quiet environment, blood pressure measurements were taken from both arms using a suitable cuff and pulses were monitored. Anthropometric body weight measurements were performed. Height was measured with the feet bare and together, leaning perpendicular to the height measurement ruler. BMI was calculated as body weight (kg) divided by the square of height in meters (BMI=kg/m2). Laboratory procedures of the study were performed in the Biochemistry Laboratory of Adana City Training and Research Hospital. Laboratory results from the date of abdominal USG were used. Venous blood was drawn from the antecubital vein after at least 8 hours of overnight fasting from the patients and the control group during routine controls. Laboratory measurements of participants were measured using automated laboratory methods (Abbott Aeroset, Minneapolis, MN) and appropriate commercial kits (Abbott). The FIB-4 score is calculated using the formula: (Age × AST) / [Platelet count × (ALT)^(1/2)].

2.2. Liver ultrasonography and liver stiffness measurements

All patients had liver ultrasound screening utilising a high-resolution USG device (Philips EPIQ 7) with a 1- to 5-MHz high-

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resolution convex probe (Philips Health Care, Bothell, WA). A liver ultrasound was conducted following a minimum fasting period of 8 hours, utilising B-mode ultrasound in greyscale to evaluate liver dimensions and parenchymal echogenicity. Hepatosteatosis was evaluated. Participants were assessed separately by two seasoned radiologists. Ultrasound operators have 10 years or more of experience.

LS measurements were performed with the FibroScan® Mini 430 device (Echosens, France). Subjects were evaluated independently by two experienced internal medicine specialist. FibroScan was considered successful only when at least 10 valid readings were obtained and the interquartile range (IQR)-to-median ratio of the 10 readings was ≤.3. Participants' LS levels were determined in kPa units. LS>8 kPa was defined as a marker of significant liver fibrosis used in this study.

2.3. Statistical analysis

All analyses were performed using the statistical software package SPSS 24.0 (Chicago, IL, USA). The Kolmogorov-Smirnov test was used to assess whether the distribution of continuous variables was normal. Continuous variables in group data were expressed as mean ± standard deviation. Categorical variables were expressed as numbers and percentages. Statistical significance level was accepted as $p < 0.05$.

3. RESULTS

The mean age of the patients was 59.4±7.38 years. The mean HbA1c was 6.70±1.81 and the mean duration of diabetes was 6.79±5.67 years. ±Mean AST was 25.9±13.0, mean ALT was 28.4±12.4, and mean platelet count was 232.9±68.2. USG imaging was performed in 474 (36.9%) of 1282 patients and MASLD was diagnosed in 341 (71.9%) of these patients. The mean FIB-4 score of 341 patients diagnosed with MASLD was 0.72±0.29 and the FIB-4 score≥ was 1.3 in 45 patients. All of these 45 patients had LS measurements≥ of 8 kPa. Fibroscan imaging was performed in 231 of 341 patients with a diagnosis of MASLD. The mean LS measurement of 231 patients was 5.73±2.45 and 52 (22.5%) patients had LS measuremtns≥ of 8 kPa (table 1).

Table 1.

Demographic, clinical, laboratory, ultrasonography findings and liver stiffness measurement of patients with type-2 dm

Variables	Patient with type 2 DM (n=1282)
Age (year)	59.4±7.38
Gender (M/F,n)	706/576
Systolic blood pressure (mmHg)	120.4±8.99
Diastolic blood pressure (mmHg)	65.7±6.52
Body mass index (kg/m2)	27.8±4.48
Waist circumference, cm	95.1±6.59
Basal heart rate (pulse/minute)	76.0±8.12
Fasting plasma glucose, mg/dL	107.4±41.6
HbA1c, %	6.70±1.81
Diabetes duration (year)	6.79±5.67
White blood cell (10^3/ μL)	7.38±1.74
Hemoglobin (g/dL)	13.4±1.59
Platelet (10^3/ μL)	232.9±68.2
Creatinine (mg/dL)	0.76±0.24
Sodium (mmol/L)	137.8±3.11
Potassium (mmol/L)	4.47±0.38
Aspartate aminotransferase (u/L)	25.9±13.0
Alanine aminotransferase (u/L)	28.4±12.4
Triglycerides, mg/dL	158.0±93.4
HDL cholesterol, mg/dL	44.6±10.4
LDL cholesterol, mg/dL	126.8±31.7
Cholesterol	329.5±99.0
CRP (mg/L)	1.44±0.87
USG imaging, n	474 (36.9%)
US-confirmed MAFLD diagnosis, n (n:474)	341 (71.9%)
CC liver size, cm (n:474)	14.2±2.02
Fib-4 index (n:341)	0.72±0.29
Fib-4 index≥1.3, n (n:341)	45 (13.1%)
Fibroscan imaging, n	231
Liver stiffness, kPa (n:231)	5.73±2.45
Liver stiffness≥8 (kPa), n (n:231)	52 (22.5%)

HDL: high density lipoprotein, LDL: low density lipoprotein, CRP: c reaktif protein, Fib-4: fibrosis-4, kPa: kilopascal, USG: ultrasonography, DM: diabetes mellitus.

4. DISCUSSION

The main findings of our study were that the rate of MASLD in patients with DM who underwent USG imaging was 71.9% and the rate of LS measurements≥ of 8 kPa in patients who underwent fibroscan imaging was 22.5%. These findings show that the rate of USG imaging in patients diagnosed with DM in outpatient clinics is low. Patients should be screened for microvascular complications during outpatient clinic examinations and should also be screened for MASLD.

