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Medical Journal of Mugla Sitki Kocman University

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On Behalf of Mugla Sitki Kocman University School Of Medicine

Prof. Dr. Süleyman Cüneyt KARAKUŞ (Dekan / *Dean*)

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İletişim / *Correspondence*

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AMAÇ VE KAPSAM

Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi, Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesinin süreli yayın organıdır ve Nisan, Ağustos ve Aralık aylarında olmak üzere yılda 3 sayı yayınlanmaktadır. Derginin yayın dili Türkçe ve İngilizcedir.

Dergide, tıbbın her dalı ile ilgili prospektif, retrospektif ve deneysel araştırmalar, olgu sunumu ve derlemeler yayınlanır. Yayınlanan makalelerde konu ile ilgili en yüksek etik ve bilimsel standartlarda olması ve ticari kaygılarda olmaması şartı gözetilir. Yayın için gönderilen çalışmalar; orijinal, başka bir dergide değerlendirme sürecinde olmayan ve daha önce basılmamış olması koşullarıyla kabul edilir.

Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi; TR Dizin, Google Akademik, Crossref, Türkiye Atıf Dizini, Türk Medline, Academic Keys ve Research Bible Index tarafından indekslenmektedir.

Dergide yayınlanacak olan yazılar http://dergipark.gov.tr/muskutd web sayfası üzerinden gönderilmelidir. Yazım kuralları, teknik bilgiler ve diğer gerekli formlara bu sayfadan erişilebilir. Gönderilen yazılardaki tüm içerikler yazarların sorumluluğundadır.

Bu dergide yer alan yazı, makale, fotoğraf ve illüstrasyonların elektronik ortamlarda dahil olmak üzere kullanma ve çoğaltma hakları Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi'ne aittir. Yazılı ön izin olmaksızın materyallerin tamamının ya da bir bölümünün çoğaltılması yasaktır. Her hakkı saklıdır. Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi'nde yayınlanan içerikler yazar(lar)a aittir. Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi, dergi editörleri, çalışanları ve yayıncı bu yazılar için mali, hukuki ve diğer yönlerden sorumluluk kabul etmemektedir.

AIMS AND SCOPE

Medical Journal of Mugla Sitki Kocman University is a periodical of Medical School of Mugla Sitki Kocman University and is published three times per year; in April, August, and December. The Medical Journal of Mugla Sitki Kocman University's publication languages are both Turkish and English.

The articles which could be prospective or retrospective on investigational studies, case reports and reviews of every aspect of medicine are published. The studies should have paramount ethical and scientific standards as well as no commercial concerns. Articles are accepted for publication on the condition that they are original, are not under consideration by another journal, or have not been previously published.

The Medical Journal of Mugla Sitki Kocman University is indexed by TR Dizin, Google Scholar, Crossref, Türkiye Atıf Dizini, Türk Medline, Academic Keys and Research Bible.

All manuscripts must be submitted electronically on the http://dergipark.gov.tr/muskutd. Instructions for authors, technical information, and other necessary forms can be accessed over this web page. Authors are responsible for all content of the manuscripts.

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YAZARLARA BİLGİ

https://dergipark.org.tr/tr/pub/muskutd/writing-rules

Genel Bilgiler

Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesinin süreli yayın organı olup özel sayılar hariç düzenli olarak yılda üç sayı olarak yayımlanır. Tıbbın her dalı ile ilgili prospektif, retrospektif ve deneysel araştırmalar, olgu sunumu ve derlemeler yayınlanmak için değerlendirilmektedir. Konu ile ilgili etik ve bilimsel standartlar olması ve ticari kaygıların olmaması şartı gözetilir. Yazarlar tarafından, başka bir dergide değerlendirme sürecinde olmayan ve daha önce basılmadığı beyan edilen yazılar incelemeye alınır. Editör onayı sonrasında en az yurt içi-yurt dışı iki hakem incelemesinden geçip gerek görüldüğü takdirde istenen değişiklikler yazarlar tarafından yapılıp hakemlerce kabul edildikten sonra yayımlanır.

Bilimsel Sorumluluk

Yazar olarak belirtilmiş tüm kişiler çalışmayı planlamalı veya gerçekleştirmeli, çalışmanın yazılmasında, gözden geçirilmesinde ve son halinin onaylanmasında rol almış olmalıdır. Kriterleri karşılayan bir metnin ortaya çıkması tüm yazarların sorumluluğudur.

Etik Sorumluluk

Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi, etik ve bilimsel standartlara uygun yazıları yayımlayarak bilimin doğru bir şekilde ilerlemesine katkı sağlamayı hedeflemektedir. Bu kapsamda, çalışmaların bilimsel etiğe uygunluğu önemlidir. Etik ilkeler COPE (Committee on Publication Ethics) tarafından hazırlanan yönerge (https://publicationethics.org/resources/resources-and-further-reading/international-standards-editors-and-authors) temel alınarak Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi tarafından benimsenmiş ve yazarlar, hakemler ve editörler tarafından da benimsenmesi önerilmektedir. Bu önerilerin bir kısmı aşağıda verilmiştir.

Yazarların Etik Sorumlulukları:

- Çalışmayla ilişkili veri kayıtlarını düzenli tutmak ve olası bir talep üzerine bu verilere erişim verebilmelidir.
- Gönderdiği makalenin başka bir yerde yayınlanmadığından veya kabul edilmediğinden emin olmalıdır.
- İnsan veya hayvan denek içeren tüm çalışmalar için ulusal ve uluslararası yasalara ve yönergelere uygun olmasını sağlamak, (örneğin, WMA Helsinki Bildirgesi, NIH Laboratuar Hayvanlarının Kullanımına İlişkin Politika, Hayvanların Kullanımına İlişkin AB Direktifi) gerekli onayların alındığını onaylamak, denek mahremiyete saygı göstermek. Çalışmasına dair ilgili etik kurul onaylarını ve araştırma detaylarını çalışmanın "Gereç ve Yöntem" kısmında belirtmek.
- Herhangi bir çıkar çatışması durumunda, makalesiyle ilgili etik bir ihlal tespit ettiğinde bunu editör ve yayıncı ile paylaşmak, hata beyanı, zeyilname, tazminat bildirimi yayınlamak veya gerekli görüldüğü durumlarda çalışmayı geri çekmelidir.

Hakemlerin Etik Sorumlulukları:

- Editörün karar verme sürecine katkıda bulunmak için makaleyi objektif olarak zamanında incelmeli ve sadece uzmanlık alanı ile ilgili çalışma değerlendirmeyi kabul etmelidir.
- Değerlendirmeyi nesnel bir şekilde sadece çalışmanın içeriği ile ilgili olarak yapmalıdır.
- Dini, siyasi ve ekonomik çıkarlar gözetmeden çalışmayı değerlendirmelidir.
- Yayınlanacak makalenin kalitesini yükseltmeye yardımcı olacak yönlendirmelerde bulunmalı ve çalışmayı titizlikle incelemelidir. Yorumlarını yapıcı ve nazik bir dille yazara iletmelidir.
- Editör ve yazar tarafından sağlanan bilgilerin gizliliğini korumalı, kör hakemliğe aykırı bir durum varsa editöre bildirmeli ve çalışmayı değerlendirmemelidir.
- Potansiyel çıkar çatışmalarının (mali, kurumsal, işbirlikçi ya da yazar ve yazar arasındaki diğer ilişkiler) farkında olmalı ve gerekirse bu yazı için yardımlarını geri çekmek konusunda editörü uyarmalıdır.

Editörlerin Sorumlulukları:

- Cinsiyet, dini veya politik inançlar, yazarların etnik veya coğrafi kökenleri üzerine ayrım yapılmaksızın görevlerini yerine getirirken dengeli, objektif ve adil bir şekilde hareket etmelidir.
- Dergiye gönderilen çalışmaları içeriğine göre değerlendirmeli, hiçbir yazara ayrıcalık göstermemelidir.
- Olası çıkar çatışmalarını önlemek adına gerekli önlemleri almalı ve varsa mevcut beyanları değerlendirmelidir.
- Etik ihlali niteliğinde bir şikayet olması durumunda, derginin politika ve prosedürlerine bağlı kalarak gerekli prosedürleri uygulamalıdır. Yazarlara, gelen şikâyete cevap vermek için bir fırsat vermeli, çalışma kime ait olursa olsun gerekli yaptırımları uygulamaktan kaçmamalıdır.
- Derginin amaç ve kapsamına uygun olmaması durumunda gelen çalışmayı reddetmelidir.

Tüm araştırma makalelerinde (retrospektif çalışmalarda dahil olmak üzere), çalışma için Etik Kurul Onayı alınmalı ve Etik Kurul Onayının alındığı yer, tarih (gün, ay ve yıl olarak) ve onay numarası Gereç ve Yöntem bölümünde belirtilmelidir. İnsan ile ilgili tüm çalışmalarda Helsinki Deklarasyonu'na (World Medical Association Declaration of Helsinki http://www.wma.net/en/30/publications/10policies/b3/index.html) göre çalışmanın yapıldığı mutlaka belirtilmelidir. Olgu sunumlarında, hastadan (ya da yasal vasisinden) tıbbi verilerinin yayınlanabileceğine ilişkin yazılı hasta onam belgesi alındı cümlesinin hasta onam tarihi ile birlikte belirtilmesi gereklidir. Hayvan deneyleri için laboratuvar hayvanlarının bakım ve kullanımı konusunda kurumsal veya ulusal yönergelerin takip edilmeli ve bildirmelidirler. Yazarların çalışmalarında kullandıkları cümlelerinden editör ve yayın kurulu sorumlu değildir. Bilimsel, hukuki ve etik sorumluluğu yazarlara aittir.

Sorumlu yazar, gönderilen çalışmanın başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını belirtmelidirler. Çalışmanın bir kısmı kongrede sözlü veya poster bildiri olarak sunuldu ise başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

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Kabul edilen yazının tüm kullanım ve yayın hakkı derginin olur ve izinsiz olarak başka bir yerde yayınlanamaz.

Değerlendirme: Tüm makaleler çift-kör değerlendirme yöntemi kullanılarak en az iki yerli veya yabancı hakem tarafından değerlendirilir. Makalelerin değerlendirilmesi, bilimsel önemi, orijinalliği göz önüne alınarak yapılır. Yayına kabul edilen yazılar editörler kurulu tarafından içerik değiştirilmeden yazarlara haber verilerek yeniden düzenlenebilir.

İntihal taraması: Dergiye gönderilen makaleler format ve intihal açısından kontrol edilir. Formata uygun olmayan veya intihal benzerlik oranı yüksek (%20'den az olmalıdır) makaleler değerlendirilmeden sorumlu yazara geri gönderilir.

Çıkar çatışması: Çalışmaları ile ilgili taraf olabilecek tüm kişisel, ticari bağlantı veya çalışma için doğrudan veya dolaylı olarak maddi destek veren kurum var ise yazarlar; kullanılan ticari ürün, ilaç, firma ile ticari hiçbir ilişkisinin olmadığını veya varsa nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar vs.), editöre sunum sayfasında bildirmek zorundadır. Herhangi bir çıkar çatışmasının olmadığı durumda metin içerisinde 'Yazarlar çıkar ilişkisi olmadığını beyan eder' şeklinde ifade edilmelidir.

Lisan

Derginin yayın dilleri Türkçe ve İngilizcedir. Türkçe metinlerde Türk Dil Kurumu'nca (www.tdk.gov.tr) yayınlanan Türkçe sözlük temel alınmalıdır. Gönderilmiş makalelerdeki tüm yazım ve imla hataları, anlam ve verileri değiştirmeksizin editör tarafından düzeltilebilir. Metnin kurallara uygun olarak düzenlenmesi yazarların sorumluluğundadır.

Telif Hakkı Bildirimi

Telif hakkı devrini bildirmek için kapak mektubunda 'Bu makalenin telif hakkı; çalışma, basım için kabul edilmesi koşuluyla Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi'ne devredilir' şeklinde belirtilmelidir. Yazarlara ücret ödenmez.

Yazı Tipleri

Derleme: Derlemeler yeni veya tartışmalı alanlara ışık tutmalıdır. Türkçe ve İngilizce başlık ve tek paragraflık özetler ve anahtar kelimeler içermelidir. Dergi editörü derleme yazımı için davette bulunur.

Orijinal makaleler: Orijinal makaleler temel veya klinik çalışmalar veya klinik denemelerin sonuçlarını bildirir. Makale dili Türkçe veya İngilizce fark etmeksizin Türkçe özet, İngilizce özet, giriş, gereç ve yöntemler, bulgular/sonuçlar, tartışma, teşekkür (gerekliyse), kaynaklar ve şekiller ve tablolardan oluşmalıdır.

Olgu Sunumu: Tıbbın her alanındaki önemi olan olgu sunumlarını yayınlanır. Türkçe özet, İngilizce özet, giriş, olgu, tartışma, kaynaklardan oluşmalıdır.

Yazı Gönderimi

Tüm yazılar elektronik ortamda http://dergipark.gov.tr/muskutd adresi üzerinden gönderilmelidir.

Yazının Hazırlanması

Yazı hazırlığı iki satır aralıklı, satır numaraları verilmiş ve Times New Roman 12 punto karakter büyüklüğünde yapılmalıdır. Sayfalar başlık sayfasından başlamak üzere, sağ alt köşesinden numaralandırılmalıdır. Makale sistemine yüklenen word (*.doc, *.docx) dosyasının başlık sayfasında yazarlara ait isim ve kurum bilgileri yer almamalıdır.

Kapak Mektubu: Kapak mektubu gönderilen makalenin kategorisini, daha önce başka bir dergiye gönderilmemiş olduğunu, çıkar ilişkisi bildirimini, yayın hakkı devri bildirimini ve varsa çalışmayı maddi olarak destekleyen kişi ve kurumların adlarını mutlaka içermelidir.

Başlık sayfası: Bu sayfada çalışmanın tam Türkçe ve İngilizce ismi ve kısa başlığı olmalıdır. Katkıda bulunanların tüm yazarların isimleri, çalıştıkları kurumları ve ORCID numaraları listelenmelidir. Ücretsiz olarak bireysel ORCID numaraları http://orcid.org adresinden alınabilmektedir. Basım sürecinde dergi editörü ile iletişimde bulunacak olan yazışma yazarı belirtilmelidir. Çalışmanın bir kısmı kongrede sözlü veya poster bildiri olarak sunuldu ise başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

Özet ve Anahtar Kelimeler: Özet 250 kelimeyi geçmemelidir. Çalışmanın amacını, yöntemi, bulgu ve sonuçları özetlemelidir. En fazla 5 anahtar kelime verilmelidir. Kelimeler birbirlerinden virgül (,) ile ayrılmalıdır. İngilizce kelimeler Index Medicus'taki Medical Subjects Headings listesine uygun olmalıdır www.nlm.nih.gov/mesh/MBrowser.html. Türkçe anahtar kelimeler Türkiye Bilim Terimleri (TBT)'ne uygun olarak verilmelidir www.bilimterimleri.com

Giriş: Kısa ve açık olarak çalışmanın amaçlarını tartışmalı, çalışmanın neden yapıldığına dair temel bilgileri içermeli ve hangi hipotezlerin sınandığını bildirmelidir.

Gereç ve Yöntemler: Açık ve net olarak yöntem ve gereçleri açıklanmalıdır. İlk vurgulamada kullanılan araç ve cihazların model numaraları, firma ismi ve adresi (şehir, ülke) mutlaka belirtilmelidir. Tüm ölçümler metrik birim olarak verilmeli ve ilaçların jenerik adları kullanılmalıdır.

İstatistiksel Değerlendirme: Tüm çalışma makaleleri istatistiksel olarak değerlendirilmeli ve uygun plan, analiz ve bildirimde bulunmalıdır. p değeri yazı içinde belirtilmelidir. Kullanılan istatistik yöntem açıkça belirtilmelidir.

Sonuçlar: Sonuçlar metin, tablo ve şekiller kullanılarak sunulmalıdır. Tablo ve metinler tekrarlanmamalıdır. p değeri yazı içinde belirtilmelidir (p=0.014 gibi).

Tartışma: Çalışmanın farklılıklarına ve sonuçlarına vurgu yapılmalıdır. En önemli bulgu kısa ve net bir şekilde belirtilmeli, gözlemlerin geçerliliği tartışılmalı, aynı veya benzer konulardaki yayınların ışığında bulgular yorumlanmalı ve yapılan çalışmanın olası önemi belirtilmelidir. Çalışmanın esas bulgularının kısa ve özlü bir paragrafla vurgulanması önerilir.

Teşekkür: Yazarlar araştırmaya katkıda bulunan ancak yazar olarak yer almayan kişilere teşekkür etmelidir.

Tablo, Resim, Şekil ve Grafikler: Tüm tablo, resim, şekil, grafik ve diğer görseller ana metnin içinde geçiş sıralarına uygun şekilde, ardışık olarak numaralandırılmalıdır. Kullanılan görsellerde hasta ve doktor kimlikleri içeren bilgiler ve kurum adları görülmeyecek şekilde hazırlanmalıdır. Tablolar ana metin içinde kaynak listesinin sonrasında sunulmalıdır. Tablolar JPEG, TIFF veya diğer görsel formatlarda gönderilmemelidir. Mikroskopik şekillerde açıklayıcı

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bilgilere ek olarak, büyütme oranı ve kullanılan boyama tekniği de belirtilmelidir. Görseller sisteme minimum 300 DPI çözünürlükte yüklenmelidir. Şekil, resim, grafik ve fotoğrafların her biri ayrı *.jpg* veya *.gif* dosyası olarak sisteme eklenmelidir. Şekiller metin içinde kullanım sıralarına göre Arabik (1, 2, 3, v.b.) rakamla numaralandırılmalı ve metinde parantez içinde gösterilmelidir. Grafiklerde kullanılan çizgiler yayın hazırlığı aşamasında yeniden boyutlandırma sırasında meydana gelecek bozulmaları engellemek amacıyla yeterli kalınlıkta olmalıdır. Tablolarda kullanılan kısaltmalar tablo altlarında tanımlanmalıdır. Tablo ve şekil başlıklarında ve tablonun yazı içinde anılmasında Roma (I, II, II, v.b.) rakamları kullanılmamalıdır.

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Dergi makaleleri için örnek

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Komite veya yazar grupları için örnek

The Standard Task Force, American Society of Colon and Rectal Surgeons: Practice parameters for the treatment of haemorrhoids. Dis Colon Rectum 1993;36:1118-20.

Kitaptan konu için örnek

Milson JW. Haemorrhoidal disease. In: Beck DE, Wexner S, eds. Fundamentals of Anorectal Surgery. 1 1992; 192-214. 1a ed. New York: McGraw-Hill

Kitap için örnek

Bateson M, Bouchier I. Clinical Investigation and Function, 2nd edn. Oxford: Blackwell Scientific Publications Ltd, 1981.

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ORİJİNAL MAKALE / ORIGINAL ARTICLE

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Factors Associated with the Progression of Aortic Aneurysms: A Single-Center Experience

Aort Anevrizmaları Progresyonu ile İlişkili Faktörler: Tek Merkez Deneyimi

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Öz

Aort anevrizmaları (AA), yetişkinlerde önemli mortalite sebebidir. Çalışmamızda, torasik aort anevrizması (TAA) ve abdominal aort anevrizması (AAA) ile ilişkili etyolojik faktörleri araştırmayı amaçladık. Çalışmamız 181 bireyi (98'i TAA ve AAA tanılı, 83'ü kontrol grubu) içermektedir. Aort anevrizma (AA) grubunda %72.4'ü erkekti. AA grubunda %57.1'i TAA, %42.9'u AAA tanılıydı. Aorta çapı 41-108 mm aralığında olanlar AA grup içine alındı. İnisiyal serum biyokimya değerleri ve 2 ardışık bilgisayarlı tomografi anjiografi ölçümü değerlendirildi ve her birey için yıllık aort çapı genişlemesi ölçüldü. AA grup ve kontrol grubu ortalama yaşı sırasıyla 62.89±13.55 ve 68.10±11.69 idi (p=0.007), hipertansiyon oranı (p=0.021) daha yüksekti. TAA grubu daha yüksek AST (p=0.016) ve trombosit değerlerine (p=0.010) sahipti. AAA grubunda ise yüksek nötrofil/lenfosit oranı (NLR) (p=0.044) mevcuttu. AAA grubunda erkek oranı %90.5'ti. Sigara kullanımı AAA grubunda daha belirgindi (p=0.08). Bir cm/yıldan daha hızlı anevrizma büyüme hızı oranı, TAA ve AAA gruplarında sırasıyla %25 ve %75 idi. TAA ile yüksek AST ve yüksek trombosit değeri arasında korelasyon mevcuttu. AAA ise erkek cinsiyet, sigara kullanımı ile yakından ilişkili bulundu.