The Cappadocia cohort study conducted with 2797 patients in Türkiye revealed a high prevalence of hepatic steatosis (60.1%) among the participants in abdominal USG examinations[11]. In another retrospective study including 10-year data (2007-2016) of 113239 individuals, the overall prevalence of NAFLD in Türkiye was found to be 48.3%. In this study, DM was shown to be an independent factor associated with NAFLD[12]. In another multicentre study on the awareness of MAFLD in patients with type 2 DM, USG examination was performed in 1731 (27.6%) of 6283 patients and MAFLD was diagnosed in 69.9% of the cases. In addition, it was reported that 24.4% of patients with MAFLD confirmed by USG had advanced fibrosis risk (FIB-4 index ≥ 1.3)[3]. In a pooled systemic review and meta-analysis of 156 studies and 1832125 patients, the prevalence rate of NAFLD in type 2 DM was 65.04% and 35.54% of these patients had clinically significant fibrosis (f2-f4)[13]. Diabetes and MASLD have analogous risk factors. These variables lead to systemic insulin resistance and elevated circulating free fatty acids, which are subsequently deposited in the liver, resulting in MASLD. The buildup of hepatic fat enhances insulin resistance in the liver, stimulates inflammatory pathways, elevates oxidative stress, and results in hepatic fibrosis[14]. In our study, we found that the rate of MASLD was 71.9% among patients with DM who had USG imaging. Our findings are compatible with other studies showing an increased frequency of MASLD in patients with DM in Türkiye. However, the rate of hepatic steatosis imaging with abdominal USG in patients with DM is unfortunately low. In our study, we found that the rate of USG imaging in patients diagnosed with DM was 36.9%. Considering the frequency of MASLD in patients with USG imaging, it is seen that a significant number of patients without imaging are missed and awareness is low. The findings suggest that MASLD is underdiagnosed in patients with DM and therefore should be screened. The first guidelines recommending general screening for NAFLD/MASLD in patients with DM were published by EASL, EASD in 2016. These guidelines recommended general screening for NAFLD/MASLD by liver USG in patients with type 2 DM. In case of steatosis, calculation of FIB-4 was recommended[15]. In the following years, with increasing data on the high prevalence of advanced fibrosis and cirrhosis in patients with DM, EASL published an update to clinical practice guidelines on non-invasive testing in 2021. The first step in this update is the calculation of FIB-4 and fibroscan should be performed if a value ≥ 1.3 is obtained. If the LS value is ≥8 kPa, the patient must be sent to a hepatologist. A lower number indicates that advanced fibrosis may be reliably excluded[16]. This method has been articulated in other recent guidelines from several worldwide hepatology and endocrinology groups. In 2023, the AASLD issued new guidelines recommending the screening for advanced fibrosis in all patients with diabetes mellitus, a disease that promotes development to cirrhosis. In accordance with the EASL recommendations, the initial stage is FIB-4. If FIB-4 is more than or equal to 1.3, a fibroscan or MR elastography is advised based on availability[17]. The 2023 recommendations released by the ADA also advocated a comparable strategy[18]. According to these assumptions, clinical practice recommendations advocate for the screening of MASLD and advanced liver fibrosis in individuals with diabetes mellitus utilising liver fibrosis scores and/or fibroscan.

MASLD correlates with an elevated risk of cirrhosis, cardiovascular disease, and malignancy. Individuals with MASLD remain asymptomatic until the onset of severe hepatic illness. The timely identification of MASLD is essential to avert disease advancement and related consequences. Liver biopsy is the definitive approach for

diagnosing MASH. Nonetheless, its invasiveness and possible consequences restrict its extensive application[19]. Non-invasive methods, such as fibroscan, have been established to identify fibrosis. Fibroscan has demonstrated high sensitivity in identifying MASLD and substantial fibrosis[20]. According to meta-analyses, fibroscan has an excellent diagnostic accuracy for the diagnosis of advanced fibrosis and cirrhosis in patients with MASLD (AUROC close to 0.90). However, fibroscan does not have as high sensitivity in detecting low fibrosis levels as in detecting high fibrosis levels[9]. In our study, we used the FIB-4 index, which is a simple non-invasive scoring test. In 341 patients with MASLD, we found 45 (13.1%) patients with FIB-4$\geq$ 1.3, which can indicate the risk of advanced fibrosis. All of these patients had an LS value above 8. In 231 patients with MAFLD who underwent fibroscan, we found 52 (22.5%) patients with an LS$\geq$ of 8 kPa indicating advanced fibrosis. 7 patients had a FIB-4 score below 1.3 although the LS value was above 8. Although FIB-4 score is a simple, noninvasive, good initial test, it may be insufficient to exclude advanced fibrosis. While the negative predictive value of the FIB-4 test is high in detecting fibrosis (FIB-4<1.3 excludes fibrosis with a high probability), its positive predictive value is low (FIB-4$\geq$ 1.3 identifies fibrosis with a non-high probability). In addition, the accuracy of FIB-4 is low in young individuals[21]. Studies have reported that FIB-4 excludes advanced fibrosis in 55-60% of patients and fibroscan should be performed in the remaining 40-45%[22]. Our study was compatible with these data. The fact that the FIB-4 score was low in some patients with an LS value above 8 suggests that patients with MASLD should be evaluated with fibroscan in addition to the FIB-4 score. The lack of fibroscan imaging in most centres is an important problem. It should be aimed to increase the number of fibroscans in centres.

Previous research has emphasised a bidirectional relationship between MASLD and DM. On the one hand, MASLD is a known risk factor for the development of DM and its complications; on the other hand, DM increases the risk of progression towards MASH and advanced liver fibrosis[23]. Substantial epidemiological evidence from large studies suggests that MASLD is an independent risk factor for cardiovascular disease morbidity and mortality. Cardiovascular diseases are the leading cause of death for MASLD[24]. While individuals with type 2 DM already have an increased cardiovascular risk, cardiovascular mortality and morbidity increase with delayed diagnosis and failure to treat MASLD. Therefore, MASLD screening rates should be increased in patients with DM and effective treatment should be provided rapidly in diagnosed individuals.

FIB-4 index and fibroscan, which are noninvasive methods, can be used to evaluate LS in diabetic patients. Our findings show that MASLD is underdiagnosed in patients with DM in internal medicine clinics, clinicians' awareness should be increased about the high prevalence of MASLD and the risk of advanced fibrosis, and these patients should be subjected to USG imaging, the FIB-4 index should be used, and if possible, they should be referred to centers where fibroscan is performed. Current guidelines recommend a two-stage strategy in which the FIB-4 score is followed by an imaging technique (most commonly fibroscan). We believe that diabetes specialists should presently occupy a favourable position to actively manage patients with diabetes mellitus, not only to mitigate their risk of developing micro- and macrovascular complications but also to alleviate the disease burden linked to cirrhosis, hepatocellular carcinoma, and cardiovascular disease.

Our study had some limitations. Our study was single-centred. New studies with a larger number of patients and multicentre are needed. We used the fibroscan method for LS evaluation. Further studies can be performed using magnetic resonance elastography, another sensitive and non-invasive method. We did not classify the diabetic patients according to the duration of the disease, whether they were newly diagnosed or not and the oral antidiabetics used. Follow-up studies can be performed in this regard.

5. CONCLUSIONS

Despite the increasing prevalence of MASLD in diabetes, rates of MASLD screening and awareness are low. We recommend early screening of MASLD, which is associated with advanced liver fibrosis and increased cardiovascular mortality and morbidity in patients with DM, with liver USG, measurement of FIB-4 score and LS evaluation with fibroscan in centres where possible.

Authors Contribution

HAO, EG, DDO, FNA, BSA, BI, MCE, BBK, IA, CD, AGM, TS and HES conceived and designed the experiments, performed the experiments, analyzed the data, contributed reagents/materials/analysis tools, prepared figures and/or tables, authored or reviewed drafts of the paper, approved the final draft.

The Declaration of Conflict of Interest

The authors have no conflicts of interests to declare.

The Declaration of Ethics Committee Approval

Adana City Training and Research Hospital Ethics Committee approved the study with decision number 319 dated 02.01.2025.

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Mid Term Evaluation of Patients Undergoing Surgery for Tetralogy of Fallot with 24 Hour Rhythm Holter and Cardiopulmonary Exercise Testing

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Objective: This study aimed to obtain mid-term evaluation of exercise capacity and arrhythmias with cardiopulmonary exercise testing (CPET) and 24-hour rhythm Holter in Tetralogy of Fallot (TOF) patients who underwent surgery.

Materials and Methods: The study group consisted of patients over 6 years of age who had undergone complete correction surgery for TOF, while the control group consisted of healthy children of a similar age group who did not have any heart disease. Echocardiography, 24-hour Holter monitoring and CPET were applied to both groups.

Results: Study group included 14 patients who were operated on due to TOF and 9 healthy children as the control group. During echocardiographic examination; aortic diameter, pulmonary annulus, right ventricular (RV) systolic and diastolic areas were found to be significantly larger in the patient group (p=0.044, p=0.017, p=0.05, p=0.012 respectively). Myocardial performance index (Tei index-MPI) calculated from mitral and tricuspid valve annulus was found to be significantly higher in the patient group (p=0.05 for both). During CPET, stroke volume and VO2max levels were significantly smaller in patients (p=0.004, p=0.044 respectively).

Conclusion: Although operated TOF patients are asymptomatic in the mid-term, the exercise capacity in these patients is lower than in healthy individuals and this decrease is related to right ventricular size and dysfunction.

Keywords: Tetralogy of Fallot, Exercise Capacity, Arrhythmia

1. INTRODUCTION

Tetralogy of Fallot is the most common cyanotic congenital heart disease in adults. Native disease consists of four different anatomical features: 1) Obstruction of the right ventricular outflow tract, 2) Non-restrictive large ventricular septal defect, 3) Dextroposition of the aorta, 4) Right ventricular hypertrophy. Initial corrective surgery for TOF using cardiopulmonary by-pass was performed in 1955.[1] Nowadays, corrective operation is performed with a mortality rate less than 5% in many centers throughout the world.[2] However during long term follow-up of operated patients there is still increased morbidity and mortality risks. Pulmonary insufficiency and stenosis are the most common hemodynamic problems in patients, which develop due to patches and muscle resections in the right ventricular outflow tract, leading to enlargement and dysfunction of the right ventricle. These structural and functional changes of the right ventricle may also cause electrocardiographic changes, arrhythmia and even sudden death.[3]

CPET is widely used in the diagnosis and monitoring of the patients with heart disease. CPET evaluates exercise capacity, visible response to exercise, helpful in determination of life expectancy and prognosis. CPET also define the risks of arrhythmia and sudden death in postoperative patients with TOF. The commonly used stimulation modes in exercise testing include bicycle ergometers, treadmills, total body workout equipment, etc., among which the first two are the most frequently used ones.[4]

Pulmonary regurgitation (PR), which is seen especially in those with transannular patch repair and leads to progressive right ventricular dilatation, is the most common residual lesion after TOF repair. The degree of PR and exercise tolerance tests show a negative correlation. Therefore, in asymptomatic patients, CPET could give objective information about the

function of the heart and can be a useful tool for deciding the optimal time for pulmonary valve replacement (PVR) in the presence of significant RV dilation with or without dysfunction.[5]

The aim of the study was mid-term evaluation of exercise capacity and arrhythmias with 24-hour rhythm Holter and CPET in TOF patients who underwent surgery. In addition, it was aimed to reveal the relationship between CPET results and echocardiographic findings.

2. MATERIAL AND METHODS

In this observational cohort study; between July 2016 - December 2016 we enrolled 14 patients with TOF who underwent total correction and followed up by Marmara University Pediatric Cardiology Department. Control group consisted of 9 healthy children with similar age and gender characteristics, without any cardiac or systemic illness. The ages of the patient and control groups participating in the study were between 5 and 20 years.

Patient files were retrospectively analyzed. Chest x-ray, 12-lead ECG, 24-h Holter monitoring, echocardiography were performed. Plasma Pro-BNP values of the patients were recorded. In echocardiographic studies; M-Mode, two-dimensional (2D) echocardiography and tissue Doppler imaging (TDI) techniques were used. All patients underwent CPETwith using Cortex ML3B device. Modified Bruce protocol was used with an individualized ramp protocol exercise stress testing. The following parameters were recorded constantly throughout the exercise test: Peak

oxygen uptake VO_{2max}, predicted VO_2 (%), as well as CO_2 elimination VCO_2, peak heart rate (PHR), respiratory exchange ratio (RER = VCO_2/VO_2), VE/VCO_2, VE/VO_2. The PHR reached was calculated as the percentage of expected HR at maximum exercise according to age. Stroke volume was calculated indirectly by dividing the VO_{2max} value by PHR.

This study was conducted with the approval of local Clinical Research and Ethics Committee (Date: 01.04.2016, Decision No: 09.2016.216) of our instutition. The study complied with the principles of the Declaration of Helsinki.