Anahtar Kelimeler: Abdominal Aort Anevrizması, ALT, AST, Nötrofil/Lenfosit Oranı, Torasik Aort Anevrizması

Abstract

Aortic aneurysms (AA) have a significant mortality rate in population. We aimed to identify the etiologic factors associated with thoracic aortic aneurysms (TAAs) and abdominal aortic aneurysms (AAAs). Our study included 181 patients; 98 patients diagnosed with TAA or AAA made up the aortic aneurysm (AA) group, 83 patients without either condition made up the control group. Within the AA group, 72.4% of the patients were male, the patients had been diagnosed with TAA and AAA in ratio of 57.1% and 42.9% respectively. All AA group patients had an aortic diameter in range from 41 to 108 mm. Initial serum biochemical measures, two consecutive computed tomography angiography measurements were recorded, the enlargement rate per year for the aorta was calculated for all. The mean age in the AA group was 62.89±13.55 compared to 68.10±11.69 in the control group (p=0.007), higher ratio for hypertension (p=0.021). TAA patients had a higher AST level (p=0.016) and platelet counts (p=0.010) compared to control group. AAA patients had a higher mean neutrophil/lymphocyte ratio (NLR) (p=0.044) compared to control group. Among the patients with AAA, 90.5 % were male. Smoking was more prevalent in the abdominal AA group (p=0.08). An enlargement rate of more than 1 cm/year was detected in 25% of the patients with TAA and in 75% of the patients with AAA. TAA was associated with higher AST levels and higher platelet counts than were in the AAA group, whereas AAA showed strong relationships with male gender and smoking.

Keywords: Abdominal Aortic Aneurysm, ALT, AST, Neutrophil/Lymphocyte Ratio, Thoracic Aortic Aneurysm

Introduction

Aortic aneurisms (AA) have been recognized for centuries; they were even depicted in hieroglyphics from ancient Egypt (1). First try in AA was endoaneurysmorrhaphy by Rudolph Mattas in 1881 (1). AAs remained untreatable until 1951. The first AA case presented by Dr. De Bakey represented a substantial surgical advance, and the manufacturing of material used in aortic replacement has aided surgical progress. The first utilization of a homograft was also an achievement of by Dr. DeBakey, which took place in 1952 (1). Many surgeons around the world have contributed their expertise to addressing this life-threatening disease, and today successful results please patients suffering AA.

Etiological factors related to AA include smoking, older age, male gender, hypertension, chronic obstructive pulmonary disease, hyperlipidemia, atherosclerosis, white race, and a family history of AA, as well as some connective tissue diseases and syndromes such as Ehlers-Danlos type IV, Marfan, and Loeys-Dietz syndrome (2). Furthermore, some infectious diseases such as tuberculosis, syphilis, bacterial and fungal infections, in addition to inflammatory diseases, may cause AA (2). The majority of AA cases are identified without any definitive cause (3).

In the current study, we aimed to identify the etiologic factors that affect aneurysm progression in any segment of the aorta.

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Material and Method

Patient Population

This retrospective study included patients diagnosed with AA in any segment of the aorta between November 2018 and June 2022 in Muğla Sıtkı Koçman University Medical Faculty Cardiovascular Surgery Department. Ethical approval was obtained from a local review board (22/06/2022 12/II), and this study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria allowed patients who were diagnosed with an AA with a diameter of at least 41 mm and who were at least 18 years of age to be included in this study. Exclusion criteria consisted of having an aneurysm that was less than 40 mm in diameter or being younger than 18 years of age.

A power analysis performed in the G Power 3.1.2 program with a type 1 error rate of 0.05 and statistical power of 0.80 gave an effect size of 0.470. Accordingly, it was calculated that a total of 144 patients, with at least 72 patients in both groups, should be included in the planned study.

Patients (n=181) were divided into 2 groups: the aortic aneurysm (AA) group (n=98) and the control group (n=83). The AA group was divided into 2 subgroups: patients who received an endovascular intervention (EVAR/TEVAR) or surgery, and medical treatment. A flow chart of the study is shown in Figure 1.

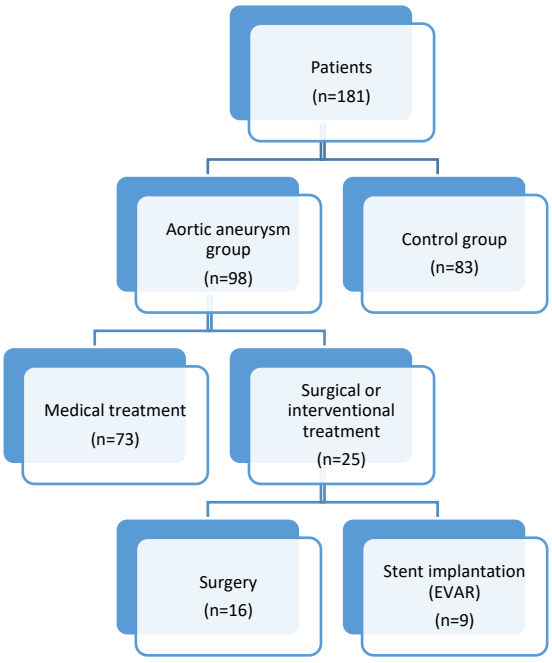

Figure 1. Demonstration of patients according to their diagnosis and treatment they received.

Two consecutive computed tomography angiography (CTA) assessments—performed with no less than 1 year between the two screenings—were evaluated for each patient. Institutional electronic database about hemogram and biochemistry, demographic features were also recorded.

Laboratory Findings

Blood samples were collected into ethylene diamine tetraacetic acid (EDTA) and analyzed using a Sysmex XN1000 hematology analyzer (Sysmex, Kobe, Japan) for white blood cell (WBC), hemoglobin (Hb), mean cell hemoglobin (MCH), red blood cell (RBC) count, platelet count, mean platelet volume (MPV), total bilirubin and direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) measurements. The neutrophil/lymphocyte ratio (NLR) was calculated by dividing the total number of neutrophils by the total number of lymphocytes. Concentrations of low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (tgl) were determined by enzymatic methods on a COBAS 8000 (c702) biochemical analyzer (Roche Diagnostics GmbH; Meinheim, Germany).

Imaging Analysis

Two consecutive measurements of AA diameters using cross-sectional CTA images were performed for each patient (no less than 1 year between two screenings). Images were obtained using a 256-slice dual energy CTA scanner (Siemens Definition Flash, Berlin, Germany) with a slice thickness of 1 mm.

Statistical Analysis

Data were analyzed with SPSS 28.0 (SPSS Inc., Chicago, IL). The Kolmogorov–Smirnov test was used to evaluate whether the distribution of continuous variables was normal. Continuous variables were compared between independent samples using independent samples t-test, and categorical variables were compared using the χ^2 test. Spearman correlation analysis was also performed to determine the level of correlation between quantitative variables. Descriptive statistics of quantitative variables were described as mean±standard deviation, median (25th–75th percentiles), and minimum–maximum. Univariate and multivariate logistic regression analyses were performed to determine the effects of risk factors on the AA enlargement rate. Receiver operating characteristic (ROC) curve analysis was applied to determine cut-off values for aortic aneurysm. Frequency and percentage (%) were given for each quantitative variable. A p value <0.05 was considered statistically significant.

Results

Demographic data for the patients in this study are shown in Table 1. Males were more common than females in both groups. The mean age was 65.28±12.96 years for all patients, 62.89±13.55

years in the AA group, and 68.10±11.69 in the control group (p=0.007). In AA group, hypertension was more frequent in ratio of 47% (p=0.021). There was no significant difference between the AA and control groups in terms of biochemical values (p>0.05). Two patients in the AA group were dead.

Table 2 shows comparative statistics for the abdominal AA (AAA) and thoracic AA (TAA) groups. Smoking habit and NLR were significantly higher in the AAA group (p=0.003 and p=0.044). However, platelet count and AST were higher in TAA group than in the AAA group (p=0.010, and p=0.016, respectively).

Table 3 shows a comparison of enlargement rate between the AAA and TAA groups; there was no significant difference between groups (p>0.05).

A high progression rate was defined as the enlargement of an aneurysm by more than 1 cm/year. A comparison of aneurysm-enlargement rate between the AA and the control group showed that the AAA group had a significantly higher progression rate (p=0.002) (Table 4).

Table 1. Patient characteristics of the AA and control groups.

Variables	**AA** (n=98)	**Control** (n=83)	p
Gender			
Male	71 (72.4)	67 (80.7)	0.259c
Female	27 (27.6)	16 (19.3)	
Age	62.89±13.55	68.10±11.69	**0.007**[s]
Smoking	45 (45.9)	45 (54.2)	0.266[c]
Hypertension	54 (65.1)	47 (48)	**0.021**[c]
Medical treatment	73 (74.5)[b]	83 (100)[a]	**<0.001**[c]
AA graft replacement	8 (8.2)[b]	0 (0)[a]	**<0.001**[c]
EVAR	9 (9.2)[b]	0 (0)[a]	**<0.001**[c]
AAA graft replacement	8 (8.2)[b]	0 (0)[a]	**<0.001**[c]
Exitus	2 (2)	0 (0)	0.501[c]
WBC	8.04 (6.01-10.08)	7.65 (5.98-9.13)	0.367[m]
Hb	13.40 (11.40-14.73)	13.30 (12.10-14.90)	0.586[m]
MCH	28.90 (27.75-30.13)	29.20 (27.70-30.50)	0.409[m]
RBC	4.74 (4.02-5.24)	4.64 (4.21-5)	0.475[m]
PLTx1000	220 (176.75-259.25)	234 (180-278)	0.214[m]
MPV	10.80±1.18	10.70±0.88	0.509[s]
NLR	2.41 (1.65-4.01)	2.31 (1.68-3.59)	0.774[m]
AST	18 (16-23.50)	17 (13-22)	0.166[m]
ALT	16 (13-22.25)	17 (12-23)	0.899[m]
T blr	0.48 (0.33-0.64)	0.51 (0.34-0.68)	0.793[m]
D blr	0.21 (0.16-0.27)	0.21 (0.16-0.29)	0.731[m]
HDL	50.35 (39.75-63.25)	49.20 (41-58)	0.770[m]
LDL	106.05 (85.75-124.25)	103 (83-124)	0.963[m]
Tgl	114 (85-167.50)	114 (81-167)	0.629[m]

[c]: Chi-Square test, [s]: Independent samples t-test, [m]: Mann Whitney U test. Descriptive statistics are expressed as mean ± standard deviation, median (25th-75th percentiles), or frequency (percentage). The same letters in the same row indicate the similarity between column percentages, and different letters indicate the difference between column percentages. AA: Aortic aneurysm, EVAR: Endovascular aortic repairment, AAA: Abdominal aortic aneurysm. WBC (white blood cell), Hb (hemoglobin), MCH (mean cell hemoglobin), RBC (red blood cell), plt (platelet counts), MPV (mean platelet volume), NLR (neutrophile–lymphocyte ratio), AST (aspartate aminotransferase), ALT (alanine aminotransferase), t blr (total bilirubin), d blr (direct bilirubin), HDL (high- density lipoprotein), LDL (low-density lipoprotein), tgl (triglyceride).

HDL, LDL, tgl, AST, ALT, WBC, Hb, MCH, RBC; When the effect of PLT, MPV, NLR, t blr, d blr, initial diameter (D1) and second diameter (D2) values were analyzed by univariate logistic regression (LR) analysis to determine if these variables affect enlargement rate>1. The effects of HDL, WBC, D1 and D2 variables on enlargement rate were statistically significant (p<0.05) while other variables were not (p>0.05). HDL increase had a protective effect of 0.958 against an enlargement rate >1 cm. As WBC, D1 and D2 values increase, the risk of an enlargement rate >1 cm increases by 1.173, 1.529 and 2.148 times, respectively (p<0.05). The variables having statistically significant effect on enlargement rate regarding univariate LR were analysed by multivariate LR. However, since there is a high level of correlation between D1 and D2 (r=0.885, p<0.001), D2 variable is excluded from multivariate LR analysis. According to the final results, it was determined that HDL had no significant effect on enlargement rate (p=0.065). As WBC and D1 value increase, the risk of an enlargement rate >1cm increases by 1.173 and 1.560 times, respectively (p<0.05) (Table 5).

The cut-off point for WBC variable for diagnosis of the disease was calculated as >8.82 by ROC-curve analysis. The sensitivity and specificity rates were found to be 38.78% and 73.49%; respectively, however, it was not statistically significant (p=0.364) because the WBC variable had a low rate of determination on enlargement rate (Nagelkerke R2=6%).

Table 2. Comparative statistics of abdominal and thoracic aortic aneurysm subgroups.

Variables	**Diagnosis** Total n=98		P
	AAA (n=42)	**TAA** (n=56)	
Gender			
Male	38 (90.5)	33 (58.9)	**0.001**[c]
Female	4 (9.5)	23 (41.1)	
Age	65 (57.50-72.25)	64 (55-71.50)	0.628[m]
Smoking	25 (59.5)	20 (35.7)	**0.033**[c]
Hypertension	23 (54.8)	24 (42.9)	0.335[c]
Medical treatment	26 (61.9)[a]	47 (83.9)[b]	**<0.001**[c]
AA graft replacement	0 (0)[a]	8 (14.3)[b]	**<0.001**[c]
EVAR	9 (21.4)[a]	0 (0)[b]	**<0.001**[c]
AAA graft replacement	7 (16.7)[a]	1 (1.8)[b]	**<0.001**[c]
Exitus	1 (2.4)	1 (1.8)	1.000[c]
Enlargement rate			
≤1	34 (81)	53 (94.6)	0.051[c]
>1	8 (19)	3 (5.4)	
WBC	8.07 (5.61-10.44)	8.01 (6.17-9.71)	0.926[m]
Hb	13.40 (11.23-14.58)	13.35 (11.43-14.78)	0.994[m]
MCH	28.80 (27.98-30.53)	29 (27.50-29.88)	0.497[m]
RBC	4.67 (4.01-5.25)	4.78 (4.04-5.26)	0.796[m]
PLTx1000	189.50 (169.75-245.25)	233.50 (197.75-284.75)	**0.010**[m]
MPV	10.70 (10.05-11.13)	10.65 (9.93-11.65)	0.951[m]
NLR	3.13 (1.79-5.88)	2.19 (1.51-3.76)	**0.044**[m]
AST	17.30 (14.75-19.40)	19.40 (16-26)	**0.016**[m]
ALT	15.50 (12.75-18)	16 (13-23.75)	0.585[m]
T blr	0.47 (0.35-0.64)	0.49 (0.30-0.66)	0.928[m]
D blr	0.21 (0.16-0.33)	0.21 (0.15-0.27)	0.595[m]
HDL	45 (40.25-56.05)	53 (39.25-65)	0.269[m]
LDL	99.14±27.27	110.73±35.25	0.080[s]
Tgl	111.50 (73.88-145.50)	119 (89.25-186.50)	0.539[m]

[c]: Chi-Square test, [s]: Independent samples t-test, [m]: Mann Whitney U test. Descriptive statistics are expressed as mean ± standard deviation, median (25th-75th percentiles), or frequency (percentage). The same letters in the same row indicate the similarity between column percentages, and different letters indicate the difference between column percentages. TAA: Thoracic aortic aneurysm, AAA: Abdominal aortic aneurysm, AA: Aortic aneurysm, EVAR: Endovascular aortic repairment, WBC (white blood cell), Hb (hemoglobin), MCH (mean cell hemoglobin), RBC (red blood cell), plt (platelet counts), MPV (mean platelet volume), NLR (neutrophile–lymphocyte ratio), AST (aspartate aminotransferase), ALT (alanine aminotransferase), t blr (total bilirubin), d blr (direct bilirubin), HDL (high- density lipoprotein), LDL (low-density lipoprotein), tgl (triglyceride).

Mortality was reported for two patients in the AA group. The first of these patients died after an AAA repair with graft interposition. He was 82 years old, and during the postoperative period he could not be weaned from ventilatory support due to his comorbid chronical obstructive pulmonary disease; he died on the 15th postoperative day. The second patient was a 68-year-old male who died due to catheter infection and sepsis on the on the 20th postoperative day after TAA repair with supra-coronary graft interposition.

Discussion

The current study describes the postoperative outcomes of our included patients and indicates factors associated with AA. When we compared TAA and AAA with regard to possible related etiologic features of AA, we found that smoking, enlargement rate>1 cm/year, and higher NLR were significantly higher in the AAA group; in contrast, higher AST values, higher platelet counts are significantly higher in TAA group. HDL, WBC, D1 and D2 values of AA had a significant effect on enlargement rate>1 cm/year. WBC, D1 and D2 values of AA increase the risk of an enlargement rate >1 cm.

AAs may develop in all aortic segments. They can produce life-threatening complications such as aortic dissection and aortic rupture, which represent difficult clinical challenges to cardiothoracic surgery teams (4).

The normal aortic wall is composed of three layers: the intima, media, and adventitia. During embryological development, the increase in medial thickness is related to an increase in the number of lamellar units (from 35 to 56), whereas there is only a minor increase in their thickness (from 12 to 17 μm) (5). However, medial growth in the abdominal aortic segment is associated with an increase in thickness of the lamellar units (from 12 to 26 μm) that is related to smooth muscle cell proliferation, but there is a minimal increase with regard to their number (from 25 to 28) (5). Therefore, the tension on lamellar units in adults is greater in the abdominal aorta than in the thoracic aorta (5). In addition, the amount of elastic tissue diminishes from the thoracic to the abdominal aorta (6). In light of this knowledge, it is believed that the thoracic aorta is better protected from aneurysm formation compared to the abdominal aorta.

Table 3. Comparative statistics of subgroups of AA according to enlargement rate.

Variables	**Enlargement rate** Total n=98		p
	≤1 *cm/year* (n=87)	>1 *cm/year* (n=11)	
Gender			
Male	61 (70.1)	10 (90.9)	0.281[c]
Female	26 (29.9)	1 (9.1)	
Age	62.64±13.48	64.82±14.63	0.619[s]
AAA	34 (39.1)	8 (72.7)	0.051[c]
TAA	53 (60.9)	3 (27.3)	
Smoking	38 (43.7)	7 (63.6)	0.352[c]
Hypertension	39 (44.8)	8 (72.7)	0.154[c]
Medical treatment	70 (80.5)[a]	3 (27.3)[b]	**0.004**[c]
AA graft replacement	6 (6.9)[a]	2 (18.2)[a]	**0.004**[c]
EVAR	6 (6.9)[a]	3 (27.3)[b]	**0.004**[c]
AAA graft replacement	5 (5.7)[a]	3 (27.3)[b]	**0.004**[c]
Exitus	2 (2.3)	0 (0)	>0.999[c]
WBC	8.16±2.86	10.68±6.07	0.201[s]
Hb	13.40 (11.50-14.70)	12.40 (10.80-15.90)	0.547[m]
MCH	29 (27.60-30.20)	28.60 (27.80-29.90)	0.657[m]
RBC	4.78 (4.02-5.27)	4.24 (3.88-5.22)	0.344[m]
PLTx1000	221 (177-259)	184 (169-295)	0.613[m]
MPV	10.86±1.22	10.36±0.73	0.181[s]
NLR	2.29 (1.61-3.94)	3.35 (1.74-8.18)	0.151[m]
AST	18 (16-23)	18 (16-26)	0.731[m]
ALT	16 (13-22)	17 (13-36.10)	0.573[m]
T blr	0.47 (0.33-0.63)	0.52 (0.23-1.08)	0.800[m]
D blr	0.21 (0.16-0.27)	0.20 (0.13-0.33)	0.804[m]
HDL	53 (41-64)	45 (36-51.10)	0.180[m]
LDL	106.10 (86-126)	91 (85.60-113)	0.434[m]
Tgl	120 (90-173)	99 (65-135.20)	0.098[m]

[c]: Chi-Square test, [s]: Independent samples t-test, [m]: Mann Whitney U test. Descriptive statistics are expressed as mean±standard deviation, median (25^{th}-75^{th} percentiles), or frequency (percentage). The same letters in the same row indicate the similarity between column percentages, and different letters indicate the difference between column percentages. AAA: Abdominal aortic aneurysm, TAA: Thoracic aortic aneurysm, AA: Aortic aneurysm, EVAR: Endovascular aortic repairment, WBC (white blood cell), Hb (hemoglobin), MCH (mean cell hemoglobin), RBC (red blood cell), plt (platelet counts), MPV (mean platelet volume), NLR (neutrophile–lymphocyte ratio), AST (aspartate aminotransferase), ALT (alanine aminotransferase), t blr (total bilirubin), d blr (direct bilirubin), HDL (high- density lipoprotein), LDL (low-density lipoprotein), tgl (triglyceride).

Another proposition for AA development is that the upregulation of common pathways in terms of reactive oxygen radical production may lead to smooth muscle cell dysfunction, extracellular matrix destruction, and aortic inflammation (7,8).