2.1. Statistical analysis

The statistical analysis of the collected patient data was carried out using IBM Statistical Package for the Social Sciences (SPSS) version 17.0. The Mann-Whitney U test, Kruskal-Wallis test, one-way analysis of variance was applied for comparing the means of continuous variables between two groups. Chi square test was used to compare nominal variables. A statistical significance was accepted when p<0.05.

3. RESULTS

14 operated TOF patients and 9 normal controls were included. In patient group; Pro-BNP levels and the duration of QRS interval measured on ECG were found to be significantly higher (p=0.014, p=0.001). A higher cardiothoracic ratio (CTR) was shown in patient group with x-Ray (p=0.010). Demographic and clinical data are tabulated and compared in Table 1.

Table 1.

Demographic, clinical and electrocardiographic findings of TOF patients and controls

	Patients(n=14)	Controls (n=9)	P value
Sex (M/F)	9/5 (%64.2)	6/3 (%66.6)	0.643
Age	13.86±4.44	14.0±2.87	0.727
BMI (kg/m^2)	20.4±4.8	19.5±5.2	0.361
Systolic Blood Pressure (mmHg)	113.7±9.9	108.4±9.6	0.219
Diastolic Blood Pressure (mmHg)	66.2±8.6	64.2±7.0	0.590
Follow-up Period(year)	11.86± 4.72		
Pro-BNP(pg/mL)	**126.2±157.3**	**27.2±19.6**	**0.014**
CTR	**0.5±0.044**	**0.39±0.05**	**0.010**
PHR	79.7±13.2	80.6±12.7	0.824
PR (ms)	152.9±27.9	155.6±38.4	0.974

Table 1. (Continued)

QTc	0.4±0.038	0.37±0.035	0.100
QRS (ms)	**141.43±42.58**	**80.00±16.67**	**0.001**

(BMI: Body mass index; Pro-BNP: Brain natriuretic peptide)

The average Ao diameter and the PA diameter of the patient group were increased significantly (p = 0.044, p=0.017). It was observed that the RV end-diastolic and end-systolic area measurements of the patient group were larger than the control group (p=0.012, p=0.05). Mitral and tricuspid valve IRT measured by TDI echocardiography in the patient group was increased compared to the control group (p= 0.021, p=0.025). ICT was determined from the mitral and tricuspid valves were found to be similar. Likewise, in the mitral and tricuspid valve; MPI was found to be significantly higher in the patient group (p= 0.05 for both). Echocardiographic measurements are demonstrated in table 2, table 3 and table 4.

Table 2.

M-Mod Echocardiographic measurements in TOF patients and controls

Controls(n=9)	Patients(n=14)	Controls(n=9)	P value
IVSd (cm)	0.83±0.15	0.78±0.11	0.570
LVEDD (cm)	4.31±0.59	4.38±0.37	0.550
LVESD(cm)	2.56±0.74	2.74±0.26	0.950
LVPWD (cm)	1.01±0.9	0.7±0.11	0.700
SF (%)	38.3±5.4	37.4±3.3	0.330
EF (%)	70 ±7.3	67.1±4.5	0.270
LA (cm)	3.1±0.71	2.8±0.56	0.610
AO(cm)	**2.8±0.61**	**2.2±0.33**	**0.044**
TAPSE(mm)	21.9±4.47	24.5±5	0.220

(IVSd: Interventricular septum thickness; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; LVPWd=left ventricular posterior wall thickness at diastole; SF: Shortening fraction; EF: Ejection fraction; LA: Left atrium; AO: Aorta; TAPSE: Tricuspid Annular Plane Systolic Excursion)

Table 3.

2D and Doppler Echocardiographic measurements in TOF patients and controls

	Patients(n=14)	Controls(n=9)	P value
RV Area (dia) (cm²)	**26.4±7.5**	**17.5±6.1**	**0.012**
RV Area (sis) (cm²)	**16.3±7.5**	**10.2±3.6**	**0.050**
PA (cm)	**2.26±0.73**	**1.47±0.65**	**0.017**
RVESV (ml)	33.8±19.7	29.4±6.1	0.680
RVEDV(ml)	80.5±32.4	75±24.3	0.700
RVEF(%)	58.2±10.8	62.4±6.1	0.700
RVFAC (%)	48 ±28.5	43.6±7.1	0.980
Mitral E (cm/sec)	1 ±0.15	0.95 ±0.11	0.390
Mitral A (cm/sec)	0.6±0.11	0.58±0.13	0.570
DT(sec)	132.5±44.6	146.6±29	0.310
IVRT(sec)	65.4±14.4	61.9±14	0.610

(RV: Right ventricular; PA: Pulmonary annulus; RVESV: Right ventricular end-systolic volumes; RVEDV: Right ventricular end -diastolic volumes; RVEF: Right ventricular ejection fraction; RVFAC: Right ventricular fractional area change; DT: Decelaration time; IVRT: Isovolumic relaxation time)

Table 4.

TDI echocardiography measurements of mitral and tricuspid valves in TOF patients and controls

	Patients(n=14)	Controls(n=9)	P value
ET (mitral) (sec)	287.5±25.7	286.2±30.8	0.256
ET (tricuspid) (sec)	272.5±16.1	263.6±17.9	0.200
IRT (mitral) (sec)	**79.4±12.8**	**66.4±1.6**	**0.021**
IRT (tricuspid) (sec)	**76 ±13.4**	**63 ±9.5**	**0.025**
ICT(mitral) (sec)	61.6±9.7	70.7±12.9	0.072
ICT (tricuspid) (sec)	80.7±12.6	74.7±12.2	0.550
MPI (mitral) (sec)	**0.53±0.06**	**0.45±0.12**	**0.050**
MPI (tricuspid) (sec)	**0.58±0.056**	**0.53±0.1**	**0.050**

(ET: Ejection time; IRT: Isovolumic relaxation time; ICT: Isovolumic contraction time; MPI: Myocardial performance index)

Seven patients (50%) could complete the 15-minute period for CPET. Eight of the patients (57.1%) were able to run to the level 5, two (14.2%) to the level 4, three (21.4%) to the level 3, and one (7.1%) to the end of the level 1. The calculated stroke volume in the patient group was lower than the control group (p = 0.004). The baseline oxygen saturation and VO_{2max} level observed in the patient group were significantly lower than the control group (p = 0.017, p=0.044). Respiratory rate, PHR, VE/VO_2, VE/VCO_2, RER values were similar in groups. 24 hour Holter monitoring revealed ventricular premature beats in 10 (71.4%) of the patients. Table 5 shows the CPET results.