Many etiologic factors were found to be related to the progression of AA, including advanced age, male sex, smoking, family history of aneurysm, family history of hypertension, and hypercholesterolemia (9,10). We found significant relationships between AAA and male sex, smoking, and familial history of AAA as reported in the literature; however, we did not find the same relationships for TAA.

Table 4. Comparison of aneurysm types according to enlargement rate.

Aneurysm type	**Enlargement rate (n / %)**		p
	≤1 *cm/year* (n=165)	>1 *cm/year* (n=16)	
AAA	54 (32.7)	12 (75)	**0.002**[c]
TAA	111 (67.3)	4 (25)	

[c]: Chi-Square test. Descriptive statistics are expressed as frequency (percentage). AAA: Abdominal aortic aneurysm, TAA: Thoracic aortic aneurysm.

Vuruşkan and Folsom demonstrated that AAA is significantly correlated with higher WBC counts and higher NLR compared with the control patients (3,4). We did not find a strong relationship of either higher WBC counts or higher NLR with AA. However, platelet counts were significantly higher in TAA group compared to AAA group.

In Cho's et al. study, AA has been found to be related to atherosclerosis and hypercholesterolemia (12). However, in the present study we did not find the same result. In our region, the Mediterranean diet is preferred. Perhaps, this habit let the blood lipid (LDL, tgl) level lower. Therefore, our results were not correlated with those in the literature.

Kang and Kawamoto's cohort studies show that increased levels of serum bilirubin protect vessels against atherosclerotic processes in peripheral arterial disease and carotid artery disease (13,14). However, we did not find any relationship between higher bilirubin levels and lower incidence of AA. In contrast, AST values are significantly higher in the TAA group.

Table 5. Univariate and multivariate logistic regression analysis results.

	Univariate logistic regression		Multivariate logistic regression	
	OR [95% CI]	p	OR [95% CI]	p
HDL	0.958 [0.919-0.998]	**0.040**	0.960 [0.919-1.003]	0.065
WBC	1.173 [1.025-1.342]	**0.020**	1.173 [1.015-1.354]	**0.030**
D1	1.529 [1.040-2.248]	**0.031**	1.560 [1.051-2.315]	**0.027**
D2	2.148 [1.469-3.140]	**<0.001**	-	-

OR: Odds ratio, CI: Confidence interval, HDL (high- density lipoprotein), WBC (white blood cell), D1: Initial diameter measurement of AA, D2: Second diameter measurement of AA.

Kirsch and Schmid's studies on TAA have focused on hereditary connective tissue disorders, bicuspid aortic valve association, and smooth muscle cell loss (5,15). In our study, there were no patients diagnosed with either connective tissue disorder or bicuspid aortic valve association.

Medical management up to surgical repair includes the control of risk factors that may prevent growth and rupture of AAs, but at present such medical therapies have limited success. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, and statins may be utilized to decrease the growth rate of AAs.

Conclusion

In the current study we found that TAA was associated with higher AST levels and higher platelet counts than were in the AAA group, whereas AAA showed strong relationships with male gender and smoking that were not observed for the TAA group.

New opportunities to determine various targets involved in vascular inflammation, cell death, extracellular matrix degradation, intramural thrombosis, and atherosclerosis of the vasa vasorum of the aortic wall are required. Relevant innovative research and studies are important and necessary.

Limitations: There are some limitations of our study. Firstly, its retrospective design may limit the ability to investigate detailed information of the patient population. Secondly, this study was designed as a single-center study; the number of patients can therefore be considered limited, and it needs to be repeated in a larger population sample. Also, no patients with Ehler-Danlos, Loeyz-Dietz or Marfan syndromes were included in this study, and there were also patients who were diagnosed with associated bicuspid aortic valve.

Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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The Evaluation of Muğla Sıtkı Koçman University Medical School Phase 2 Programme by Students

Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi Dönem 2 Programının Öğrenciler Tarafından Değerlendirilmesi

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Öz

Tıp eğitimi COVID-19 pandemisinden olumsuz etkilenmiştir. Bu çalışmanın amacı, ikinci sınıf tıp öğrencilerinin değerlendirmeleri ve koordinatörlerin raporları aracılığıyla yüz yüze ve uzaktan eğitim sisteminin avantajlarını ve dezavantajlarını araştırmaktır. Bu çalışmada, uzaktan ve yüz yüze eğitim dönemlerini karşılaştırmak için ikinci sınıf tıp öğrencilerinden alınan anketler ve koordinatörlük raporları incelendi. Kapalı uçlu sorular için Likert tipi derecelendirme ölçeği kullanıldı, açık uçlu cevaplar ise kategorize edildi. Çevrimiçi uzaktan eğitim sırasında kurul, final ve bütünleme sonuçlarının ortalamaları istatistiksel olarak yüksek bulundu. Yapılan anket ve raporlardan, uygulamalı eğitim verimliliği açısından çevrimiçi eğitimin tamamen yüz yüze eğitimin yerini alamayacağı öğrencilerden alınan yanıtlardan anlaşıldı. Bunula birlikte öğrencilerin pandemi koşullarında çevrimiçi öğrenme sürecinden memnun olduğu tespit edildi. Etkili çevrimiçi öğrenme için öğrencilerin çevrimiçi eğitime yönelik geri bildirimleri eğitmenler, kurumlar ve kurs tasarımcıları için özellikle yol gösterici olabilir. Yüz yüze eğitim çevrimiçi eğitim yöntemleri ile desteklenebilir.

Anahtar Kelimeler: Çevrimiçi Eğitim, Covid-19 Pandemisi, Geleneksel Eğitim, Tıp Eğitimi, Yüz Yüze Eğitim

Abstract

The COVID-19 pandemic has negatively impacted medical education. This study aimed to explore the pros and cons of face-to-face and distance education based on feedback from second-year students and coordinator reports. In this study, questionnaires and coordinator reports from second-year medical students were examined to compare distance and face-to-face education periods. Likert scales were used for closed-ended questions, and open-ended answers were categorized. Online distance education resulted in statistically high average scores for committee, final, and make up exams. While students indicated that online education cannot fully replace face-to-face learning in terms of applied education efficiency, they expressed satisfaction with the online learning process during the pandemic. For effective online learning, students' feedback on online education can be particularly guiding for instructors, institutions, and course designers. Face-to-face education can be supported with online education methods.

Keywords: Online Education, Covid-19 Pandemic, Traditional Education, Medical Education, Face to Face Education

Introduction

The first case of COVID-19 pandemic in the world was reported in China in December 2019. Subsequently, in recognition of the widespread proliferation of the contagion, the World Health Organization (WHO) officially classified the COVID-19 crisis as a pandemic on the 11th of March, 2020 (1). Within our national context, the inaugural COVID-19 case materialized on the very same date, the 11th of March, 2020 (2). Promptly responding to these unfolding events, the Council of Higher Education (CHE) implemented a comprehensive academic hiatus, suspending educational activities for a duration of three weeks, effective from the 16th of March, 2020 (3). Amidst the global response to the COVID-19 pandemic, health security imperatives have engendered a paradigm shift towards online learning. Notably, while online learning represents a singular recourse within the exigencies of the pandemic, the paramount significance of ensuring both student and instructor contentment underscores the efficacious educational experience (4).

This investigation encompasses the documentation provided by the Muğla Sıtkı Koçman University (MSKU) Faculty of Medicine Phase 2 coordinatorship, alongside the perspectives and appraisals voiced by Phase 2 students concerning the program under scrutiny. The focus spans two academic years: 2020-2021, which aligns with the COVID-19 pandemic era, and 2021-2022, marking the return to face-to-face education post-pandemic.

The Phase 2 program is structured into five distinct committees, each catering to a specialized realm of study: Committee-1 pertains to tissue biology, Committee-2 encompasses the circulatory and respiratory system, Committee-3 focuses on the nervous system, Committee-4 delves into the digestive system and metabolism, and Committee-5 addresses the excretory, reproductive, and endocrine systems. These committees encompass a comprehensive range of subjects, including Anatomy, Histology and Embryology, Physiology, Medical Biochemistry, Medical Microbiology, Biophysics, and Foreign Language instruction. Notably, the discipline of Biophysics is exclusively integrated into the curricula of the second and third

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committees, while the remaining subjects are consistently offered across all committees.

Furthermore, the Phase 2 program incorporates a series of practical modules to enhance students' applied competencies. Professional Skills Laboratory Practices (PSL), Problem-Based Learning (PBL), and Special Study Module (SSM) are essential components within this framework. PBL, specifically, is confined to the purview of the second committee, whereas PSL is exclusively administered within the context of the fifth committee. Conversely, the SSM finds its inclusion within the academic landscape of the third, fourth, and fifth committees.

The impact of PBL on the second committee examination and the influence of the SSM on the fifth course board assessment amount to 10 points. Students achieving a course committee average grade of 85 or higher, coupled with a minimum score of 60 or more in each individual course committee, are exempt from participating in the end-of-term examination. It is noteworthy that within a committee examination, distinct benchmarks are established for each course and corresponding practical/practice examination. The established threshold for attainment is set at 50%. In scenarios where a student's performance falls below 50% in one or more lectures contributing to the committee assessment, the disparity between the attained score in that specific subject and 50% of the cumulative score for that subject is subtracted from the overall examination score, thereby determining the ultimate grade for the course committee examination (5).

Within the realm of pedagogical strategies, feedback assumes an integral role as a facilitative component of the learning process (6). The evaluation of instructional methodologies encompasses a diverse array of tools, ranging from peer assessments, self-appraisals, external expert evaluations, mentor analyses, teaching portfolios, to student feedback. These evaluative mechanisms consistently contribute to the enhancement of curriculum design and the elevation of educational standards (7).

Demonstrating a commitment to comprehensive assessment, the Assessment and Evaluation Commission of our academic institution employs a structured questionnaire upon the culmination of each course committee. This questionnaire employs closed-ended and open-ended questions to garner insights from students concerning instructors, committee content, the Phase 2 curriculum, and examinations. This student-centric approach not only captures the student perspective on the educational milieu but also serves as a platform for the articulation of their viewpoints. Additionally, the Phase 2 coordinatorship orchestrates a series of initiatives, encompassing coordinator hours, course introductions, culminating-committee evaluations, interviews with dean, program assessments, and developmental progress summaries. These combined endeavors substantiate a holistic framework for continuous evaluation, refinement, and evolution of the instructional paradigm.

In light of the persistent and escalating pandemic circumstances, compounded by directives from CHE, MSKU Faculty of Medicine undertook a transformative shift in its educational paradigm. Commencing from the 16th of March, 2020, during the 2019-2020 academic year, and extending through the entirety of the subsequent 2020-2021 academic session, the institution seamlessly transitioned its pedagogical operations to a virtual framework of distance education. This momentous adaptation was necessitated by the persistent prevalence of the pandemic. In particular, the 2020-2021 academic year witnessed the sustained implementation of online, synchronous distance instruction, facilitated by the adept utilization of the university's distance education center infrastructure and resources, thereby employing the proficient course management system (distance learning system). A meticulous endeavor was undertaken to pre-emptively upload course materials onto the distance learning system platform, thus ensuring the seamless delivery of educational content.

In the subsequent academic term, spanning the duration of 2021-2022, a discernible pivot back to conventional, face-to-face educational methodologies was observed. This transition was guided by a strategic imperative to restore in-person educational engagement, thereby facilitating a comprehensive educational experience. Throughout this period, robust mechanisms for soliciting and assimilating continuous student feedback were actively cultivated, underscoring the institution's commitment to pedagogical excellence.

In the context of practical applications in the pandemic, students encountered a notable deviation from established protocols. Under the constraints of the pandemic, the traditional engagement in practical laboratory exercises was curtailed, leading to an adaptation wherein students resorted to video-based observations in lieu of hands-on participation. The pandemic-induced restrictions engendered a transformative pivot, redefining the dynamics of practical learning and propelling an exploration of alternative modes of pedagogy.

The disruptive ramifications of the pandemic permeated various facets of the academic landscape, ushering in a series of consequential alterations. Specifically, the conventional implementation of PBL encountered hindrances, rendering it unfeasible during the academic year of 2020-2021. Consequently, the pedagogical focus shifted towards alternative avenues, as remote and online platforms became the conduit for the application of other theoretical lectures, encompassing PSL and laboratory practices.

The diminution of Foreign Language instruction by 6 hours within the 2020-2021 academic year was attributed to public holidays. Noteworthy, the introduction of the SSM marked a significant enhancement in the Phase 2 curriculum, a development observed for the first time in the subsequent academic year of 2021-2022 (Table 1).

Table 1. The instructional hours during the academic periods of 2020-2021 and 2021-2022.

	Academic Periods	
	2020-2021	**2021-2022**
Theoretical Hours	580	615*
Practice Hours	140	192**
Total Hours	720	807

*Reason for Increase in Theoretical Hours: PBL 12, Foreign Language 6, Anatomy 3, Histology and Embryology 14 hours. **Reason for Increase in Practical Hours: SSM 40, Anatomy 6, Histology and Embryology 1 and Medical Microbiology 5 hours

A notable divergence lies in the absence of the dam system during the 2020-2021 academic year, a period characterized by the prevalence of distance education. In this context, the threshold for successful completion, previously set at 85 without a final examination, underwent adjustment to a benchmark of 65.

Furthermore, compensatory arrangements were orchestrated to address the disruption in practical instruction. Remedial sessions for PSL and Anatomy practices were meticulously devised and executed in a face-to-face format, strategically inaugurated at the outset of the 2021-2022 academic year.

Phase 2 lectures in the 2020-2021 academic year were seamlessly migrated to online platforms, facilitated through the distance learning system. However, a paradigmatic transformation was evident in the subsequent academic year of 2021-2022, as the educational encounters underwent a complete transition towards traditional face-to-face education, signifying a return to familiar pedagogical methodologies.

Material and Method

The research protocol was authorized by both the Dean of MSKU Faculty of Medicine (dated 2022/451397) and the MSKU Ethics Committee (dated 2022/220076), ensuring compliance with ethical standards. Notably, the investigation upheld a stringent approach to data protection, wherein no personally identifiable or sensitive student information was incorporated into the study.

All students enrolled in the 2020-2021 and 2021-2022 academic years were invited to participate in the study on a voluntary basis to respond to the scale items. Data from students who did not consent to participate were not included. The survey data from students who agreed to participate in the study were used retrospectively. Within the study's framework, a meticulous evaluation of the MSKU Faculty of Medicine Phase 2 curriculum encompassed an appraisal of its five committees. This comprehensive assessment was conducted through a retrospective examination of responses provided by students, encompassing a questionnaire featuring a blend of nine closed-ended and one open-ended questions at the conclusion of each course committee. The qualitative data stemming from the open-ended question were systematically categorized and subjected to a thorough evaluation. Significantly, both the open-ended question and the nine closed-ended questions were designed to correlate with the prevailing mode of education, distinguishing between distance education during the 2020-2021 academic year and in-person instruction during the 2021-2022 academic year. This open-ended format facilitated an in-depth exploration of participant sentiments.

Elaborating upon the specifics of the questionnaire's closed-ended queries, comprehensive details are expounded in Table 2.

In addition to the aforementioned data sources, the analysis encompassed the Phase 2 coordinator's report, coordinatorship hours, insights garnered from the dean's interview, and student feedback extracted from the course evaluation meeting. Notably, the evaluation process incorporated feedback received from a minimum of three distinct individuals, thereby enriching the robustness of the assessment.

The evaluation parameters for the closed-ended questions within the questionnaire were appraised using a Likert-type rating scale, presenting respondents with a selection from five distinct options encompassing "strongly disagree, disagree, partially agree, agree, and strongly agree." Concomitantly, the responses to the nine closed-ended questions underwent quantification, with Strongly Disagree assigned 1 point, Disagree attributed 2 points, Partially Agree denoted as 3 points, Agree designated 4 points, and Strongly Agree associated with 5 points.

Calculation of total scores ensued by amalgamating the responses for each question within the questionnaire, subsequently multiplying these responses by their corresponding point values. The derived scores for each question were then normalized by dividing the cumulative scores by the number of participants engaged in the survey, thereby yielding the weighted average values for each question, delineated distinctly across the academic years (as delineated in Table 2).

Table 2. Weighted Average Scores Derived from Responses to Closed-Ended Queries in the Committee Evaluation Questionnaire.

Closed Ended Questions	Mean (±) SD		*p*
	2020-2021	2021-2022	
1. Instructors adhered to the stipulated commencement and conclusion times of the lectures	**3.90±0.05**	3.55±0.13	<0.001
2. The instructors recommended accessible sources of information that I could readily avail	3.78±0.05	3.66±0.10	<0.001
3. I experienced a pleasant and constructive interaction with the instructors	3.84±0.07	3.75±0.17	<0.001
4. The instructors dedicated an adequate amount of time to fostering discussions and facilitating the expression of students' personal viewpoints	3.89±0.09	3.59±0.10	<0.001
5. Adequate time was allocated for personal learning pursuits	3.58±0.16	**3.19±0.23**	<0.001
6. Adequate practical applications corresponding to the program's subject matter were available	**3.45±0.13**	3.54±0.09	<0.001
7. The practices were carried out in a way that supports my individual learning	3.49±0.12	3.57±0.10	<0.001
8. The exams accurately gauged my knowledge level and encompassed questions spanning the entirety of the knowledge taught	3.71±0.12	3.43±0.12	<0.001
9. The adoption of distance education negatively influenced the attainment of learning objectives (2020-2021) The adoption of face-to-face education positively influenced the attainment of learning objectives (2021-2022)	3.55±0.21	**3.76±0.13**	<0.001

It is noteworthy that the numerical scale was assigned corresponding levels of interpretation: 1 point represented a state considerably below expectations, 2 points signified a level below expectations, 3 points indicated an alignment with expectations, 4 points indicated performance surpassing expectations, and 5 points reflected an achievement substantially beyond expectations.

The information amassed within our investigation underwent rigorous analysis employing the software application "SPSS for Windows 23.0." Descriptive statistical techniques, encompassing frequency (n), percentages (%), mean ± standard deviation (SD), were harnessed to elucidate the dataset's characteristics. Disparate continuous variables characterized by a normal distribution were juxtaposed through Student's t-test (specifically, the independent samples t-test) for comparison, with a significance threshold of $p<0.05$ deemed statistically significant. Additionally, the narrative was enriched with the inclusion of notable appraisals and insights derived from the responses to open-ended questions.

Results

The MSKU Phase 2 Turkish Medicine Program witnessed an enrollment of 179 students during the academic year 2020-2021, while the subsequent academic year, 2021-2022, recorded a slightly reduced student count of 157. The research scope encompassed surveys from committees, specifically those with a participation rate of 50% or greater, while omitting the first committee survey of the 2020-2021 academic year and the third committee survey of the 2021-2022 academic year.

Based on the outcomes of the closed-ended survey administered to students enrolled in the Turkish Medicine program during the 2020-2021 academic year, the most favorable rating was garnered by the inaugural query, "Instructors adhered to the stipulated commencement and conclusion times of the lectures." Conversely, the sixth inquiry, "Adequate practical applications corresponding to the program's subject matter were available," received the lowest rating, signifying an area of concern.

In correlation with the students closed-ended questionnaire outcomes for the subsequent academic year, 2021-2022, the ninth query emerged as the highest scorer, affirming that "The adoption of face-to-face instruction positively influenced the attainment of learning objectives." Conversely, the fifth question, "Adequate time was allocated for personal learning pursuits" received the lowest evaluation. Remarkably, this particular question exhibited the most prominent discrepancy in average ratings between the two academic years, a trend expounded upon in Table 2.

The academic landscape of the 2020-2021 year, characterized by the online education, notable statistical elevation was discerned in the academic achievements of students across board exams, final examinations, and make-up assessments. A demonstrable correlation between the adoption of distance education and the attainment of elevated grades emerged as a salient observation.

There were fewer students in the 2021-2022 academic year. Paradoxically, within the initial phase of resuming face-to-face education after the pandemic, a notable increase was observed in the proportion of students to retake the Phase 2, The juxtaposition of these phenomena is comprehensively illustrated in Table 3.

Table 3. Mean of Examination Scores Across Different Years.

	Academic Periods	
	2020-2021	2021-2022
Committee 1 Exam Score	78.1±12.1	63.4±16.8
Committee 2 Exam Score	79.5±12.8	58.5±15.8
Committee 3 Exam Score	84.9±9.8	58.1±19.4
Committee 4 Exam Score	84.2±11	67.4±18.8
Committee 5 Exam Score	84.5±11.7	72.3±18.2
Final Exam Score	82.96±9.8	65.7±19.4
Make-up Exam Score	52±5.7	46.8±21.8
Rate of Participation in Make-Up Exam	1.67	2.14
Number of Students Required to Repeat Phase 2	3	22
Total Number of Students	179	157

The open-ended question in the study garnered responses from a minimum of three distinct individuals, and these feedbacks were subsequently subjected to a comprehensive categorization. Within each categorized segment, affirmative and adverse remarks were meticulously organized based on their respective frequencies of occurrence, resulting in a descending sequence from the most prevalent to the least. This systematic presentation strategy was employed to facilitate a comparative evaluation between the two academic years, effectively illustrated through the juxtaposition of data in both Table 4 and Table 5.

Discussion

Our nation has been confronted with the contemporary challenges of the COVID-19 pandemic, necessitating an immediate shift towards remote learning, and the consequential impact of the Kahramanmaraş-centered earthquake, which reverberated across 11 provinces. In light of these adverse circumstances, conventional in-person instruction has been supplanted by distance education as a viable alternative (8). The subsequent adoption of online learning for distance education has engendered a constellation of concerns encompassing student contentment, the efficacy of both practical and theoretical lessons, the safeguarding of examination integrity, and the complex interplay of psychological well-being, spanning stress and anxiety, in tandem with health issues arising from prolonged screen exposure and heightened internet utilization.

Table 4. Grouped Positive Responses From The Open-Ended Question Within The Committee Evaluation Questionnaire.

2020-2021 Academic Year	2021-2022 Academic Year
Positive feedback regarding the execution of the lectures	
The faculty members and the administrative office demonstrated dedicated efforts to ensure the seamless advancement of education and training during the epidemic.	Face-to-face education is useful, I am inclined to continue with traditional education rather than transitioning to online platforms.
The pandemic situation was effectively handled, fostering a secure and productive working environment.	Following the pandemic, face-to-face learning provided a sense of liberation.
I perceive the distance education process as proficient and fruitful.	I express contentment with both the instructional content and the teaching methodology.
The viability of distance education can be extended to theoretical courses.	The student affairs offered valuable assistance.
	Participation in the PBL yielded productive outcomes.
The theoretical lectures are of high quality and yield favorable outcomes.	Engagement with the SSM proved to be a productive endeavor.
The opportunity to revisit theoretical lessons later proved beneficial and significantly useful.	
The provision of extra time for revision facilitated a more efficient learning experience.	
The synchronous delivery of lessons facilitated effective tracking of the curriculum.	
Engaging in remote learning allowed me to study more comfortably at home and allocate time for personal endeavors.	
Positive feedback about exams	
During the pandemic, distance education emerges as the most fitting mode of education.	The examination effectively assessed our understanding of the subject matter.
	I am content with the comprehensive disclosure of the laboratory exam scores.

Table 5. Grouped Negative Responses From The Open-Ended Question Within The Committee Evaluation Questionnaire.

2020-2021 Academic Year	2021-2022 Academic Year
Negative feedback regarding the execution of the lectures	
Distance education posed challenges from both social and educational perspectives, and it fell short in meeting my needs. The process left me feeling aimless and sapped my energy for keeping up with the coursework.	There is a need for dedicating more time to individual study.
The extended duration of virtual lessons, delivered through computer screens, led to certain health issues.	The syllabus is intensive.
Allocating more time for individual study is essential.	The lecture hours of some committees are long and intense.
Remote practical lessons lacked effectiveness, failing to provide robust individual learning and leaving information retention inadequate. Incorporating additional practice videos should be made and compensating for the absence of face-to-face models and cadavers should be made up.	Adhering to the stipulated lesson duration is important.
Financial constraints and the psychological impact of remote teaching adversely affected the educational experience.	Scheduled breaks should align with the program, avoiding consecutive lectures.
Excessive lecture hours on some committees demanded prolonged computer use, which detrimentally impacted health.	Increasing the hours of practices would be beneficial.
It's advisable not to exceed the prescribed duration of lessons.	It is inefficient to teach more than 2 hours a day from the same branch.
Enhanced instructor communication would be beneficial.	Distributing course hours evenly across the week enhances efficiency.
Coordinating lesson topics more effectively is desirable.	The syllabus underwent frequent changes.
The absence of PBL training was notable.	Coordination between lecture topics should be enhanced.
Epidemic-related restrictions impeded my ability to venture outdoors, given the discordance between curfew hours and the curriculum for those under 20.	The brief break following a committee exam is insufficient; additional days off post-exams are necessary to prepare mentally for the next committee.
	Having new lectures during the exam week detrimentally affects my studying.
	I struggle to keep up with the lecture pace.
	Providing extra points for laboratory notebooks would be beneficial.
Negative feedback regarding the instructional materials	
Uploading the presentation slides onto the online platform before the lesson is beneficial.	Uploading the presentation slides onto the online platform before the lesson is beneficial.
Lecture slides could include more textual content, or instructors could provide additional notes regarding the topic.	Enhancing the level of detail in the lecture notes would be advantageous.
	The presence of English-language slides had a negative impact.
Negative feedback about exams	
I encountered issues like freezing during the exam, delayed loading of photo questions, and waiting for the next question in the committee exam, causing concerns about time management and inducing stress.	The distribution of questions in the theoretical exam was uneven.
After moving on from a question in the exam, I recalled the answer later but was unable to revisit it, leading to a negative impact.	Insufficient pre-exam information for the first face-to-face exam resulted in stress.
The lack of suitable resources and an effective study environment hindered my exam and lecture performance.	I desire to know how many points I scored in each branch within the exam.
Implementing a camera system during exams is essential.	Theoretical exam questions were challenging.
A more balanced distribution of question difficulty in exams would be beneficial.	
Given the challenges of distance education, the passing grade or the passing grade without a final should be reduced and the conditions should be alleviated.	

Medical faculties have persistently endeavored to curtail the extent of traditional lectures, harness technological innovations to enhance the pedagogy of laboratory sessions, foster an environment conducive to active and autonomous learning, and promote personalized and interdisciplinary educational approaches (9). Within our own academic setting, students enrolled in Phase 2 courses consistently conveyed a feedback of elevated theoretical course load, reflecting in the feedback submitted over successive academic years. Guided by the amalgamation of student insights and scholarly discourse, we posit that an augmentation of dedicated self-study periods could potentially yield advantageous outcomes.

The emergence of the COVID-19 pandemic precipitated a transformative shift towards virtual education, introducing formidable hurdles within the domain of medical pedagogy. Health educators, in response, have been compelled to strategize and tailor their instructional methodologies to align with the exigencies of the prevailing circumstances (10). Notably, the efficacy of online learning hinges upon a constellation of variables, spanning content relevance, user interface sophistication, cultivation of a collaborative learning community, and the optimization of learning outcomes, all of which play a pivotal role in fostering contentment among students and faculty members alike (11). Within the precincts of our faculty, the seamless integration of course materials within the distance learning system has facilitated effortless accessibility for students. Additionally, to ensure a smooth transition, a comprehensive distance learning system user manual, enriched by instructional videos, has been furnished to both students and educators. Furthermore, a dedicated initiative encompassing specialized training courses has been orchestrated for educators, fostering their adeptness in navigating digital educational platforms. This comprehensive approach collectively underscores our commitment to embracing the digital paradigm and engendering a robust online learning ecosystem.

Within the scope of our present inquiry, students enrolled in the 2020-2021 academic year expressed contentment concerning the communicative efficacy and adaptability exhibited during the period of online learning. However, the protracted duration of exclusively online instruction yielded certain challenges, manifesting as health-related issues, psychological implications, ineffectual practical lessons, and the conviction that virtual education inadequately substitutes traditional in-person interactions. Collaborative activities during online learning were perceived as cumbersome, rendering distance education less efficient. Additionally, students voiced grievances pertaining to inadequate resources and examination-related predicaments. Conversely, during the subsequent academic year of 2021-2022, students testified to their satisfaction with face-to-face education, perceiving greater autonomy and a reluctance to revert to online learning. This revelation, congruent with existing scholarly discourse (12,13), accentuates a pronounced preference for in-person pedagogy. Nonetheless, even within the context of conventional classroom-based instruction, students notably registered concerns about the intensity of the curriculum and the dearth of time allocated for independent study. Crucially, a common feedback thread emerged from our investigation, where students in both educational modalities articulated the imperative for instructors to adhere to prescribed course durations, allocate augmented time for individual study, and optimize the sequential arrangement of courses within the curriculum. Supplementary recommendations included the timely uploading of course materials onto the distance learning system prior to lessons, the provision of more comprehensive lecture notes, and a preference for lecture slides to be presented in the native language. Moreover, student perspectives extended to the examination realm, with a discernible plea for balanced question difficulty levels in assessment instruments. The comprehensive analysis encapsulated a nuanced tapestry of student viewpoints, enriching our understanding of the educational landscape and pinpointing areas primed for targeted improvements.

During the academic term of 2021-2022, a significant addition materialized in the form of the SSM, an inaugural inclusion within the Term 2 curriculum, endowing students with 10 European Credit Transfer and Accumulation System (ECTS) credits. This novel module, spanning a two-hour weekly commitment within the 3rd, 4th, and 5th committees, elicited favorable satisfaction among students. Notably, the phase 2 committee exams introduced practical assessments for Anatomy, Histology and Embryology, as well as Medical Microbiology courses, supplementing the conventional theoretical evaluations. Remarkably, a noteworthy shift transpired in the administration of exam results. Initially, the results of the practical and theoretical exams were announced as a single score. However, in response to student feedback following the first committee assessment, the Phase 2 coordinatorship adopted a new approach, meticulously delineating practical examination results for each individual course. This granular reporting of practical exam scores garnered student approval, underscoring their contentment with this refined assessment reporting mechanism. During the pandemic, the implementation of practical exams rendered unfeasible within the context of distance education.

In a comprehensive examination involving over 230,000 undergraduate students, as conducted by Bettinger et al., a discernible pattern emerged indicating that engagement in online coursework corresponded to a decrease in student academic performance by approximately one-third of a standard deviation (14). Curiously, in stark contrast to existing scholarly literature, our own investigation unveiled a contrary outcome, characterized by an augmentation of grade point averages. This anomaly could potentially be attributed to the inherent advantages of distance education, such as unrestricted access to educational resources and course materials, alongside the flexibility to revisit and reinforce subject matter at one's convenience. Parallelly, while the CHE introduced a regulatory framework pertaining to online instruction, entrusting the execution to individual universities, distinct operational choices have ensued. In the

context of MSKU Faculty of Medicine, the matter of exam invigilation has been an area of intensive inquiry. Notably, the decision was made to abstain from mandating the use of cameras during exams, primarily due to factors encompassing the absence of camera-equipped devices among certain students. Moreover, the imposition of mandatory camera activation could potentially raise concerns surrounding the infringement of personal privacy, invoking potential legal ramifications. The implementation of a nationwide directive mandating the utilization of cameras during exams is envisaged as a potential avenue to substantially mitigate the prevalent issue of exam security across universities. Concurrently, the orchestration of additional factors influencing academic achievement are important. Notably, within the framework of in-person instruction, the congruence of instructors with stipulated course commencement and conclusion times appears less pronounced in contrast to the online educational period. This variance might significantly impact student motivation and overall success. Furthermore, the transition to conventional face-to-face teaching has been notably hindered by circumstantial challenges brought about by the enduring repercussions of the COVID-19 pandemic. In particular, instructors grappled with disruptions stemming from COVID-19 infections or potential illnesses, which impeded their ability to maintain strict adherence to the prescribed curriculum. Conclusively, an additional consideration surfaces from the absence of the "dam system" during the 2020-2021 academic year, coinciding with the prevalence of distance education. This variance in evaluation methodology may have contributed to the elevation of students' board examination grades.

Amid the exigencies posed by the pandemic, participants at Manisa Celal Bayar University Faculty of Medicine expressed contentment with the online e-PBL sessions. However, alongside this contentment, it was underscored that while online learning was satisfactory, it remained clear that it could not wholly supplant the irreplaceable value of in-person instruction (15). Within our academic setting, an immersive one-week PBL module, encompassing 10 ECTS credits, is administered as part of the 2nd Term Committee. Notably, the continuity of PBL instruction was momentarily disrupted during the period of distance education, but it was subsequently reinstated and effectively reinstated during the 2021-2022 academic year. Importantly, the academic year 2022-2023 marked the inauguration of e-PBL sessions, a novel and pioneering approach in our faculty.

When the studies are examined, it is seen that the difficulties experienced in medical education during the pandemic were emerged, and solutions and innovations for the continuation of medical education were determined (16). It is observed that the use of technology in lessons can enable students to learn more interactively and help the learning process (17). There are also studies showing that three-dimensional visualization is a significantly more effective learning method compared to traditional methods (18).

The integration of online learning within the realm of medical education encompasses an array of advantageous attributes, notably cost-efficiency, heightened temporal and spatial flexibility, and the inherent ability to seamlessly integrate updated content (19). Furthermore, the assimilation of e-learning platforms furnishes medical students with a valuable opportunity to acclimate themselves to the evolving landscape of web-based medicine, replete with burgeoning digital health services (16). Notably, the survey respondents, comprising students, conveyed reservations concerning their access to adequate devices, in addition to grappling with internet connectivity issues and speed-related constraints. Moreover, the predicament of sharing a single device among multiple users posed an obstacle to attending synchronous lessons. This predicament substantiates the premise that prioritizing investments in the realm of online education, coupled with the establishment of standardized practices, is a prudent course of action, poised to address these issues and optimize the learning environment.

Conclusion

The insights garnered from students' perspectives on both online and in-person learning hold the potential to furnish valuable insights for educators, institutions, and curriculum designers. This trove of feedback equips them with the necessary insights to curate enriching and effective online learning encounters while also harnessing technology adeptly in conventional classroom settings. A paradigm shift towards innovation in medical education beckons, inviting a reevaluation of both established and contemporary instructional paradigms. Through the lens of this study's findings, a dual-pronged objective emerges: to contribute to the advancement of both traditional and distance education, ultimately bolstering the caliber of educational provision. Presently, the utilization of online distance learning remains unbounded, deployed sporadically and for indeterminate durations. In light of this, we advocate for the widespread proliferation of internet connectivity and accessible online learning tools across the educational spectrum, thereby preemptively curbing the emergence of opportunity disparities and embracing a more forward-looking, contemporary approach to education.

Conflict of interest statement

The authors hold no affiliations or relationships that could give rise to any potential conflicts of interest.

Ethics Committee Approval: In the course of this investigation, strict adherence was observed to the entirety of the guidelines delineated in the "Higher Education Institutions Scientific Research and Publication Ethics Directive." No actions that contravene the principles outlined in the directive's section titled "Actions Contrary to Scientific Research and Publication Ethics" were undertaken. Furthermore, formal authorization was procured for the execution of this study from the MSKU Faculty of Medicine (dated 2022/451397) and the MSKU Ethics Committee (dated 2022/220076).

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Risk of Recurrence After Anti-Seizure Medication Discontinuation

Nöbet Önleyici İlaç kesimi Sonrası Rekürrens Riski

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Öz

Uygun nöbet önleyici ilaç tedavisi ile epilepsi hastalarının yaklaşık 2/3'ünde nöbetsizlik sağlanabilmektedir. Uzun süreli nöbetsizlikten sonra hem hastalar hem de hekimler için ilaçların kesilmesi fikri ön plana çıkmaktadır. Biz de bu çalışma ile nöbet önleyici ilaç tedavisi kesilen hastalarda nöbet nüks oranlarını ve nüksü etkileyen faktörleri araştırmayı amaçladık. Çalışmaya 50 hasta dahil edildi. Hastaların 28'i (%56) kadındı, yaş ortalaması 41.28±14.58 yıl ve ortalama epilepsi süresi 15.20±9.90 yıldı. Hastaların 14'ünde (%28) nüks gözlendi. Nüks risk faktörleri incelendiğinde, nöbetsizlik süresi arttıkça nüks riskinin azaldığı tespit edildi. Çalışmamız nöbet önleyici ilaçların kesilmesinden sonra nüks riskinin ilaç kesim öncesi nöbetsizlik süresi uzadıkça azaldığını desteklemektedir. Ancak, ilacı bırakma kararının hasta bazında bireyselleştirilmesi gerektiği unutulmamalıdır.

Anahtar Kelimeler: Epilepsi, Nöbet Önleyici İlaç Kesimi, Nöbetsizlik, Nüks

Abstract

With appropriate anti-seizure medication, long-term seizure freedom can be achieved in about 2/3 of patients with epilepsy. After long-term seizure freedom, the idea of medication discontinuation arises for both patients and physicians. In this study, we aimed to investigate seizure recurrence rates and the factors affecting recurrence in patients whose anti-seizure medication treatment was discontinued. Fifty patients were included in the study. Twenty-eight (56%) patients were female, with a mean age of 41.28±14.58 years and a mean duration of epilepsy of 15.20±9.90 years. Recurrence was observed in 14 (28%) patients. When the recurrence risk factors were analyzed, it was observed that the risk of recurrence decreased as the seizure-free period increased. Our study supports that the risk of relapse after discontinuation of anti-seizure medications decreases as the seizure-free period is prolonged. However, it should not be forgotten that the decision to discontinue medication should be individualized.

Keywords: Epilepsy, Anti-Seizure Medication Discontinuation, Seizure-Free, Recurrence

Introduction

Although epilepsy is one of the most common chronic neurological diseases, long-term seizure freedom can be achieved in approximately 2/3 patients with appropriate anti-seizure medications (ASMs) (1). However, long-term use of ASMs has several adverse effects on many systems, including the kidneys, liver, central nervous system, and fertility, as well as negative impacts on the quality of life and economic status of patients (2). Consequently, after a long-term absence of seizures, the idea of discontinuing medication arises for both patients and physicians. Predicting the risk of seizure recurrence after discontinuation is the most important point in the decision and timing of medication discontinuation. In previous studies, it was claimed that medication discontinuation should be discussed with patients who have achieved seizure freedom for 2 to 5 years after treatment with ASMs. However, it was reported that the risk of recurrence after medication discontinuation should be carefully evaluated (3-7). As studies on recurrence rates after medication discontinuation increased, many new algorithms that may indicate the risk of recurrence were developed. It was emphasized in many studies that the risk of recurrence is never guaranteed to be zero (8). Additionally, to emphasize that epilepsy is not a disease that can be ultimately cured, the International League Against Epilepsy (ILAE) Task Force introduced a new definition. They suggested using the term 'resolved' to describe a situation where the individual no longer has active epilepsy. This terminology underscores that while the person might not currently experience epileptic events, there is no absolute assurance that the condition will not recur in the future. The task force further stated that the risk of recurrence can depend on multiple factors such as the type of epilepsy, age, syndrome classification, etiology, treatment, and various other factors (9). In recent studies, recurrence rates have been demonstrated to vary between 12% and 67% (10).

We aimed to investigate the seizure recurrence rates and the factors affecting recurrence in patients

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in whom treatment of ASMs was discontinued in our clinic. We want to underline the importance of continuous monitoring and individualized patient management even after a period of seizure freedom.

Material and Method

This study was approved by the ethics committee of Antalya Training and Research Hospital (2024/072). The files of all patients who were followed up in the epilepsy outpatient clinic of Antalya Training and Research Hospital between 2012 and 2023 were retrospectively reviewed. Patients with a definite diagnosis of epilepsy according to the ILAE 2014 definition of epilepsy (9), and who self-discontinued their medication for any reason, and all epilepsy patients whose anti-seizure medication was completely discontinued under physician control after 2 years or more of seizure-free status, were included in the study. Age, gender, age at onset, duration of the disease, seizure type, epilepsy type, family history, parental consanguinity, history of febrile convulsions, etiology of the disease, neurological examinations, cranial magnetic resonance imaging (MRI) findings, ASMs used, last discontinued ASMs, seizure-free period and electroencephalogram (EEG) findings before and after medication discontinuation were recorded.

Patients younger than 18 years of age, patients who had seizures during the discontinuation of ASMs, patients who voluntarily discontinued the medication but had not been seizure-free for a period of 1 year before discontinuation, patients who did not present to the hospital in the last 6 months after discontinuation and patients with a follow-up period of less than 1 year after drug discontinuation were excluded from the study.

Statistical Method

The data were analyzed with IBM SPSS V23. The conformity to the normal distribution was examined by the Shapiro-Wilk test. Yates correction, the Fisher-Exact test, and the Fisher-Freeman-Halton test were used to compare categorical variables between groups. Mann-Whitney U test was performed for the comparison of non-normally distributed data according to the binary group. The effect of independent variables on the recurrence time was analyzed by Cox regression analysis. Log Rank (Mantel-Cox) test was utilized to compare the duration of recurrence according to the number of seizure-free years. The results of the analyses were presented as mean±standard deviation and median (minimum- maximum) for quantitative data and frequency (percentage) for categorical data. The significance level was taken as $p<0.05$.