Table 5.

CPET variables of TOF patients and controls

	Patients(n=14)	Controls(n=9)	P value
PHR (bpm)	164.2±24.1	168.7±12.9	0.825
Stroke Volume (ml)	**135.3±36.9**	**184.7±32.4**	**0.004**
MinO$_2$ saturation(%)	**90.6±9.6**	**97.2±1.5**	**0.017**
VO$_2$ (max)(ml/kg/min)	**29.2±10.37**	**31.44±7.43**	**0.044**
VO2(%)	41.4±15.5	46.1±10.7	0.470
VE/VO$_2$slope	28.8±3.8	29.3±4.0	0.975
VE/VC0$_2$slope	25.9±1.8	26.8±2.4	0.256
RER	1.12±0.09	1.18±0.17	0.613

Supraventricular premature beats were detected in six patients (42.3%) which were clinically insignificant and did not need medical treatment.

4. DISCUSSION

PR is the most important complication in operated TOF patients. Although variable degrees of PR related to operated TOF can be tolerated for many years, PR in some patients becomes severe and is associated with dilatation and dysfunction of the RV and subsequently the left ventricle, therefore contributes to long-term morbidities, including exercise intolerance, arrhythmia and possibly sudden death.[6] PVR is performed in patients with operated TOF to protect the RV from the adverse effects of chronic volume overload, and there is no consensus on the optimal timing of PVR in operated asymptomatic patients.

The higher frequency of right bundle branch block characterized by long QRS duration in TOF patients who underwent surgery has been attributed to the effect of cardiac surgery. Right ventricular enlargement and QRS prolongation greatly increase the risk of symptomatic arrhythmia. The most sensitive predictor of life-threatening ventricular arrhythmia is a QRS duration of ≥180 msec on the resting ECG.[7] In our

study, the QRS duration was longer in the patient group. Additionally, four patients had an increased QRS duration over 180 ms and two of these patients underwent PVR surgery. In our study, Pro-BNP levels of the patient group were found to be higher than the control group. In the study of Çetin et al showed that Pro-BNP levels were higher in adult operated TOF patients who underwent CPET; it was stated that PHR and VO_{2max} levels were lower and exercise durations were shorter.[8] In our study no correlation was found between PHR and Pro-BNP levels. But there was a correlation between higher Pro-BNP levels and lower $VO_{2max,}$ levels in patient group.

Cardoso et al. showed that there was a positive correlation between follow-up time and diastolic dysfunction.[9] In our study patient group tricuspid valve MPI which was measured to evaluate right ventricular function, was found to be significantly higher. Abd El Rahman et al stated that restrictive state in RV leads to decreased RV compliance and decrease in ICT, which results in underestimation of MPI.[10] In our study, patient group had longer IRT in both tricuspid and mitral valves; while ICT was similar in both groups.

In the postulate developed by French physiologist Bernheim, it was revealed that the left ventricle functionally affects the right ventricle. Later studies showed that the right ventricle also affected the left ventricle, this was called the 'reverse Bernheimeffect.'[11] It has been shown that in operated TOF patients, left ventricular functions deteriorate as the follow-up period increases. Left ventricular dysfunction is more common as the age at surgery is delayed. Exposure of the myocardium to long term hypoxia is also one of the factors causing this condition.[12] Therefore, multipl studies indicated that the total correction operation must be performed before the age of one.[13] In our study, left ventricular EF and SF measurements were found to be similar in both groups, however MPI measured from the lateral annulus of the mitral valve was higher in the patient group and higher BNP levels were found in patient group.This finding indicate the presence of left ventricular dysfunction in operated TOF patients.

Studies showed that, nearly one third of adults with operated TOF have an aortic root diameter≥40 mm.[14] Patients in our study have larger Ao and PA diameters than the control group. Previous studies indicated that there is a direct association between pulmonary regurgitation and PA diameter.[15]

CPET is an important tool used in the management of adults with operated TOF. In patients with TOF, assessment of exercise capacity at any given time and its changes over time are important in determining the impact of residual hemodynamic lesions and the need for intervention. Giardiani and colleagues showed that adult TOF patients with predicted VO_2 39% were at greater risk for cardiac-related death.[16] We demonstrated that the achievable VO_{2max} values of the patient group were lower than the control group. But there was no difference $VO_2(\%)$ levels between groups. Carvalho et al have suggested a significant relation between the degree of pulmonary regurgitation and stroke volume or PHR.[17] We found that the stroke volume of the patient group was lower than the control group.

Shafer et al. demonstrated that VO_2 (%) values, baseline O_2 saturation and VE/VCO_2 slope were worse in adult TOF cases than healthy controls.[18] In our study, while the baseline O_2 saturation of the patient group were lower than the control group, no difference was detected in terms of VE/VCO_2 and VO_2 (%) values.

Diller et al. showed that adults with congenital heart disease VO_{2max} ≤15.5 ml/kg/min are at an increased risk of major adverse cardiovascular events.[19] In our study, we detected lower VO_{2max} levels in TOF patients. There isn't any threshold VO_{2max} level spesific for TOF patients yet.

In one multicentre study showed that 43% of adults with operated TOF had experienced at least 1 sustained arrhythmia or arrhythmia intervention and prevalence of atrial tachyarrhythmias was 20.1%.[20] Harrison et al identified monomorphic ventricular tachycardia in 18 of 254 operated TOF patients.[21] None of our patients had clinically significant rhythm abnormalities.

In conclusion, even after successful surgery; the patients with TOF have decreased exercise capacity in objective assessment and this is

related to hemodynamic problems and ventricular functions. Further studies are needed for determining the optimal timing for re-intervention.

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The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

The Declaration of Ethics Committee Approval

University of Marmara Ethics Committee approved the study with decision number 09.2016.216 dated 01.04.2016.