Results

The medical records of 3200 patients who were followed up in the epilepsy outpatient clinic of Antalya Training and Research Hospital between 2012 and 2023 were analyzed. Fifty patients who had discontinued anti-seizure medication and met the appropriate criteria were included in the study. Twenty-eight (56%) of the patients were female, with a mean age of 41.28±14.58 years and a mean duration of epilepsy of 15.20±9.90 years. Recurrence was observed in 14 (28%) patients. Nine (18%) patients discontinued their medication on their own, and recurrence developed in 55.5% of these patients. This group constituted 35.7% of the patients with recurrences. Recurrence was observed in 10 (71.5%) patients within the first year and 80% of these patients had recurrence within the first 6 months. While 3 (21.4%) patients developed recurrence within the 2nd year, 1 (7.1%) patient had recurrence within the 3rd year.

Patients were divided into two groups: those with recurrence and those without recurrence, and no difference was observed between age, gender, epilepsy type, duration of epilepsy, presence of etiology, presence of pathology on cranial MRI, and EEG abnormalities both during and after discontinuation (Table 1).

The effect of independent risk factors on recurrence was analyzed by Cox regression analysis with univariate and multiple models. When the results of the univariate model were analyzed, the risk of recurrence was 24.96 times higher in generalized epilepsy compared to focal epilepsy ($p=0.009$). The risk of recurrence increased 1.379 times as the seizure-free period decreased ($p=0.023$). In the multiple model, the risk of recurrence increased 1.488 times as the seizure-free period decreased ($p=0.034$). Other variables had no statistically significant effect ($p>0.050$) (Table 2).

The recurrence time did not differ when the seizure-free periods were divided into 2 groups: >5 years and ≤5 years ($p=0.516$). The mean recurrence time was 76.455 months in the 5 years or less group and 91.165 in the >5 years group (Table 3) (Figure 1).

Table 1. Comparison results according to recurrence.

	Recurrence		Total	Test	p
	Available (n=14)	N/A (n=36)	(n=50)	statistics	
Age	40.07±13.14 37.00(24.00-67.00)	41.75±15.26 38.50(22.00–70.00)	41.28±14.58 37.50(22.00-70.00)	237.000	0.746[a]
Gender					
Female	6 (42.9)	22 (61.1)	28 (56)	0.723	0.395[b]
Male	8 (57.1)	14 (38.9)	22 (44)		
Etiology					
Yes	6 (42.9)	20 (55.6)	26 (52)	0.242	0.623[b]
No	8 (57.1)	16 (44.4)	24 (48)		
Etiology					
Perinatal injury	1 (16.7)	1 (5)	2 (7.7)		
Febrile convulsions	2 (33.3)	2 (10)	4 (15.4)		
CNS Infection	0 (0)	2 (10)	2 (7.7)		
Head Trauma	3 (50)	8 (40)	11 (42.3)	4.460	0.718[d]
SAH-CVD	0 (0)	3 (15)	3 (11.5)		
Brain Tumor	0 (0)	2 (10)	2 (7.7)		
Other	0 (0)	2 (10)	2 (7.7)		
Age at Epilepsy Diagnosis (years)	21.00±15.05 17.00	28.00±16.47 25.00	26.04±16.25 22.50	174.000	0.092[a]
Duration of epilepsy (years)	19.07±9.37 16.00	13.69±9.81 11.00	15.20±9.90 13.50	163.500	0.056[a]
Epilepsy Type					
Focal	9 (64.3)	25 (69.4)	34 (68)		
Generalized	1 (7.1)	0 (0)	1 (2)	2.350	0.406[d]
Unclassified	4 (28.6)	11 (30.6)	15 (30)		
History of Status Epilepticus					
Yes	1 (7.1)	4 (11.1)	5 (10)	---	1.000[c]
No	13 (92.9)	32 (88.9)	45 (90)		
Cranial MRI Findings					
Lesion available	5 (35.7)	16 (44.4)	21 (42)	0.059	0.808[b]
Lesion N/A	9 (64.3)	20 (55.6)	29 (58)		
Used medication					
Monotherapy	12 (85.7)	28 (77.8)	40 (80)	----	0.704[c]
Polytherapy	2 (14.3)	8 (22.2)	10 (20)		
ASM					
Levetiracetam	6 (42.9)	12 (33.3)	18 (36)		
Carbamazepine	3 (21.4)	10 (27.8)	13 (26)		
Oxcarbazepine	0 (0)	5 (13.9)	5 (10)		
Valproate	3 (21.4)	4 (11.1)	7 (14)	6.141	0.550[d]
Lamotrigine	1 (7.1)	3 (8.3)	4 (8)		
Topiramate	0 (0)	1 (2.8)	1 (2)		
Zonisamide	0 (0)	1 (2.8)	1 (2)		
Phenytoin	1 (7.1)	0 (0)	1 (2)		
Duration of epilepsy until remission (years)	13.21±7.43 11.50	10.08±8.16 6.50	10.96±8.02 8.50	173.000	0.087[a]
Duration of use of Discontinued ASM (years)	8.21±4.51 9.50	7.61±5.45 5.50	7.78±5.16 7.00	217.500	0.454[a]
Duration of seizure-free (years)	3.71±2.74 3.50	6.33±4.49 5.00	5.6±4.25 4.50	163.000	0.053[a]
EEG on discontinuation of ASM					
Abnormal	4 (28.5)	5 (13.9)	9 (18)	0.649	0.422[d]
Normal	10 (71.5)	31 (86.1)	41 (82)		
EEG after discontinuation of ASM					
Abnormal	3 (21.5)	3(9.1)	6 (12)	0.631	0.427[d]
Normal	11 (78.5)	33 (91.9)	44 (88)		
Previous DiscontinuationAttempt					
Yes	2 (14.3)	1 (2.8)	3 (6)	---	0.186[c]
No	12 (85.7)	35 (97.2)	47 (94)		
Reason for Discontinuation					
Seizure freedom	9 (64.3)	32 (88.9)	41 (82)	---	0.094[c]
Self- discontinuation	5 (35.7)	4 (11.1)	9 (18)		

[a]Mann-Whitney U test, [b]Yates correction, [c]Fisher-Exact test, [d]Fisher-Freeman-Halton test, mean±s. deviation, median (minimum - maximum), frequency (percentage). CNS: Central Nervous System, SAH: Subarachnoid Haemorrhage, CVD: Cerebrovascular Disease, MRI: Magnetic Resonance Imaging, ASM: Anti-seizure Medication, EEG: Electroencephalogram

Table 2. Analysing the risk factors affecting the duration of recurrence by Cox regression analysis

	Univariate		Multiple	
	HR (95%CI)	p	HR (95%CI)	p
Age at Epilepsy Diagnosis	0.977 (0.939 – 1.016)	0.241	0.989 (0.912 – 1.073)	0.795
Seizure Frequency	1.006 (0.995 – 1.017)	0.295	1.007 (0.989 – 1.026)	0.429
Epilepsy Type (Reference: Focal)				
Generalized	24.96 (2.198 – 283.453)	**0.009**	3.932 (0.025 – 613.591)	0.595
Unclassified	1.061 (0.326 – 3.453)	0.921	1.147 (0.158 – 8.322)	0.892
History of Status Epileptikus (Reference: None)	0.631 (0.081 – 4.912)	0.660	0.879 (0.084 – 9.204)	0.915
ASM (Reference: Monotherapy)	0.58 (0.13 – 2.596)	0.476	0.322 (0.04 – 2.581)	0.286
Duration of epilepsy until remission	1.042 (0.981 – 1.108)	0.183	1.063 (0.92 – 1.227)	0.406
Duration of use of Discontinued ASM	1.014 (0.919 – 1.119)	0.777	1.133 (0.916 – 1.4)	0.250
Duration of seizure freedom	0.725 (0.55 – 0.956)	**0.023**	0.672 (0.465 – 0.971)	**0.034**
Reason for Discontinuation (Reference: seizure freedom)	2.83 (0.945 – 8.475)	0.063	3.39 (0.645 – 17.805)	0.149

HR (95% CI): Hazard rate (95% confidence interval). ASM: Anti-seizure Medication

Discussion

In our study, the relapse rate was 28% after discontinuation of ASMs. In previous studies, a wide range of relapse risk after discontinuation of ASMs has been reported, ranging from 12% to 67% (11). In a recent study by Li et al. this rate was found to be 29.8%, similar to our study. They also argued that the high risk of recurrence was related to the use of multiple ASMs and EEG findings after seizure freedom (10). In a previous study conducted in our country in which recurrence rates after discontinuation of ASMs were analyzed, this rate was observed to be 19.3% (12). Moreover, in a study conducted by Vurucu et al., the recurrence rate was found to be 19.2%, and it was argued that the recurrence rate was relatively low, and this was due to patients with low-risk factors in the study population (13). The slightly higher recurrence rates in our study may be due to the inclusion of patients who self-discontinued their medication. We thought that this situation was significant because it reflected real-life data.

Table 3. Comparison of the duration of recurrence based on the number of seizure-free years

	Average survival time (months) (95% CI)	P
Number of seizure-free years		
≤5	76.455 (60.126–92.783)	0.516
>5	91.165 (67.481–114.848)	
Total	86.009 (71.007–101.011)	

*Log Rank (Mantel-Cox) test

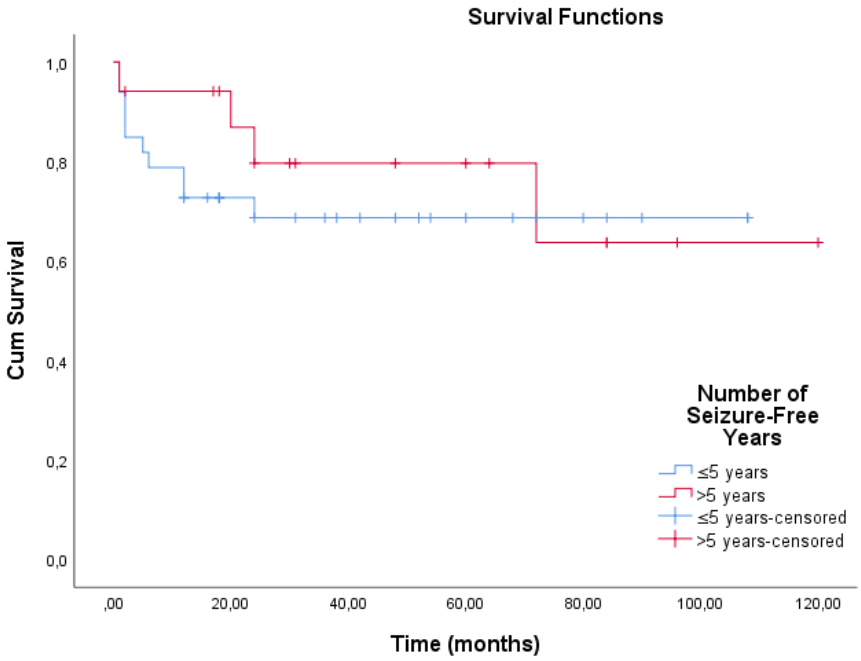

Figure 1. Kaplan Meier univariate analysis of the relationship between seizure-free years and duration of recurrence

The National General Practice Study of Epilepsy in the United Kingdom identified a 3-year recurrence risk of 44% after a seizure-free period of 6 months, 32% after 12 months, and 17% after 18 months. Although there is insufficient data on the risk of seizure recurrence after a long period of seizure-free and medication-free life, it has been reported that delayed recurrences are rare after 5 years and that the annual risk of seizures is probably very low 10 years after discontinuation of anti-seizure medication (9). Also, in many studies, it has been shown that the period with the highest risk of seizure is in the first 2 years (14,15). In our study, this rate was observed to be higher in the first year, and the risk rate was considerably higher, especially in the first 6 months.

In many studies, in order to compare the link between the timing of discontinuation and recurrence rates, seizure-free periods before medication discontinuation were classified as 2 years, 2–5 years, and 5 years. It was reported that the longer the remission period was maintained, the lower the risk of relapse after discontinuation, although no difference was observed between the periods (4,16). In our study, when we classified the patients as below 5 years and above 5 years, we observed that there was no significant difference between the two groups in terms of recurrence, but the recurrence rate decreased as the seizure-free period increased in compliance with other studies.

In a study conducted by Bouma et al. on a pediatric population, an inverse correlation was found between the duration of ASM use and the risk of relapse (17). In another study, evidence was presented that previous use of multiple ASMs, the presence of abnormal EEG during discontinuation, and the presence of a structural lesion in the etiology of epilepsy increased the risk of recurrence (10,18-22). On the other hand, Benhadis et al. argued that female patients should be more careful because of the high risk of recurrence in the presence of abnormal EEG after medication discontinuation (23). In our study, the risk of recurrence was statistically significantly higher in patients with generalised epilepsy, and no relation was found with any of the previously described risk factors such as gender, epilepsy duration, age at onset, or abnormal EEG findings.

Although data on seizure control in patients with relapse after medication discontinuation are limited, while seizures can be controlled again in 64-91% of patients, there are data on difficulty in seizure control and development of drug-resistant seizures at rates ranging from 7 to 19%, however, no predictive factor has been shown for this situation (24-26). In the Medical Research Council Antiepileptic Medication Discontinuation Study, it was shown that the risk of seizure recurrence was similar between patients who relapsed after discontinuation of ASMs and patients who relapsed while continuing treatment. Therefore, it has been argued that the detected resistances are perhaps related to the natural course of the disease (27). In our study, seizures were not resistant to treatment in any patient with a recurrence. The seizures of all patients were controlled after the initiation of treatment. In addition, in a study by Cho et al. evaluating 104 patients who underwent anti-seizure medication discontinuation for the second time, it was observed that 41.3% of the patients were seizure-free for at least 2 years. Therefore, it is argued that relapse after discontinuation of anti-seizure treatment does not mean that the treatment will last for life, and that drug discontinuation may be tried again at a later time, but it should be kept in mind that the threshold for a cessation attempt may be slightly higher in such cases (28,29).

This study has several limitations. Firstly, the small number of patients is one of the limitations. The reason for the lower number of patients with medication discontinuation may be due to the fact that our center is a tertiary epilepsy center and therefore, especially medication-resistant epileptic patients are referred. Additionally, multicentre randomised controlled studies with a large sample size may lead to more precise results. The fact that retrospective nature of the study is another limitation. Although patients were followed up for at least one year, not all patients had equal follow-up periods. Considering that the rate of discontinuation of ASMs may also affect seizure recurrence, no evaluation could be made in this regard since we did not have information about the discontinuation periods of the medication in some patients.

Conclusion

In conclusion, our study supports that the risk of relapse after discontinuation of ASMs decreases as the seizure-free period is prolonged. However, it should not be forgotten that the decision to discontinue medication should be individualized. When making a decision, the risk of relapse should be evaluated and shared with the patient or the patient's relatives. The patient's work and social life, the expectation of a license, drug interactions, side effects, and even the risk of teratogenicity should all be taken into consideration and discussed with the patient. A joint decision should be reached together with the patient.

Conflict of interest statement

In our study, there is no financial conflict of interest with any institution, organization, person and there is no conflict of interest between the authors.

Ethics Committee Approval: This study was approved by the human ethics committee of Antalya

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An Evaluation of Patients Aged 90 and Over Who Admitted to the Emergency Department

Acil Servise Başvuran 90 Yaş ve Üstündeki Hastaların Değerlendirilmesi

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Öz

Dünyada yaşlı nüfus oranının her geçen gün arttığı görülmektedir. Bununla birlikte acil servislerde de yaşlı hasta başvurusu oranı artmaktadır. Bu çalışmada acil servise başvuran 90 yaş ve üstündeki hasta grubunu analiz etmek amaçlanmıştır. Bu çalışmada 01.01.2022-31.12.2022 tarihleri arasında ikinci basamak olarak hizmet veren bir sağlık kuruluşunun acil servisine başvuran 90 yaş ve üzerindeki hastaların retrospektif değerlendirmesi yapıldı. Hastalarda yaş, cinsiyet, başvuru zamanı, başvuru şikâyeti, tanı, en sık hasta yatırılan klinikler ve sonlanım şekilleri değerlendirildi. Sonuçlar ortalama±standart sapma (SS) veya frekans (yüzde) şeklinde verilmiş ve $p<0.05$ istatistikî olarak anlamlı kabul edilmiştir. Çalışmada 754 hasta değerlendirildi. Yaş ortalaması 92.4±2.38'di. Kadın hasta oranı (%70.7) daha fazlaydı. En çok başvuru hafta içi mesai saatlerinde ve yaz aylarında yapıldı. En sık başvuru nedenleri nefes darlığı, düşme ve karın ağrısı oldu. En sık pnömoni, ekstremite kırığı ve akut böbrek yetmezliği teşhisi konuldu. Hastalarda en sık görülen ek hastalık hipertansiyondu. Hastaların %72.2'si acil servisten taburcu edildi. En sık hasta yatırılan klinikler göğüs hastalıkları, dahiliye ve ortopedi oldu. Hastanede ortalama yatış süresi 6 (1-91) gün olmuştur. Acil serviste veya yatırıldığı klinikte ölümle sonlanan hasta sayısı 63'tür (%8.3). En sık ölüm nedeni pnömoni ve akut miyokard infarktüsü oldu. Çalışmamızda ileri yaşlı hastalarda en sık pnömoni teşhisi konulduğu görüldü. Acil servise kişinin genel durumunda bozulma ile başvuran geriatrik hasta popülasyonunda pnömoni olabileceği mutlaka düşünülmelidir.

Anahtar Kelimeler: Acil Servis, Geriatri, Hospitalizasyon

Abstract

It is seen that the rate of elderly population in the world is increasing day by day. However, the rate of elderly patient admissions in emergency departments is also increasing. In this study, a group of patients over the age of 90 who admitted to the emergency department was analyzed. In this study, a retrospective evaluation was made of patients aged over 90 who admitted to the emergency department of a secondary care health institution between 01.01.2022 and 31.12.2022. The information about patients' age, gender, time of acceptance, acceptance complaint, diagnosis, clinics where patients were most frequently admitted, and their results were evaluated. Results are presented as mean±standard deviation (SD) or frequency (percentage), and $p<0.05$ was considered statistically significant. 754 patients were evaluated in the study. The mean age was 92.4±2.38. The proportion of female patients was higher (70.7%). Most acceptance were made during weekday working hours and summer months. The most common reasons for accept were shortness of breath, falling and abdominal pain. The most common diagnoses were pneumonia, extremity fracture and acute renal failure. The most common co-morbidity in the patients was hypertension. 72.2% of the patients were discharged from the emergency department. The clinics where patients were most frequently admitted were chest diseases, internal medicine and orthopedics. The average length of hospitalization was 6 (1-91) days. The number of patients who died in the emergency department or in the hospitalized clinic was 63 (8.3%). The most common causes of death were pneumonia and acute myocardial infarction. In our study, pneumonia was diagnosed most frequently in elderly patients. Pneumonia should be considered in the geriatric patient population presenting to the emergency department with deterioration in general condition.

Keywords: Emergency Service, Geriatrics, Hospitalization

Introduction

The ratio of the elderly population and the number of patients is increasing day by day in our country and all over the world. It is predicted that Turkey will be the most populous country in Europe in 2050 in terms of the elderly population (1). As the proportion of the elderly population increases in society, it is necessary to conduct current research and find solutions to the health problems and problems seen in this age group.

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The concept of old age covers the period of time between living things reaching biological adulthood and the end of the reproductive period until death. Old age should be evaluated socially, physically and psychologically. Physiologically, lung vital capacity decreases, kidney functions slow down, decreased gastrointestinal motility, slowdown of central nervous system functions and weakening of the immune system are observed (2). When looked at from a psychological perspective, it is seen that learning, problem solving, psychomotor skills, perception capacity and the capacity of a person to adapt to his environment change with age (3). With this change, the ability of elderly patients to cope with changes in the living environment and stress factors decreases. This situation causes the elderly to face diseases more frequently. A large proportion of the elderly population struggles with many diseases at the same time, and as a result, it is seen that emergency departments are applied more frequently than the normal patient population (4-6). It will be easier for physicians to know the reasons why

geriatric patients are more frequently admitted to the emergency department and the current approaches to be taken during the diagnosis and treatment process (7).

The World Health Organization (WHO) considers the population over the age of 65 as the elderly population (3). We observed that patients over 65 years of age were evaluated in most of the studies in the literature on the subject. We think that life expectancy is increasing in the world and in our country and the average age of geriatric patients applied to the emergency department is increasing day by day. Therefore, in this study, we wanted to set the age limit higher in geriatric patients admitted to the emergency department and to conduct a special study for this age range. We aimed to analyze the demographic data in the group of patients over 90 years of age admitted to the emergency department, to analyze the most common reasons for admission, hospitalization rates and the most common diagnoses and clinics in which inpatients were followed up. We wanted to investigate the effect of the presence of chronic diseases on the outcome of the patients. With the increase in the elderly population in the world day by day, we anticipate that isolated studies in advanced age ranges, as we have determined in our study, will increase. We think that our study will be effective in creating a preliminary idea for the literature in this respect.