Copyright Statement

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Factors Affecting the Etiology of Isolated Thalamic Infarcts and Thalamic Infarcts with Extrathalamic Involvement: The Stroke Center Experience

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Objective: The thalamus is a control point that is a gateway for all sensory impulses except smell and contributes to regulating the sleep-wake process. Therefore, infarcts of the thalamus cause a diversity of symptoms along with a diversity of vascular anatomy. The fact that thalamic infarcts are mostly considered lacunar infarcts seems to create inadequacy in understanding the etiology. This study aimed to compare the etiologic, diagnostic, and therapeutic parameters of thalamic infarction.

Materials and Methods: This retrospective study analyzed 230 patients with thalamic infarction among 820 stroke patients admitted between January 2019 and April 2022. Patients with hemorrhagic stroke, malignancy, or infection were excluded. Demographic data, comorbidities, imaging results, and treatments administered were evaluated. All these results were analyzed in two subgroups: isolated thalamic and extrathalamic involvement.

Results: Bilateral thalamic involvement was 8.386 times more common in patients with extrathalamic participation. Patients using dual antiaggregants had 2.207 times higher isolated thalamic involvement, while those on oral anticoagulants had 2.378 times higher extrathalamic involvement. Pathologies in the basilar and vertebral arteries increased the risk of extrathalamic involvement by 2.660 times ($p < 0.001$).

Conclusion: Thalamic infarcts cannot be considered exclusively lacunar. Extrathalamic involvement has been associated with worse functional scores and arterial pathologies. The protective effects of dual antiaggregants and oral anticoagulants vary depending on whether the thalamic infarct is extrathalamic or not, emphasizing the need for individualized therapies.

Keywords: Thalamus; Stroke, Extrathalamic involvement, Antiaggregant

1. INTRODUCTION

The thalamus is a cerebral structure located in the dorsal part of the diencephalon, between the cerebral cortex and the midbrain, consisting of several interconnected gray matter nuclei separated by laminae of white matter and providing transmission between the cerebral cortex and peripheral structures, the spinal cord or brainstem.[1,2] The thalamus, which is considered a gateway for afferent signals from all systems except the sense of smell, provides filtration of incoming motor and sensory signals and transfers them to the cerebral cortex. As such, it governs our sensitivity to heat, light, and physical touch, and controls the flow of visual, auditory, and motor information. It plays a role in motivation and sleep-wake processes and controls proprioceptive sensation. The thalamus is involved in the modulation of these functions and is thus responsible for purposeful conscious behavior.[3]

Thalamic infarcts are known to occur most commonly with an etiology of small vessel disease and may show unilateral or bilateral involvement.[4-6] The thalamus is supplied by the polar artery (posterior communicating artery), paramedian thalamic-subthalamic arteries, inferolateral (thalamogeniculate) arteries, and posterior choroidal arteries (medial and lateral). These are all branches of the posterior cerebral artery (PCA). Considering that all arteries supplying the thalamus are terminal arteries, it can be assumed that thalamic infarctions are mostly lacunar and the etiology is small vessel disease. However, in vertebral and/or basilar artery-related infarcts in which the PCA is also affected, different clinical pictures may occur

according to the characteristics of the arterial area affected by the infarct due to extrathalamic involvement as well as signs of thalamus involvement.[1,7,8] The incidence of PCA infarcts is 5-10% of all ischemic strokes and the most common causes are atherosclerosis and embolism. However, causes other than thrombotic processes such as dissection, hemorrhage, migraine, Moyamoya disease, fibromuscular dysplasia, mitochondrial diseases, reversible cerebral vasoconstriction syndrome, vertebrobasilar dolichoectasia and vasculitis, and central nervous system infections may also be involved in the etiology.[7,9-11]

Due to the differences in the localization of the affected vessel and the differences in the etiological causes, it is important to make an etiological evaluation of patients with isolated thalamic infarcts and patients with thalamic infarcts with extrathalamic involvement. In addition to this, it is an absolute necessity for the treatment of acute stroke to be directed towards this etiologic cause for the treatment to be applied correctly. Therefore, this study aimed to compare the diagnostic and therapeutic parameters of thalamic infarcted patients with isolated thalamic involvement and thalamic infarcted patients with extrathalamic involvement and to evaluate the relationship with etiologic causes.

2. MATERIAL AND METHODS

In this study, patients admitted to our hospital with a diagnosis of thalamic infarction were retrospectively analyzed. History and demographic data from all patients were recorded. Neurologic examination records including detailed tests of somatosensory functions and motor performance were also evaluated.

We retrospectively analyzed 820 patients with a diagnosis of stroke who were hospitalized and treated in our hospital between January 2019 and April 2022. Among these patients, patients without thalamic involvement, patients whose hospitalization and follow-up could not be performed by us after diagnosis, patients with malignancy, patients associated with infection, and patients diagnosed with hemorrhagic stroke were excluded. Ethics committee approval was obtained for the study (The Ethics Committee of the Antalya Education and Research Hospital approved this study (Number: 2024-152 KN: 7/11).

230 patients with thalamic stroke were included in the study and analyzed retrospectively. Etiological factors such as age, gender, lateralization, hypertension, diabetes mellitus, coronary and peripheral artery disease, history of previous cerebrovascular events, history of dementia, history of seizures, smoking, presence of atrial fibrillation, and family history were evaluated and recorded. In addition, functional assessments such as cognitive impairment, hemoglobin (Hb), Mean Corpuscular Volume (MCV), platelet, Mean Platelet Volume (MPV), hemoglobin A1C (HbA1c), and hyperlipidemia (HL) results, and medication history were recorded. In addition, the results of imaging scoring systems Alberta Stroke Program Early CT Score (ASPECT), Fazekas Scale and Computed tomographic angiography (CTA), tissue plasminogen activator (tPA) and Endovascular thrombectomy EVT procedures and Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria were recorded (Table-1,2).

Table 1.

Identification of risk factors for isolated thalamus involvement and extrathalamic involvement (Demographic data)

| | Extrathalamic involvement | | | Univariate | |
	No	Yes	Total	OR (%95 CI)	p
Age	69,1 ± 13,1	70,6 ± 13,7	69,8 ± 13,4	1,008 (0,989-1,028)	0,399
Gender					
Female	55 (55,6)	44 (44,4)	99 (43)	Reference	
Male	67 (51,1)	64 (48,9)	131 (57)	1,194 (0,707-2,016)	0,507
Lateralization					
Unilateral	121 (54,5)	101 (45,5)	222 (96,5)	Reference	
Bilateral	1 (12,5)	7 (87,5)	8 (3,5)	8,386 (1,015-69,301)	**0,048**
Hypertension					
(-)	52 (55,9)	41 (44,1)	93 (40,4)	Reference	
(+)	70 (51,1)	67 (48,9)	137 (59,6)	1,214 (0,715-2,060)	0,473
Diabetes Mellitus					
(-)	69 (51,9)	64 (48,1)	133 (57,8)	Reference	
(+)	53 (54,6)	44 (45,4)	97 (42,2)	0,895 (0,530-1,513)	0,679
Coronary Arterial Disease					
(-)	89 (55,3)	72 (44,7)	161 (70)	Reference	
(+)	33 (47,8)	36 (52,2)	69 (30)	1,348 (0,766-2,373)	0,300
Peripheral Arterial Disease					
(-)	119 (53,6)	103 (46,4)	222 (96,5)	Reference	
(+)	3 (37,5)	5 (62,5)	8 (3,5)	1,926 (0,449-8,254)	0,378
Cerebrovascular Disease					
(-)	97 (52,4)	89 (47,6)	186 (80,4)	Reference	
(+)	24 (54,5)	20 (45,5)	44 (19,1)	0,882 (0,458-1,698)	0,707
Dementia					
(-)	116 (52,5)	105 (47,5)	221 (95,2)	Reference	
(+)	6 (66,7)	3 (33,3)	9 (3,9)	0,984 (0,725-1,335)	0,917
Seizure					
(-)	121 (53,3)	106 (46,7)	227 (98,7)	Reference	
(+)	1 (33,3)	2 (66,7)	3 (1,3)	2,283 (0,204-25,536)	0,503

Table 1. (Continued)

Smoking					
(-)	102 (51,8)	95 (48,2)	197 (85,7)	Reference	
(+)	20 (60,6)	13 (39,4)	33 (14,3)	0,698 (0,329-1,481)	0,349
Atrial Fibrillation					
(-)	107 (54,9)	88 (45,1)	195 (84,8)	Reference	
(+)	15 (42,9)	20 (57,1)	35 (15,2)	1,621 (0,784-3,352)	0,192
Family History					
(-)	121 (52,8)	108 (47,2)	229 (99,6)		
(+)	1 (100)	0 (0)	1 (0,4)		

Table 2.

Identification of risk factors for isolated thalamus involvement and extrathalamic involvement (Test results, imaging results, and scoring systems)

	Extrathalamic involvement*			Univariate	
	No	Yes	Total	OR (%95 CI)	p
Cognitive Impairment					
(-)	106 (58,9)	74 (41,1)	180 (78,3)	Reference	
(+)	15 (31,3)	33 (68,8)	48 (20,9)	1,362 (0,874-2,123)	0,172
Hb	12,8 ± 1,8	12,7 ± 2,2	12,8 ± 2	0,960 (0,843-1,093)	0,538
MCV	83,9 ± 10,2	84,5 ± 7,6	84,1 ± 9,1	1,008 (0,979-1,037)	0,610
Plt	242,7 ± 84,1	249,8 ± 78	246 ± 81,2	1,001 (0,998-1,004)	0,510
MPV	10,8 ± 1	10,8 ± 1	10,8 ± 1	1,038 (0,797-1,353)	0,781
Hba1C	6,9 ± 1,9	7,2 ± 2,1	7,1 ± 2	1,083 (0,947-1,238)	0,245
HL					
(-)	110 (53,4)	96 (46,6)	206 (89,6)	Reference	
(+)	12 (50)	12 (50)	24 (10,4)	1,146 (0,492-2,669)	0,752
Medication Use					
No medicine	2 (40)	3 (60)	5 (2,2)	1,716 (0,281-10,471)	0,558
Single antiaggregant	41 (48,2)	43 (51,8)	84 (37,3)	1,363 (0,795-2,335)	0,260
Double antiaggregant	64 (64)	36 (36)	100 (43,5)	2,207 (1,292-3,768)	**0,004**
Oral anticoagulant	15 (35,7)	26 (64,3)	41 (18,3)	2,378 (1,188-4,760)	**0,014**
ASPECT Score					
<6	18 (43,9)	23 (56,1)	41 (17,8)	1,563 (0,792-3,086)	0,198
≥6	104 (55)	85 (45)	189 (82,2)	Reference	

Table 2. (Continued)

Fazekas Score					
0 - 1	84 (53,5)	73 (46,5)	157 (68,3)	0,9744 (0,541-1,645)	0,838
2 - 3	38 (52,1)	35 (47,9)	73 (31,7)	Reference	
CTA					
(-)	83 (63,4)	48 (36,6)	131 (57,0)		
(+)	39 (39,4)	60 (60,6)	99 (43,0)	2,660 (1,554-4,553)	**<0,001**
tPA					
(-)	117 (54,2)	99 (45,8)	216 (94,7)	Reference	
(+)	4 (33,3)	8 (66,7)	12 (5,3)	2,364 (0,691-8,084)	0,170
EVT					
(-)	120 (53,8)	103 (46,2)	223 (97,8)	Reference	
(+)	1 (20)	4 (80)	5 (2,2)	4,660 (0,513-42,356)	0,172
TOAST					
Large-artery atherosclerosis	9 (47,4)	10 (52,6)	19 (8,3)	1,41 (0,54 - 3,68)	0,482
Cardioembolism	16 (42,1)	22 (57,9)	38 (16,5)	1,75 (0,85 - 3,6)	0,131
Small-vessel occlusion	16 (59,3)	11 (40,7)	27 (11,7)	0,87 (0,38 - 2,01)	0,750
Stroke of other determined etiology	1 (33,3)	2 (66,7)	3 (1,3)	2,54 (0,23 - 28,65)	0,451
Stroke of undetermined etiology	80 (55,9)	63 (44,1)	143 (62,2)	Reference	

*n (%); mean ± s.deviation
Abbreviations: mRS: Modified Rankin Scale, Hb: Hemoglobin, MCV: Mean Corpuscular Volume, Plt: Platelet, MPV: Mean Platelet Volume, HbA1c: Hemoglobin A1c, HL: Hyperlipidemia, ASPECT: Alberta Stroke Program Early CT Score, CTA: Computed Tomographic Angiography, tPA: tissue plasminogen activator, EVT: Endovascular thrombectomy and TOAST Criteria: Trial of Org 10172 in Acute Stroke Treatment Criteria

Data were analyzed with IBM SPSS V23. Mann-Whitney U test was used to compare the values. Pearson chi-square and Continuity correction tests were used to analyze categorical data. A significance level of $p<0.05$ was taken.