Material and Method

In this study, patients aged 90 and over who applied to the emergency department of a secondary healthcare institution between 01.01.2022 and 31.12.2022 were evaluated. The study was conducted by retrospective file review method in electronic environment and is an observational, descriptive study. The data of the patients were collected by the researchers between 25.07.2023-01.09.2023 and statistical analysis was performed and then the article was written. In addition to data such as age, gender, accept time, the patient's complaint of acceptance, diagnosis and if hospitalization was performed, the hospitalization diagnosis and the hospital clinic were determined. In hospitalized patients, additional diseases recorded in the system were also detected and added to the patient data. How many days the patient stayed in the hospital through the system and how he left the hospital as a result were evaluated by evaluating the physician's notes. Data collection was done retrospectively through the hospital electronic data system. The epicrisis of the patients was also taken into consideration in obtaining the data. Patients who did not generate sufficient data were excluded from the study (Figure 1). Approval for the study was received by Hacıbektaş Veli University Non-Interventional Clinical Research Ethics Committee with decision number 2023/05 dated 21/07/2023.

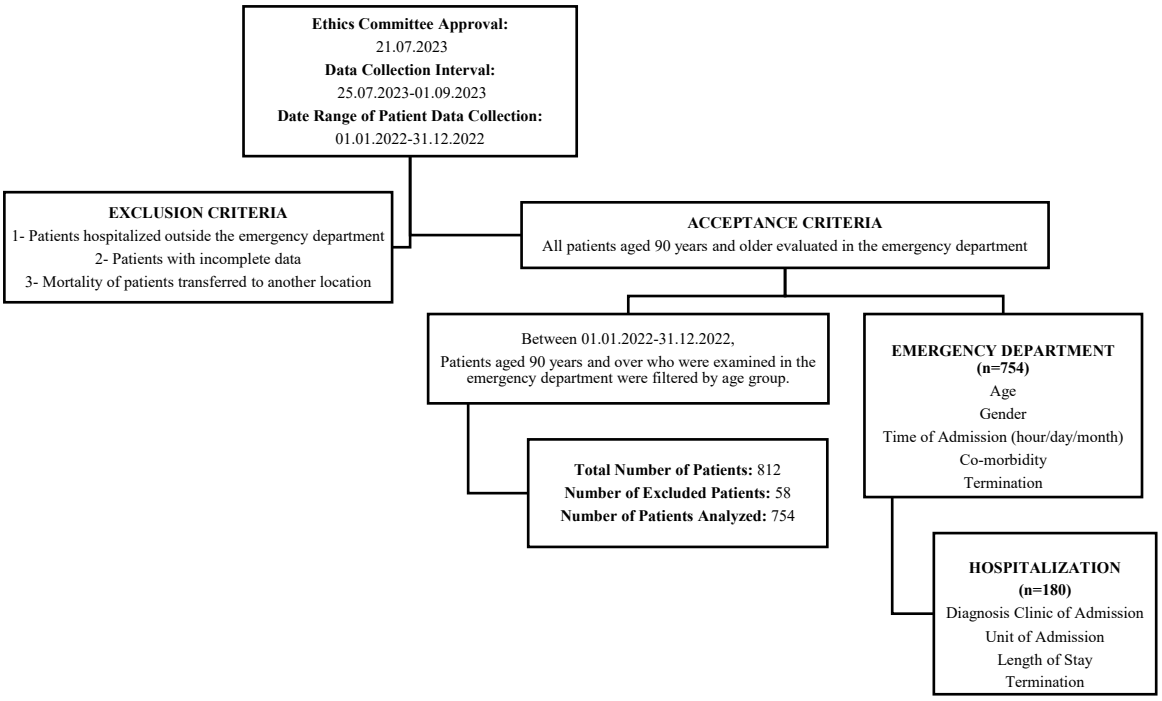

Figure 1. Flow chart showing study times.

Package analyzes data for Social Sciences for Windows 21.0 (SPSS 21.0) program was used. As statistical analysis, descriptive statistics (frequency, percentage distribution) and chi-square test were used to compare categorical variables between two groups. Results are presented as mean±SD, or frequency (percentage), and $p<0.05$ was considered statistically significant.

Results

Within the scope of the study, 754 patients were examined. The average age of the patients was 92.4±2.38. When evaluated by gender, 70.7% of the patients were women. Patients were evaluated according to the time of admission and it was observed that 76% of admissions were made on weekdays. Acceptance intervals were divided into three according to time intervals. The most common time of admission was between 08.00-16.00 (55%), followed by 16.00-24.00 (35.8%) and the least common time of admission was between 24.00-08.00 (9.2%). When admissions were analyzed by months, it was observed that admissions were higher in summer months (Figure 2). The most common reasons for admission are given in Table 1 and the most common reasons for admission were shortness of breath and cough. The complaints of admission according to gender were compared and a significant difference was observed between the two variables (Chi square: 34.732 p=0.019). Across the table, the only admission complaint that was more common in men was urinary tract symptoms. Significant differences were observed in admission complaints according to seasons (Chi-square: 94.390, p=0.038) (Table 2). Among the patients, there were a total of 209 cases that were not discharged from the emergency department but were decided to be hospitalized, referred, refused treatment, or ended in death. The diagnoses made in these cases are given in table 3. According to this result, the three most frequently diagnosed diseases were pneumonia, extremity fracture and acute renal failure. It was observed that there was no significant difference between patient gender and diagnoses (Chi-square: 16.747, p=0.669). Comorbidities were examined in the admitted patients and are shown in Figure 3. According to this result, the most common comorbidities were hypertension (HT) (65.3%), previous surgery, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), chronic renal failure (CRF) and cerebrovascular disease (CVD). (Figure 3).

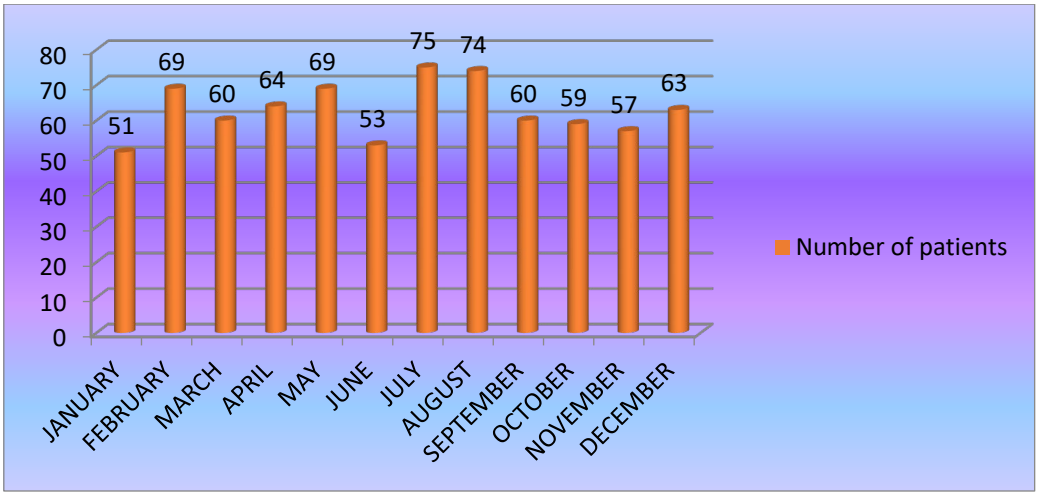

Figure 2. Distribution of patient applications by months.

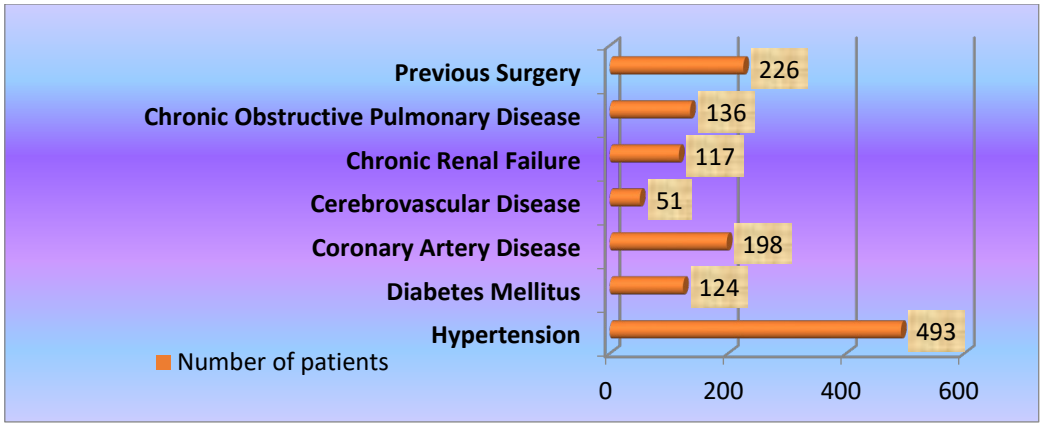

Figure 3. Distribution of additional diseases seen in patients

Table 1. Complaints of the patients admitted to the emergency department and their distribution according to gender*.

Admission Complaint	Number of Patients	Ratio (%)	Female	Male	p value
Shortness of Breath and Cough	143	18.9	106[a]	37[a]	
Fall	91	12.1	59[a]	32[a]	
Stomachache	73	9.7	49[a]	24[a]	
Weakness and Resentment	59	7.8	43[a]	16[a]	
Nausea, Vomiting, Diarrhea	59	7.8	44[a]	15[a]	
High Blood Pressure	51	6.8	39[a]	12a	
Soft Tissue Trauma	46	6.1	35[a]	11[a]	
Nutritional Disorder	35	4.6	25[a]	10[a]	
Chest Pain	44	5.8	28[a]	16[a]	
Muscle and Joint Pain	44	5.8	35[a]	9[a]	p=0.019
Urinary Tract Symptoms	40	5.3	16[a]	24[b]	
Upper Respiratory Tract Infection	19	2.5	14[a]	5[a]	
Dizziness	12	1.6	10[a]	2[a]	
Allergy	12	1.6	7[a]	5[a]	
Headache	11	1.5	11[a]	0[b]	
Neurological Symptoms**	6	0.8	5[a]	1[a]	
Epistaxis	3	0.4	3[a]	0[a]	
Eye Pain, Stinging, Burning	3	0.4	2[a]	1[a]	
Hypoglycemia / Hyperglycemia	3	0.4	2[a]	1[a]	
TOTAL	**754**	**100**	**533**	**221**	

*The same letters in the table indicate similarity between groups, while different letters indicate difference. **Extremity weakness, speech disorder, convulsion, etc.

545 (72.3%) of the patients were discharged from the emergency department. Of the other patients, 180 were hospitalized. The clinics that admitted the most patients were chest diseases, internal medicine and orthopedics. The discharge status of the patients from the emergency department and the clinic where they were hospitalized, and the distribution of patient admissions by clinic are given in detail in Table 4. The mean length of hospitalization of the hospitalized patient group was 6 (1-91) days. The majority of hospitalized patients (55%) stayed in the hospital between 1-7 days (Table 4). No significant relationship was found between hospitalization times according to patient diagnosis (Chi-square: 110.838, p=0.127). The relationship between the type of discharge from the emergency department and the presence of chronic disease is given in Table 5. In the study, the total mortality rate in the emergency department and inpatients was 8.3%. The most common causes of death were pneumonia and acute myocardial infarction.

Table 2. Comparison of complaints according to seasons*.

Variables	Season				p
	Winter (*n*=183)	Spring (*n*=193)	Summer (*n*=202)	Autumn (*n*=176)	
Admission Complaint					
Shortness of Breath and Cough	31 (16.9)[a]	44 (22.8)[a]	39 (19.3)[a]	29 (16.5)[a]	
Fall	17 (9.3)[a]	25 (13.0)[a]	29 (14.4)[a]	20 (11.4)[a]	
Stomachache	19 (10.4)[a]	13 (6.7)[a]	26 (12.9)[a]	15 (8.5)[a]	
Weakness and Resentment	12 (6.6)[a]	20 (10.4)[a]	21 (10.4)[a]	6 (3.4)[a]	
Nausea. Vomiting. Diarrhea	16 (8.7)[a]	17 (8.8)[a]	12 (5.9)[a]	14 (8.0)[a]	
High Blood Pressure	13 (7.1)[a]	14 (7.3)[a]	14 (6.9)[a]	10 (5.7)[a]	
Soft Tissue Trauma	10 (5.5)[a]	6 (3.1)[a]	15 (7.4)[a]	15 (8.5)[a]	
Nutritional Disorder	7 (3.8)[a.b]	5 (2.6)[b]	7 (3.5)[a.b]	16 (9.1)[a]	
Chest Pain	8 (4.4)[a]	9 (4.7)[a]	13 (6.4)[a]	14 (8.0)[a]	p=0.038
Muscle and Joint Pain	15 (8.2)[a]	12 (6.2)[a]	8 (4.0)[a]	9 (5.1)[a]	
Urinary Tract Symptoms	11 (6.0)[a]	13 (6.7)[a]	6 (3.0)[a]	10 (5.7)[a]	
Upper Respiratory Tract Infection	9 (4.9)[a]	3 (1.6)[a]	3 (1.5)[a]	4 (2.3)[a]	
Dizziness	5 (2.7)[a]	1 (0.5)[a]	1 (0.5)[a]	5 (2.8)[a]	
Allergy	4 (2.3)[a]	1 (0.5)[a]	3 (1.5)[a]	4 (2.3)[a]	
Headache	3 (1.6)[a]	4 (2.1)[a]	1 (0.5)[a]	3 (1.7)[a]	
Neurological Symptoms**	3 (1.6)[a]	2 (1.0)[a]	1 (0.5)[a]	0 (0.0)[a]	
Epistaxis	0 (0.0)[a]	1 (0.5)[a]	2 (1.0)[a]	0 (0.0)[a]	
Eye Pain. Stinging. Burning	0 (0.0)[a]	1 (0.5)[a]	0 (0.0)[a]	2 (1.1)[a]	
Hypoglycemia / Hyperglycemia	0 (0.0)[a]	2 (1.0)[a]	1 (0.5)[a]	0 (0.0)[a]	

The data are expressed as n (%). *The same letters in the table indicate similarity between groups. while different letters indicate difference. **Extremity weakness. speech disorder. convulsion. etc.

Table 3. Distribution of patients who were not discharged from the emergency department according to diagnosis and gender.

Diagnosis	Number of Patients	Ratio (%)	Female	Male	p value
Pneumonia	42	5.3	28	14	
Extremity Fracture	30	3.7	20	10	
Acute Renal Failure	28	3.4	20	8	
Electrolyte Disturbance	20	2.4	12	8	
Cerebrovascular Disease	13	1.6	10	3	
Sepsis	11	1.3	8	3	
Acute Coronary Syndrome	11	1.3	8	3	
Gastrointestinal Bleeding	11	1.3	8	3	
Hepatobiliary Disease	9	1.2	8	1	
COPD* Exacerbation	7	0.9	4	3	
Pulmonary Embolism	7	0.9	7	0	p=0.717
Ileus	5	0.7	3	2	
Urogenital Pathologies	4	0.5	2	2	
Urinary Tract Infection	3	0.4	1	2	
Pleural Effusion / Empyema	2	0.3	2	0	
Heart Failure	1	0.1	1	0	
Epilepsy	1	0.1	1	0	
Shingles Infection	1	0.1	0	1	
Mesentery Ischemia	1	0.1	1	0	
Follow-up After Surgery	1	0.1	0	1	
Diabetic Ketoacidosis	1	0.1	1	0	
TOTAL	**209**	**100**	**145**	**64**	

*Chronic Obstructive Pulmonary Disease

Discussion

The incidence of chronic diseases increases with the elderly population. This situation also affects the number of elderly patients admitted to the emergency department and hospitalization rates with exacerbation of the existing disease or acute diseases that will occur.

In the literature, there are generally studies on cases over the age of 65. In this study, we analyzed patients aged 90 and over, which is an older age group. It was observed that 208614 patients applied to the emergency department annually in the center and date range where our study was conducted, and 754 of these patients were 90 years old and over. Varıslı et al. In their study analyzing patients over the age of 65, they stated that the rate of patients over the age of 85 was 21.3% (8). In the study conducted by Bedel et al. on patients over 65 years of age, 10.8% of the admission rate was in patients over 85 years of age. (9). Celik et al. In another study conducted by et al. on geriatric patients, it was observed that the oldest patient was 90 years old, and the rate of patients over the age of 85 was stated as 10.1% (10). In a study conducted abroad, admission of patients over 80 years of age was found to be higher than the studies conducted in our country (11). Depending on the centers where the studies are conducted and the average age of the patients admitted may vary. We think that living conditions and sociodemographic factors may also be effective in this regard. In our study, since the age group over 90 years was evaluated in isolation, age group-specific ratios could not be made as in other studies evaluating patients over 65 years of age.

In our study, we found that 70.7% of the patients were female. Kekec et al. reported that 50.5% of the cases were female in their study (2). Varıslı et al. reported 56% female (8), Bedel et al. 52.9% male (9), Celik et al. 52% female (10), Oktem et al. 54.7% female (12). Similarly, gender comparison was made according to age in some of the studies and it was observed that the female sex ratio was more prominent in patients older than 85 years (8,9,13). In our study, only those over the age of 90 were examined and the female gender ratio resulted similar to the literature. From these results, it can be concluded that men's lifespan is shorter than women or they are admitted to hospital less frequently.

When we analyzed the admission times of the patients, we found that the most common time of admission was during working hours (55%), on weekdays (76%) and the most common month of admission was July (9.9%). In a study, it was observed that geriatric patients were mostly admitted to the emergency department between 18.00-23.59 hours (35.7%) and in the summer months (25.6%) (13). In a study by Oktem et al. similar to our study, it was observed that emergency department admissions in geriatric patients were during working hours (08.00-16.00) and in summer months (12).

In this study, we observed that patients were most commonly admitted to the emergency department because of shortness of breath, cough, falls and abdominal pain. In a similar study, the most common reasons for admission were cardiac symptoms, fatigue and general condition disorder (2). In another study, the most common complaints were abdominal pain, chest pain and shortness of breath (9). In another study, 49.8% of patients had respiratory, 30.6% cardiac and 29.5% pathologic abdominal

findings (8). In some studies, it was reported that the most common reasons for admission to the emergency department were cardiac and respiratory (13-17). Dundar et al. analyzed patients admitted with abdominal pain over the age of 65 years and reported that the rate of patients admitted with abdominal pain in this age group was 12.4% (13). In the study by Oktem et al. the most common reasons for admission were musculoskeletal disorders, gastrointestinal system disorders and traumas (12). In a study conducted by Aslaner in 2019, the first and second reasons for admission of geriatric patients within 72 hours were examined. According to the results, the reasons for first and second admission were generally the same and the most common reasons for admission were musculoskeletal pain, shortness of breath, hypertension and abdominal pain (18). As in our study, we can say that the reasons for admission in elderly patients are generally due to respiratory and cardiac reasons. We think that the differences seen in the studies are related to the region where the studies were conducted, the scope of the study and the centers where the study was conducted.

In trauma cases, patients over the age of 65 require more treatment than younger patients, and this rate rises to 50% in people over the age of 80 (19). In a study conducted in Erzurum, the most common cause of trauma was falls (82%) (20). Schwab et al. and Osler et al. in their studies on geriatric trauma patients, it was stated that the most common cause of trauma was falls (21,22). In our study, admissions due to falls ranked second among tens of internal complaints with a rate of 12.1%. This shows that traumas have an important place in the elderly population. We think that the weakening of muscle strength and reflexes with aging increases injuries due to falls and trauma. Therefore, we anticipate that injuries will decrease with the necessary precautions against trauma in the elderly age group.

Table 4. Analysis of patients' outcome and hospitalizations.

	Number of Patient (n)	**Ratio (%)**
Termination from the Emergency Department		
Discharged	545	72.2
Service	117	15.5
Intensive Care	63	8.3
Transfer to Another Center	2	0.3
Treatment Refusal	20	2.7
Excitus	7	1
TOTAL	**754**	**100**
Hospitalized Patients		
Clinic		
Chest Diseases	40	22.2
Internal Medicine	33	20.5
Orthopedics	26	14.4
Nephrology	21	11.6
Cardiology	16	8.8
Infection	16	8.8
Neurology	11	6.1
General Surgery	9	5
Anesthesia and Reanimation	3	1.6
Urology	2	1.1
Brain Surgery	2	1.1
Obstetrics and Gynecology	1	0.05
Length of Stay		
1-7 days	100	55.5
8-14 days	51	28.3
15-21 days	10	5.5
22-28 days	4	2.2
29-35 days	7	3.8
>36 days	8	4.4
Termination of inpatients		
Discharged	106	58.9
Transfer to Another Center	7	3.8
Treatment Refusal	11	6.2
Excitus	56	31.1
TOTAL	**180**	**100**

Table 5. The relationship between the mode of discharge from the emergency department and the presence of chronic disease*.