3. RESULTS

There was no difference between the two groups according to age and gender. 8 of 230 patients had bilateral thalamic involvement. The rate of extrathalamic involvement in unilateral patients was 45.5%, while the rate of extrathalamic involvement in bilateral patients was 87.5%. Extrathalamic involvement in patients with bilateral thalamic involvement was 8.386 (95% CI= 1.015-69.301) times higher than those with isolated thalamic involvement (p=0.048).

When the data in Table 2 are evaluated; there was no significant difference between isolated thalamic and extrathalamic involvement in terms of cognitive impairment, hemoglobin, MCV, platelet, MPV, HbA1c, and hyperlipidemia. When evaluated according to the history of medication (antiaggregant or anticoagulant) that the patients were taking at the time of admission; no medication, single antiaggregant use, dual antiaggregant use, and oral anticoagulant use were compared. Accordingly, isolated thalamus involvement was 2.207 (95% CI=1.292-3.768) times higher than extrathalamic involvement in patients using dual antiaggregant (p=0.004). In contrast, extrathalamic involvement was 2.378 (95% CI=1.188-4.760) times higher than isolated thalamus involvement in patients on oral anticoagulants (p=0.004). There was no significant difference between the two groups in the comparison of patients with no other drug use and patients with single antiaggregant use. There

was no difference between the two groups in terms of ASPECT score and Fazekas score indicating lesion burden. Again, when compared according to TOAST criteria, there was no significant difference in both groups according to TOAST subgroups. In addition, isolated thalamic and extrathalamic involvement was compared according to the treatments applied to the patients and the results of both groups were similar in terms of tissue plasminogen activator therapy and endovascular thrombectomy. Finally, the risk of pathology in the basilar artery and vertebral arteries on CTA was 2.660 (95% CI=1.554-4.553) times higher in extrathalamic involvement than in isolated thalamic involvement (p<0.001).

4. DISCUSSION

The thalamus is a structure with important roles in the sleep-wake cycle, mediating cortical stimulus responses, emotions, sensory (gustatory, somatosensory, visual, and auditory) information processing and connection to the cortex, and many other cognitive functions.[12] Thalamic ischemia is a stroke localization that can be frequently seen both in isolation and in association with infarcts involving other structures.[13] The functional complexity of the nuclei of the thalamus and the potential for different variations in the arteries supplying the thalamus result in wide variations in the clinical presentation of thalamic infarcts.[4]

There are many studies in the literature on the relationship between the different arterial anatomy of the thalamus and stroke. Especially publications on Percheron artery infarcts have started to appear frequently in the literature. However, there are no studies on the etiology of isolated thalamic infarcts.[14-16]

In our study, involvement outside the thalamus was observed in a total of 108 patients. These patients were compared with patients with isolated thalamus involvement. Bilateral thalamus involvement was approximately 8 times more common in patients with extrathalamic involvement than in patients with isolated thalamus involvement. Although subgroup analysis could not be performed in this group due to the small number of patients, it was thought that the presence of bilateral thalamus and simultaneous extrathalamic involvement may be associated with percheron artery infarcts. There are articles supporting this in the literature.[15,16] The view that thalamic infarcts are predominantly lacunar infarcts does not fit the data of this study.[17,18]

The most important data of the study is the estimation of the risk related to the protective effect of the medical treatment (antiaggregant or anticoagulants) used by the patients before stroke. In the study, patients without medication, patients using single or dual antiaggregants, and patients using oral anticoagulants were compared. Accordingly, the results of single antiaggregant use were similar in terms of isolated thalamic stroke or stroke with extrathalamic involvement. However, isolated thalamic stroke was approximately 2.2 times higher than stroke with extrathalamic involvement in patients on dual antiaggregants. On the contrary, stroke with extrathalamic involvement was 2.3 times higher than isolated thalamic stroke in patients using oral anticoagulants. Accordingly, dual antiaggregant use was found to be a protective factor in terms of extrathalamic involvement. In addition, oral anticoagulant use was found to be a protective factor for isolated thalamic involvement. When these statistically significant differences obtained in terms of medical treatments are considered from an etiologic point of view, it was concluded that single antiaggregants used in the treatment of small vessel disease in the etiology of thalamic infarction did not make a significant difference in terms of isolated thalamic involvement and extrathalamic involvement. As a result, the choice of medications used for secondary prophylaxis due to previous cerebrovascular disease and/or coronary disease affected the infarct area in these patients. In patients with extrathalamic involvement, conditions such as stenosis, plaque, or dissection in large vessels increase extrathalamic involvement significantly.[19,20]

The study has some limitations. First, it is a retrospective study. Controlled prospective studies will be necessary to form a more definite opinion. Secondly, the areas of involvement of patients with extrathalamic participation are quite large and show differences. Finally, the

sample numbers in some subgroups are quantitatively low, although statistically significant.

In conclusion, it has been shown in this patient group that thalamic infarcts cannot be explained only by lacunar infarction etiology. Therefore, the etiology of thalamic infarcts should be investigated in more detail. In our study, results that were contrary to what is known in terms of medical treatment of thromboembolic processes were shown. Prospective studies with large samples are needed for more precise information.

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The Declaration of Ethics Committee Approval
The Ethics Committee of the Antalya Education and Research Hospital approved this study (Number: 2024-152 KN: 7/11). Informed consent was obtained from all subjects and/or their legal guardians. All methods were carried out in accordance with relevant guidelines and regulations. All experiments were performed by relevant guidelines and regulations.

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