Chronic Disease / Final**	Discharge	Service Hospitalization	Intensive Care Hospitalization	Transfer to Another Center	Treatment Refusal	Excitus	p value
HT							
Absent	210(80.5)[a]	30(11.5)[a]	15(5.7)[a]	1(0.4)[a]	2(0.8)[a]	3(1.1)[a]	**0.009**
Present	335(68.0)[b]	87(17.6)[b]	48(9.7)[a]	1(0.2)[a]	5(1.0)[a]	17(3.4)[a]	
DM							
Absent	468(74.3)[a]	90(14.3)[a]	48(7.6)[a]	2(0.3)[a]	4(0.6)[a]	18(2.9)[a]	**0.035**
Present	77(62.1)[b]	27(21.8)[b]	15(12.1)[a]	0(0.0)[a]	3(2.4)[a]	2(1.6)[a]	
CAD							
Absent	420(75.5)[a]	80(14.4)[a]	38(6.8)[a]	2(0.4)[a]	6(1.1)[a]	10(1.8)[a]	**0.004**
Present	125(63.1)[b]	37(18.7)[a]	25(12.6)[b]	0(0.0)[a]	1(0.5)[a]	10(5.1)[b]	
CVD							
Absent	508(72.3)	107(15.2)	59(8.4)	2(0.3)	7(1.0)	20(2.8)	0.678
Present	37(72.5)	10(19.6)	4(7.8)	0(0.0)	0(0.0)	0(0.0)	
CRF							
Absent	474(74.4)[a]	88(13.8)[a]	53(8.3)[a]	2(0.3)[a]	5(0.8)[a]	15(2.4)[a]	**0.036**
Present	71(60.7)[b]	29(24.8)[b]	10(8.5)[a]	0(0.0)[a]	2(1.7)[a]	5(4.3)[a]	
COPD							
Absent	449(72.7)	90(14.6)	56(9.1)	2(0.3)	6(1.0)	15(2.4)	0.361
Present	96(70.6)	27(19.9)	7(5.1)	0(0.0)	1(0.7)	5(3.7)	
SURG							
Absent	373(70.6)	91(17.2)	46(8.7)	1(0.2)	5(0.9)	12(2.3)	0.352
Present	172(76.1)	26(11.5)	17(7.5)	1(0.4)	2(0.9)	8(3.5)	

Values are expressed *n* (%). *The same letters in the table indicate similarity between groups. while different letters indicate difference. **HT: Hypertension. DM: Diabetes Mellitus. CAD: Coronary Artery Disease. CVD: Cerebrovascular Disease. CRF: Chronic Renal Failure. COPD: Chronic Obstructive Pulmonary Disease. SURG: Previous Surgery.

In our study, when we looked at the order of diagnosis in patients planned to be hospitalized, it was seen that the most common were pneumonia, extremity fracture, acute renal failure, electrolyte disorder and cerebrovascular disease. Kekec et al. in their study, the most common diagnoses were heart failure, acute coronary syndrome, stroke, oncological and hematological diseases and renal failure (2). Satar et al. in their study, they stated that the most common diagnoses in patients were stroke, oncological emergencies, chronic renal failure, myocardial infarction and heart failure (4). Bedel et al. observed that 20.2% of patients over the age of 65 admitted to the emergency department were due to cardiovascular diseases, 14.3% oncologic diseases, 11.1% respiratory system diseases, 10.1% gastroenterologic diseases, 6.5% trauma and 5.5% neurologic diseases (9).

In our study, the clinics with the most frequent hospitalizations were chest diseases, internal medicine and orthopedics clinics. In a similar study, patients were most frequently admitted to internal medicine, neurology, cardiology, pulmonology and orthopedics clinics (2). Bedel et al. in their study, the most patients were hospitalized in internal medicine and cardiology clinics (9). In the study conducted by Varıslı et al. the most hospitalized patient groups were due to cardiovascular diseases (16.5%) and infection (13.3%). The clinics where consultation is most frequently requested are internal medicine (52.2%) and neurology clinics (21.2%) (8). Similarly, in another study, the clinics with the most frequent hospitalizations were chest diseases, neurology and internal medicine clinics (23). Generally speaking, geriatric patient admissions from emergency departments were similar. In our study, more patients were hospitalized in the chest diseases clinic due to the most frequent diagnosis of pneumonia. In our study, the second most common department for extremity fractures was the orthopedics clinic. According to similar studies, more patients were admitted to the orthopedics clinic and we thought that this was related to the harsh winter months and the high number of falls due to icing in the center where our study was conducted.

According to the literature, additional diseases for which they receive chronic treatment are common in the geriatric patient population (5,24). In one study, it was observed that 87.3% of patients over the age of 65 had at least one chronic disease (23). Varıslı et al. in their study, it was observed that the most common comorbidities in patients were HT (63%), DM, CAD, heart failure (HF), COPD and CKD (8). According to the results of a study conducted in Turkey, the most common chronic disease was HT (30.7%), followed by osteoarthritis, HF, DM and CAD (25). In our study, HT was the most common comorbidity (65.3%), followed by previous surgery, CAD, COPD, DM, CRF and LVH, respectively. When we look at the discharge and hospitalization rates of the geriatric patient population admitted to emergency departments, we see that the majority of patients are treated symptomatically in the emergency department and discharged. In our study, the hospital discharge rate was 72.2% from the emergency department and

58.8% in hospitalized patients. In similar studies, Bedel et al. reported discharge rates from the emergency department. 77.2% (9), Celik et al. 53.7% (10), Oktem et al. they reported it as 79.4% (12). Satar et al. in their study, the hospitalization rate was stated as 59.35% (4). We predict that the diversity seen in these rates is due to the different service levels of the centers where the studies are carried out. In our study, the number of cases that ended in death was 7 in the emergency department and 56 in inpatients, 8.3% of the total admissions. The most common causes of death were pneumonia and acute myocardial infarction. Bedel et al. in their study, the most common cause of death in the emergency department was acute myocardial infarction (9).

Conclusion

As a result, apart from trauma, pneumonia, acute renal failure and deterioration in general condition due to electrolyte disturbance should be considered in the foreground in the elderly patient group. It is predicted that the rate of elderly patients admitted to the emergency department will increase every year and it is necessary to know the elderly patient group well (26). Assuming that the average age of the elderly patients admitted to emergency departments is increasing every year, we analyzed patients aged 90 years and older in this study. In the literature, similar results were generally obtained in the studies on the subject and the majority of the studies were conducted with a patient population over 65 years of age. We think that our study will contribute to the literature in this respect. Similarly, by analyzing current data, we foresee that the establishment of separate departments for the evaluation of elderly patients in each health institution will be more efficient in the diagnosis and treatment process.

Limitations: Since the COVID-19 pandemic was on going during the period of our study, the higher number of pneumonia diagnoses may be related to the process. In addition, since the studies in the literature were generally conducted on patients aged 65 years and older, we could only compare our study with these data.

Ethics Committee Approval: Approval was received by Hacıbektas Veli University Non-invasive Clinical Research Ethics Committee, decision number 2023/05 dated 21/07/2023.

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Hypermobility Spectrum Disorders, Functional Constipation and Voiding Dysfunction in School-Aged Children: Are They Related to Each Other?

Okul Çağındaki Çocuklarda Hipermobilite Spektrum Bozuklukları, Fonksiyonel Kabızlık ve İşeme Disfonksiyonu: Birbirleriyle İlişkili midir?

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Öz

Hipermobilite spektrum bozuklukları, tanısı konmuş sistemik romatolojik bir hastalık olmaksızın kas-iskelet sistemi bulguları ve yaygın eklem hipermobilitesi ile kendini gösterir. Hipermobilite spektrum bozuklukları, disfonksiyonel işeme bozuklukları ve fonksiyonel kabızlık gibi klinik durumlar için risk oluşturabilir. Amacımız okul çağındaki çocuklarda hipermobilite spektrum bozuklukları, işeme disfonksiyonu ve fonksiyonel kabızlık sıklığını saptamak ve birbirleriyle ilişkilerini değerlendirmektir. Bu kesitsel çalışmaya okul çağındaki 947 çocuk (6–15 yaş) dahil edildi. Bir pediatrik romatolog tüm çocukları hipermobilite tanısı koymak için Beighton Hipermobilite Skoru kullanarak muayene etmiş ve fonksiyonel kabızlık tanısı ise bir pediatrik gastroenterolog tarafından konulmuştur. İşeme disfonksiyonu tanısını koymak için bir pediatrik nefrolog tarafından Disfonksiyonel İşeme ve İnkontinans Semptomları Skorlaması kullanılmıştır. İşeme disfonksiyonu genç yaş grubunda, anne eğitim düzeyi düşük olanlarda, gelir düzeyi düşük olanlarda ve idrar yolu enfeksiyonu öyküsü olanlarda daha sık görüldü (sırasıyla p<0.001, p=0.027, p=0.035, p<0.001). İdrar yolu enfeksiyonu öyküsü olan çocuklarda da kabızlık prevalansı daha yüksekti (p=0.001) ve kabızlık görülme sıklığı, işeme disfonksiyonu olan çocuklarda olmayanlara göre belirgin şekilde daha yüksekti (p<0.001). Hipermobilitesi olan ve olmayan çocuklar arasında işeme disfonksiyonu ve kabızlık oluşumu açısından istatistiksel olarak anlamlı bir fark bulunamadı (p>0.05). Hipermobilitesi olan çocuklarda fonksiyonel kabızlık ve işeme disfonksiyonu gibi şikayetlerin arttığı hipotezini doğrulamak için daha fazla çalışmaya ihtiyaç vardır. İşeme disfonksiyonu ve/veya idrar yolu enfeksiyonu olan çocuklarda kabızlık sorgulanmalı ve etkin bir şekilde tedavi edilmelidir.

Anahtar Kelimeler: Çocuklar, Fonksiyonel Kabızlık, Hipermobilite Spektrum Bozuklukları, İşeme Disfonksiyonu

Abstract

Patients suffering from hypermobility spectrum disorders (HSDs) present with problems related to the musculoskeletal system and have generalized joint hypermobility without a diagnosed systemic rheumatological disease. HSDs represent an underlying risk factor for many clinical conditions, such as dysfunctional voiding disorders and functional constipation (FC). In this study, we investigated ways to detect the frequency of HSDs, voiding dysfunction (VD), and FC in school-aged children and assessed their relationship with each other. In this cross-sectional study, 947 school-aged children (6–15 years old) were included. A pediatric rheumatologist examined all children using the Beighton Hypermobility Score to diagnose hypermobility. FC was diagnosed by a pediatric gastroenterologist. The dysfunctional voiding and incontinence symptoms score questionnaire was used by a pediatric nephrologist to diagnose VD. VD was more frequently observed in the younger age group, those whose mothers had lower education levels, children from lower-income families, and those with a history of urinary tract infection (p<0.001, p=0.027, p=0.035, p<0.001, respectively). Children with a history of urinary tract infection also had a higher prevalence of constipation (p=0.001), and the incidence of constipation was significantly higher in children with VD compared to those without VD (p<0.001). The difference in the occurrence of VD and constipation between children with and without hypermobility was not significant (p>0.05). Further studies are needed to confirm the hypothesis that problems such as FC and VD are worse in children with hypermobility. Constipation should be investigated in children suffering from VD and/or urinary tract infections for effective treatment of these diseases.

Keywords: Children, Functional Constipation, Hypermobility Spectrum Disorders, Voiding Dysfunction

Introduction

Hypermobility spectrum disorders (HSDs) are a group of inherited diseases of the connective tissue that present with problems in the musculoskeletal system and generalized joint hypermobility without a diagnosed systemic rheumatological disease. The incidence of HSDs varies between 5% and 45% according to the age, sex, and ethnic origin of the patients (1-3).

In children, HSD is diagnosed based on the Beighton Hypermobility Score (4,5). In HSD, the most common complaint is pain that is often felt in the shoulders, arms, elbows, back, neck, and temporomandibular joint (6,7). Arthralgia, recurrent joint dislocation, subluxation, and carpal tunnel syndrome, as well as, several other conditions, such as vesicoureteral reflux, voiding dysfunction (VD), urinary tract infections (UTIs), striae gravidarum, varicocele, abdominal herniation, and mitral valve

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prolapse may accompany HSD (8,9). Pelvic floor dysfunction influences the etiopathogenesis of VD, and the incidence of VD is higher in patients with HSD than in healthy children (8,9).

Functional constipation (FC) is a clinical condition frequently reported in childhood and affects the quality of life of children and their parents. An increase in intestinal laxity due to HSD may lead to a decrease in intraluminal pressure and result in relatively slow intestinal passage. Previous studies have reported that the incidences of rectal evacuation disorders, slow transit constipation, and gastrointestinal system disorders, such as functional abdominal pain and FC, were higher in patients with HSD compared to their incidences in healthy children (10,11).

In this study, we investigated the frequency of HSD, FC, VD, and their relationships with each other in school-aged children. We hypothesized that lax pelvic floor ligaments in HSD may lead to functional gastrointestinal system disorders and dysfunctional voiding problems. As studies in this field are limited, we examined the reciprocal relationships (if any) between HSD, FC, and VD.

Material and Method

Study Design

This prospective study was conducted at Trabzon Farabi Hospital between April 2017 and June 2020. Students were screened from four different schools, which were located in different regions of Trabzon Province. The students were primary and secondary school children who were 6–15 years old. The students who met the inclusion criteria were included in the study. Primary and secondary school students in Trabzon Province were individually examined, and questionnaires were distributed among them. In total, 947 children participated in this cross-sectional study. We excluded children from the study with chronic kidney and urinary tract anomalies that cause VD, those with chronic diseases involving the gastrointestinal system that cause FC, and those with chronic rheumatological diseases. All participants were healthy and were not under any drug therapy regimen. The questionnaires requested demographic information from participants on their age, sex, education status of the parents, family income, number of siblings, voiding habits, history of UTI, constipation, and any learning or behavioral problems. The questionnaires were filled out by the parents and collected two weeks later.

Evaluation of Hypermobility Spectrum Disorders

A pediatric rheumatologist examined the physical condition of all participants and used the Beighton Hypermobility Score to diagnose HSD. For children who were 5–9 years old and those ≥10 years old, Beighton Hypermobility Score ≥5 and ≥4 were defined as the criteria for HSD, respectively. These scores were calculated based on the following criteria: (i) dorsiflexion of the metacarpophalangeal joint to ≥90°, (ii) hyperextension of the elbow to ≥10°, (iii) hyperextension of the knee to ≥10°, and (iv) placement of hands flat on the floor without bending the knees (4-5).

Evaluation of Functional Constipation

Participants were evaluated, and FC was diagnosed by a pediatric gastroenterologist who assessed the gastrointestinal symptoms of participants based on the Rome III Diagnostic Criteria for Irritable Bowel Syndrome (12). All participants filled out a questionnaire based on the Rome III criteria to assess FC. According to the Rome III criteria, complaints of irritable bowel syndrome should be present for at least three months, recurrent abdominal pain or discomfort (an uncomfortable sensation not described as pain) associated with two or more of the following: improvement with defecation, and/or onset associated either with a change in the frequency of stool, and/or in the form or appearance of stool that should be present for at least six months.

Evaluation of Voiding Dysfunction

The diagnosis of VD was based on the questionnaire for the Dysfunctional Voiding and Incontinence Symptoms Score (DVISS) of The International Children's Continence Society. The results were evaluated by a pediatric nephrologist. The obtainable DVIS scores ranged from 0 to 35 points. A DVIS score of ≥9 points suggested VD (13).

Evaluation of Urinary Tract Infection

Whether participants had a history of UTI or started antibiotherapy due to UTI was also determined by the questions asked in the questionnaire.

Statistical Analysis

All data were analyzed using SPSS 26.0. The descriptive variables are presented as numbers and percentages. The differences between categorical variables in independent groups were determined by Chi-square tests. The differences between subgroups were determined by post hoc tests. All differences were considered to be statistically significant at $p<0.05$. Power analysis was not performed at the beginning of the study. A posterior power analysis was performed and calculated using the relationship between VD and constipation as the primary hypothesis. The G*Power 3.1.9.2 program was used to perform the power analysis, and the post hoc power was found to be 99.9%.

Results

Demographic characteristics

In this cross-sectional study, 947 children (6–15 years old) were included. Among them, 52.4% were girls. Most participants (60.4%) were between 6 and 10 years old. The questions on the mother's education level, father's education level, monthly income of the family, and the number of children in the family were answered by 942, 932, 910, and 937 participants, respectively. The mothers of 335 (35.6%) children and fathers of 366 (39.3%) children were high school graduates. The families of 379 (41.6%) children had a monthly income three times the minimum wage (in Turkish liras), and 754 (80.5%) children had 2–3 siblings.

Frequency and Clinical Features of Functional Constipation, Voiding Dysfunction, and Hypermobility Spectrum Disorders

Hypermobility was observed in 155 (16.4%) children, VD in 139 (14.7%) children, and constipation in 174 (18.4%) children. Children with hypermobility most commonly had left (89.7%) and right (82.6%) metacarpophalangeal joint hypermobility. The most common complaints in children with VD were urgency (72.7%) and enuresis (56.8%). Lumpy or hard stool (54.6%) and painful defecation (45.4%) were the most common complaints in children with constipation (Table 1). When the factors affecting the frequency of VD were examined, VD was more frequently associated with younger children (6–10 years old), lower education level of the mother, lower family income level (minimum wage and below), and children with a history of UTIs ($p<0.001$, $p=0.027$, $p=0.035$, and $p<0.001$, respectively). Constipation was more common in children with a history of UTIs ($p=0.001$). The difference in the incidence of VD and constipation between children with and without hypermobility was not significant. The frequency of constipation was higher in children with VD compared to those without VD ($p<0.001$) (Table 2). Comparison within the subgroups showed that the frequency of VD differed significantly based on the maternal education level, and its frequency increased as the education level decreased ($p=0.027$). The results of post hoc tests showed that the frequency of VD differed significantly between those whose mothers received secondary school education and high school education ($p=0.040$), between those whose mothers received secondary school education and university education ($p=0.019$), between those whose mothers received primary school education and high school education ($p=0.042$), and between those whose mothers received primary school education and university education ($p=0.020$). The frequency of VD differed significantly according to the monthly income level of the family, and the frequency increased as the income level decreased ($p=0.035$). The results of post hoc tests showed a significant difference between those whose families earned the minimum wage or below and those whose families earned three times the minimum wage ($p=0.010$). The frequency of hypermobility differed significantly according to the monthly income of the family; the frequency increased with an increase in the income level ($p=0.003$). The results of the post hoc test showed a significant difference between those whose families earned the minimum wage or less and those whose families earned two times the minimum wage ($p=0.002$); the difference was also significant between those whose families earned two times and three times the minimum wage ($p=0.037$).

Table 1. The frequencies and characteristics of hypermobility, voiding dysfunction, and constipation in children.

	n	%
Hypermobilities	**155**	**16.4**
Left metacarpal	139	89.7
Right metacarpal	128	82.6
Left knee	105	67.7
Left elbow	101	65.2
Right knee	99	63.9
Right elbow	83	53.5
Left thumb	72	46.5
Right thumb	62	40.0
Trunk	15	9.7
Voiding Dysfunction	**139**	**14.7**
Urgency	101	72.7
Enuresis	79	56.8
Squatting	57	41.0
Urinary incontinence	48	34.5
Staccato urination	42	30.2
>7 urination in a day	41	29.5
Discontinuous urination	38	27.3
Painful voiding	29	20.9
Hesitancy	20	14.4
Functional Constipation	**174**	**18.4**
Lumpy or hard stool	95	54.6
Painful defecation	79	45.4
Sensation of incomplete evacuation	64	36.8
≤2 defecation in a week	48	27.6
Fecal incontinence	28	16.1
Urinary tract infection	**240**	**25.3**

Discussion

In this study, the results related to FC and VD were not significantly different between children with and without HSD. Some studies have reported that the frequency of FC and VD is higher among children with HSD, while other studies did not find a significant increase (14-16). Chelimsky et al. (14) showed that an increase in intestinal laxity leads to a decrease in intraluminal pressure and results in slow intestinal passage. Similar to the findings of our study, Khorasgani et al. (15) found no significant difference in the incidence of HSD between patients with and without FC. Zaleski et al. (17) conducted a study with 411 children and showed that FC is significantly more common in girls with HSD

(p<0.05). Adib et al. (3) conducted a similar study in a pediatric rheumatology clinic in the United Kingdom and detected chronic constipation in 30% of the patients with HSD. In this study, we detected FC in 20% of cases with HSD; however, the difference in the frequency of FC between the HSD group and the healthy control group was not significant (p=0.647). Velasco-Benitez et al. (16) evaluated 1,630 children who were 10–18 years old using the Rome IV criteria and detected functional gastrointestinal tract disorders in 267 (16.2%) patients and HSD in 306 (28.4%) patients. The differences in the results of the studies investigating the relationship between FC and HSD might be due to genetic variations associated with HSD. Variations in incidence rates may be caused by differences in sex, age, ethnic and regional characteristics of the patients, and the types of questionnaires used to detect FC (4). Unlike the findings of our study, Shulman et al. (18) did not find a significant difference between patients with and without generalized joint hypermobility in terms of the development of irritable bowel syndrome and functional abdominal pain. We speculated that dietary, oral hydration, and defecation habits are also important factors associated with the development of FC. Information on these aspects should be obtained from patients when evaluating FC. The differences between the studies may also be due to the different scoring systems used to evaluate HSD. Some researchers argue that the Beighton scoring system is insufficient to define HSD and that it needs to be improved (19).

Table 2. Comparison of hypermobility, voiding dysfunction, and constipation in children based on the contributing factors.

	Hypermobility			**Voiding dysfunction**			**Constipation**		
	n	**%**	**p***	**n**	**%**	**p***	**n**	**%**	**p***
Age groups (years)									
6-10	78	13.6	**0.005**	111	19.4	**<0.001**	103	18.0	0.719
11-15	77	20.5		28	7.5		71	18.9	
Sex									
Female	91	18.3	0.084	71	14.3	0.740	94	19.0	0.630
Male	64	14.2		68	15.1		80	17.7	
Maternal education									
Illiterate	1	9.1	0.066	3	27.3	**0.027**	3	27.3	0.514
Primary school	28	12.6		41	18.5		47	21.2	
Secondary school	23	15.3		29	19.3		24	16.0	
High school	52	15.5		41	12.2		55	16.4	
University	50	22.3		24	10.7		43	19.2	
Paternal education									
Illiterate	1	12.5	0.099	2	25.0	0.078	1	12.5	0.905
Primary school	17	12.8		21	15.8		28	21.1	
Secondary school	21	14.4		27	18.5		27	18.5	
High school	54	14.8		57	15.6		65	17.8	
University	60	21.5		27	9.7		49	17.6	
Monthly income									
Minimum wage or below	18	9.9	**0.003**	36	19.8	**0.035**	27	14.8	0.290
Minimum wage x 2	52	14.9		53	15.2		71	20.3	
Minimum wage x 3	79	20.8		44	11.6		68	17.9	
Number of siblings									
Single	16	18.8	0.199	17	20.0	0.097	18	21.2	0.266
2-3	127	16.8		101	13.4		131	17.4	
>3	10	10.2		19	19.4		23	23.5	
History of UTI									
Yes	46	19.2	0.153	53	22.1	**<0.001**	62	25.8	**0.001**
No	105	15.2		82	11.9		111	16.1	
Hypermobility									
Yes				18	11.6	0.291	31	20.0	0.647
No				121	15.3		143	18.1	
Voiding dysfunction									
Yes	18	12.9	0.291				55	39.6	**<0.001**
No	137	17.0					119	14.7	
Constipation									
Yes	31	17.8	0.647	55	31.6	**<0.001**			
No	124	16.0		84	10.9				

*Chi-square test. UTI: urinary tract infection.

Abdol-Mohammad et al. (20) evaluated 226 children (113 patients with HSD and 113 control subjects; 5–14 years old) and detected HSD in 45% of patients with VD and 17% of control subjects. The most common complaints in that study were related to UTI in girls and constipation in boys. In our study, HSD was detected in 12.9% of patients with VD, and its prevalence was not significantly different from that of the control subjects (p=0.291). de Kort et al. (9) showed that children with HSD have a higher frequency of VD and daytime urinary incontinence than healthy children because of the laxity of their pelvic floor ligaments. In girls with HSD, the frequencies of UTI, nocturnal enuresis, and daytime urinary incontinence were higher than their respective frequencies in the controls. The frequency of constipation and fecal incontinence was higher in boys with HSD. We did not find a significant relationship between HSD and VD in this study, probably because of the differences in the study populations, ethnicity, regional characteristics, sex, and age of the participants investigated in other studies. These differences in the results between studies may also suggest that voiding disorders have a multifactorial etiology involving central, spinal, and sympathetic-parasympathetic neural mechanisms, which affect functions of detrusor and sphincter, bladder filling and emptying phases, and the physiology of urination. We found that enuresis occurred in 56.8% and daily urinary incontinence occurred in 34.5% of patients with VD. In our study, the frequency of UTI was significantly higher in patients with VD and constipation ($p<0.05$ for both). The frequency of VD was significantly higher (31.6%) in patients with FC than those without FC ($p<0.001$), which was also found in other studies. Lower urinary tract symptoms are more prevalent in patients with constipation (21). We found UTI at a significantly higher (22.1%) rate in patients with VD ($p<0.001$) than those without VD. As shown in other studies, the frequency of UTI was significantly higher (25.8%) in patients with FC relative to that in healthy participants (p=0.001). However, UTI rates were similar in patients with and without HSD. Some researchers have reported higher incidence rates of lower urinary tract symptoms (vesicoureteral reflux, UTI, VD, etc.) in patients with a more complicated syndrome known as Ehlers-Danlos syndrome (22).

Limitations of the Study

As this study was conducted in one city, the conclusions derived based on the collected data cannot be generalized to the whole population. Thus, multicenter studies need to be conducted to investigate generalized hypermobility in childhood. If information on the three-day diet and fluid intake of the patients could be obtained, additional factors triggering FC might have been identified. If patients with VD who maintained a voiding diary were evaluated, we may have identified other factors affecting its etiology.

Conclusion

VD and FC are common in childhood. The relationship between HSD and these disorders is not clear. Constipation should be investigated in children with VD and/or UTIs, and the factors causing FC in these patients should be identified and treated. Some studies have shown that diffuse joint hypermobility increases problems such as FC and VD. More information might help diagnose and treat patients with HSD in future.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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Evaluation of the Contribution of Computed Tomography Findings and Neutrophil/Lymphocyte and Neutrophil/Platelet Ratios in the Diagnosis of Acute Epiploic Appendagitis

Akut Epiploik Apandajit Tanısında Bilgisayarlı Tomografi Bulguları ile Nötrofil/Lenfosit ve Nötrofil/Platelet Oranlarının Katkısının Değerlendirilmesi

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Öz

Akut epiploik apandisit (AEA) kolon çevresindeki yağla dolu keselerin enfeksiyonu veya iskemisi ile karakterize nadir bir hastalıktır. Teşhis edilmesi zordur ve ameliyat gerektiren diğer akut karın ağrısı ile karıştırılabilir. Bilgisayarlı tomografi (BT), akut epiploik apandisit tanısında altın standart tekniktir. Çalışmamız, karın ağrısı ile başvuran hastalarda AEA BT bulgularını ve tam kan sayımından elde edilen nötrofil-lenfosit ve nötrofil-trombosit oranlarının tanısal değerini değerlendirmeyi amaçlamaktadır. AEA tanısı konulan 40 hasta ve benzer karın ağrısı şikayeti olan ve tedavi için acil ameliyat gerektiren 80 hasta olmak üzere toplam 120 hastayı çalışmaya dahil ettik. Öncelikle kontrol grubundaki hasta sayısını belirlemek için güç analizi yapıldı. Kontrol grubu hastaları, akut cerrahi girişim gerektiren karın ağrısı olan hastalar arasından kura programı ile belirlendi. Kontrol grubunda akut apandisit, peptik ülser perforasyonu, kolon perforasyonu, mezenter iskemisi, üreter taşı, over torsiyonu, over kisti rüptürü ve ektopik gebelik rüptürü tespit edilen patolojiler idi. AEA grubundaki ortalama yaş 41.6 idi ve grubun çoğunluğu erkekti (%70) ve bu grupta en sık görülen şikayet karın ağrısı (%80.1) idi. Nötrofil/lenfosit ve nötrofil/platelet oranları, AEA grubunda, ameliyat gerektiren akut karın ağrısı grubuna göre anlamlı derecede düşüktü ($p<0.001$). Nötrofil/lenfosit oranı ve nötrofil/platelet oranı için kesim değerleri sırasıyla 5.80 ve 6.96 idi. Bu bulgular, nötrofil/lenfosit oranı ve nötrofil/platelet oranının akut epiploik apandisit tanısı koymaya ve onu acil cerrahi gerektiren çeşitli karın ağrısı nedenlerinden ayırmaya yardımcı olabileceğini ve potansiyel olarak gereksiz cerrahi müdahaleyi önleyebileceğini göstermektedir.

Anahtar Kelimeler: Akut Epiploik Apandisit, Akut Karın Ağrısı, Nötrofil-Lenfosit Oranı, Nötrofil-Trombosit Oranı

Abstract

Acute epiploic appendicitis (AEA) is a rare disease characterized by infection or ischemia of fat-filled sacs around the colon. It is difficult to diagnose and can be confused with other acute abdominal pain requiring surgery. Computed tomography (CT) is the gold standard technique for acute epiploic appendicitis. Our study aims to evaluate the CT findings of acute epiploic appendicitis and the diagnostic value of neutrophil-lymphocyte ratios (NLR) and neutrophil-platelet ratios (NPR). We included one hundred twenty patients, 40 of whom were diagnosed with acute epiploic appendicitis, and 80 had similar complaints of abdominal pain and needed urgent surgery for treatment. First of all, power analysis was performed to determine the number of patients in the control group. Control group patients were determined by a lottery program. Pathologies detected in the control group were acute appendicitis, peptic ulcer perforation, colon perforation, mesenteric ischemia, ureteral stone, ovarian torsion, ovarian cyst rupture, and ectopic pregnancy rupture. The mean age in the AEA group was 41.6 years, and the group was predominantly male (70%). The most common complaint of the AEA group was abdominal pain (80.1%). NLR and NPR were significantly lower in the AEA group compared to the acute abdominal pain requiring surgery group ($p<0.001$). The cut-off values for NLR and NPR were 5.80 and 6.96, respectively. These findings suggest that neutrophil/lymphocyte ratio and neutrophil/platelet ratio may help diagnose AEA and distinguish it from various causes of abdominal pain that need urgent surgery, potentially preventing unnecessary surgical intervention.

Keywords: Acute Epiploic Appendicitis, Acute Abdominal Pain, Neutrophil-Lymphocyte Ratio, Neutrophil-Platelet Ratio

Introduction

Epiploic appendages, also known as epiploic extensions, were first described by Vesalius in 1543 (1). Acute epiploic appendagitis (AEA) refers to the inflammation or ischemia of peritoneal outpouchings filled with fat located around the colon segments from the cecum to the rectosigmoid junction and the vermiform appendix, which can occur due to torsion or spontaneous venous thrombosis (2). It is usually a self-limiting condition and most commonly affects patients in the 2nd to 5th decades and prefers women and obese individuals, probably due to larger appendages. Its frequency is approximately 1.3% of cases with abdominal pain (3). It is rare in pediatric patients since epiploic appendages are not yet fully developed (4). AEA's rarity and nonspecific clinical symptoms sometimes make its diagnosis challenging.

The patient's main presenting symptoms are abdominal pain and defense during the abdominal examination. While AEA presents with symptoms similar to the acute abdomen, it is a disease that can be effectively treated conservatively; however, it can be clinically confused with conditions requiring

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surgery (5,6). Pain may be more localized than other acute abdomen reasons like diverticulitis or acute appendicitis, as there is focal peritoneal irritation (7). For diagnosis, ultrasonography (US), computed tomography (CT), and magnetic resonance (MR) imaging may be used. The ultrasonography often reveals a moderately hyperechoic, ovoid, non-compressible mass close to the colon with considerable discomfort (8,9). CT is the gold standard imaging technique for evaluating patients with acute abdominal pain of uncertain origin (10). In modern radiology technology, the diagnosis of AEA can be reliably established using CT.

The normal epiploic appendages, which are small fatty projections on the surface of the colon, are typically not easily visualized on CT images. Their density is similar to fatty tissue in the surrounding peritoneal wall and omentum, resulting in overlapping appearances. In the case of inflammation of the epiploic appendix, CT can reveal specific findings, such as an oval-shaped lesion with fat attenuation (similar to adipose tissue) surrounded by a thin hyperdense rim on CT, known as the hyperattenuating ring sign. This lesion is typically located adjacent to the colon and is linked with adjacent mesentery inflammation (Figure 1,2). Another characteristic finding is an area of significant attenuation in the center of the fatty lesion, known as the central dot sign. This central dot represents a thrombosed vein within the AEA (Figure 3).

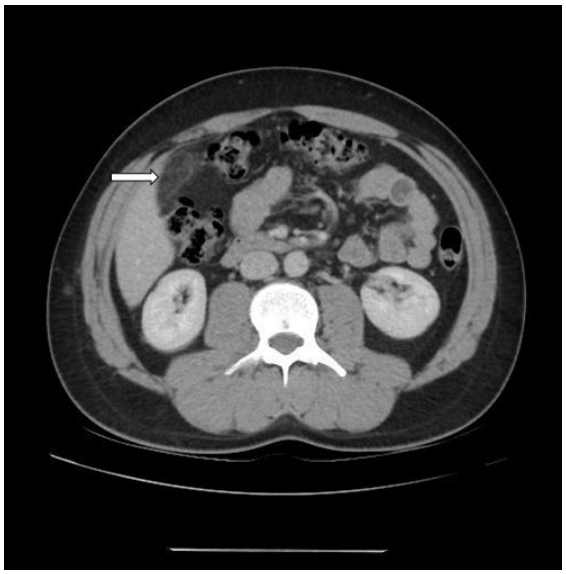

Figure 1. Axial sections of contrast enhanced CT, an oval-shaped inflamed fatty tissue area surrounded by a hyperdense ring at the level of the hepatic flexure (arrow).

The neutrophil-to-lymphocyte ratio (NLR) has been proposed to assess the extent of systemic inflammation, and NLR has been shown to correlate with worse outcomes in patients with infection (11). Also, the neutrophil-to-platelet ratio (NPR) is implicated in the inflammatory response to infections; it may affect the platelet count and the thrombotic process, which might lead to thrombosis (12).

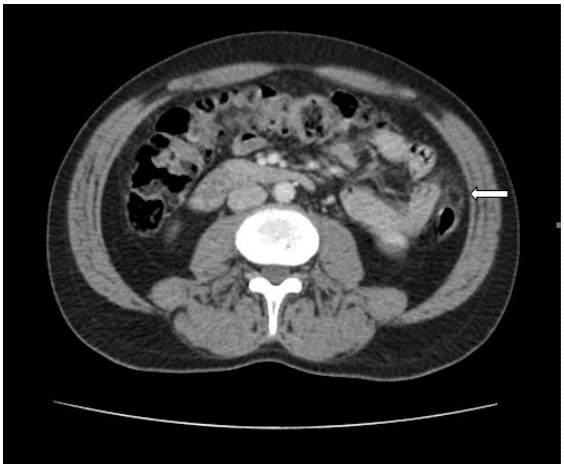

Figure 2. In axial CT scans with intravenous contrast, epiploic appendagitis is seen at the level of the descending colon. Hyperattenuated ring sign observed around inflamed fat tissue (arrow).

In this study, we aim to review the CT findings of AEA and examine the contribution of acute phase reactants, such as the neutrophil/lymphocyte ratio (NLR) and neutrophil/platelet ratio (NPR) based on complete blood count, in diagnosing the AEA. By identifying markers that can place the diagnosis of AEA among the differential diagnoses of patients presenting with AAPRS, we intend to promote conservative management and prevent unnecessary surgical procedures.

Figure 3. In axial CT scans with intravenous contrast, a hyperattenuated ring sign (big arrow) adjacent to the sigmoid colon and a focal increase in density (central dot sign) of thrombosed veins in its center (thin arrow).

Material and Method

Ethical approval

Our study was conducted according to the guidelines and regulations of the Institutional Review Board of Health Sciences University Ankara

Dışkapı Yıldırım Beyazıt Training and Research Hospital with a 36/06 approval number dated 27.03.2017.

Patient selection

By using the keywords 'epiploic appendagitis' in the abdominal CT reports from the hospital data storage system, 43 cases of epiploic appendagitis were found between January 2014 and December 2016. Since the data of 3 patients could not be accessed, they were not included in the study. The main outcome variables of the study are NLR and NPR, respectively, in terms of NLR and NPR averages between groups; In order to test the statistical significance of the differences of at least 12.52 and 278.6 at 95% power and 5% error level (two cases for each control case), it was planned to include at least 15 cases in the control group and at least 29 cases in the case group (13). For NLR, effect size d=1.3969678 and for NPR, effect size d=1.1860167 was calculated. Two control patients were taken for each case. Among the 4957 patients who applied to our hospital with acute abdominal pain between 2018-2020 and had abdominal CT for this reason, 43 people diagnosed with epiploic appendicitis were excluded. Of the 4914 patients, 3372 who did not receive acute surgical treatment were excluded, and among 1542 patients were identified. The remaining 1542 patients whose treatment resulted in acute surgery were loaded into the lottery program, and the command was given to select 80 patients for the control group.

Data collection

Demographic data, clinical characteristics, NLR, and NPR values were extracted from the patient's records. CT images of patients diagnosed with AEA were reevaluated at the location of AEA within the abdomen, lesion size, presence of linear stranding around the lesion, oval-shaped lesion with fat attenuation surrounded by a thin hyperdense rim (hyperattenuating ring sign), central hyperdensity (central dot sign), and thickening of adjacent peritoneum by radiologists. The NLR and NPR were obtained from the hemogram results of the patients. The NLR was calculated by dividing the neutrophil count by the lymphocyte count, and the NPR was calculated by dividing the neutrophil count by the platelet count obtained from complete blood counts.

Statistical analysis

The correlation between NLR, NPR, and AEA was also assessed. The $\chi 2$-test, independent t-test and Mann-Whitney U test were used to compare distributions between the two groups. The diagnostic performance of NLR and NPR was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). We used a receiver operating characteristic (ROC) curve analysis to calculate the cut-off. Statistical analysis was performed by IBM SPSS Statistics for MAC.

Results

40 patients were diagnosed with AEA, 28(70%) were male and 12(30%) were female; the mean age of the patients was 41.6±9.3. The main complaints were 80.1% abdominal pain, 9.5% groin pain, 7.8% flank pain with nausea and vomiting (2.6%), and abdominal discomfort and painful micturition.

The average time of symptoms was 4.3 days (1-15 days). In the CT scan images, AEA was located in the descending colon (28, 70%), ascending colon (3, 7.5%), cecum (2, 5%), and transverse (7, 17.5%). "hyperattenuating ring sign" was detected in 30 (75%) patients and "central dot sign" was seen in 21 (52.5%) patients. No patient underwent surgical treatment. However, 10 (25%) patients were hospitalized for medical treatments (Table 1).

42(52.5%) were male and 38(47.5%) were female of 80 patients in the AAPRS group; the mean age of the patients was 45.2±8.7. The main complaints were 65.9% abdominal pain, 15.9% groin pain, 10.2% flank pain with nausea and vomiting (8.4%), and abdominal discomfort and painful micturition. The average time of symptoms was 6.2 days (2-12 days).

Table 1. Patient Characteristics and Clinical Factors in Acute Epiploic Appendagitis (AEA) Group and Abdominal Pain Groups Requires Surgery (AAPRS) Group.

	AEA Group	**AAPRS Group**	**Statistical Test**	**p-value**
Number of Patients	40	80		
- *Male*	28 (70%)	48 (52.5%)	Chi-square test	0.104
- *Female*	12 (30%)	32 (47.5%)		
Mean Age	41.6±9.3	45.2±8.7	Independent t-test t value:2.124	0.048
Main Complaints			Chi-square test	0.174
- *Abdominal pain*	80.1%	65.9%		
- *Groin pain*	9.5%	15.9%		
- *Flank pain with nausea and vomiting*	7.8%	10.2%		
-*Abdominal discomfort and painful micturition*	2.6%	8.4%		
Average Time of Symptoms	4.3 days	6.2 days	Mann-Whitney U test U value: 174.5	0.065
Hospitalization	10 (45%)	80 (100%)	Chi-square test	0.02

In the CT scan images of the AAPRS group, the most common findings were consistent with usual abdominal emergencies causing abdominal pain, such as acute appendicitis, peptic ulcer perforation, colon perforation, mesenteric ischemia, ureteral stone, ovarian torsion, ovarian cyst rupture, and ectopic pregnancy rupture.

The mean age of the AEA Group was 41.6±9.3 years, whereas the AAPRS group had a slightly higher mean age of 45.2±8.7 years. There was a significant difference between the groups (p=0.048).

The distribution of other complaints, such as groin pain, flank pain with nausea and vomiting, and abdominal discomfort with painful micturition, differed slightly between the groups, and there was not a statistically significant difference between the groups (p=0.174).

The average time of symptoms in the AEA Group was 4.3 days. In contrast, the AAPRS group had an average time of 6.2 days, and there was a trend toward a shorter duration of symptoms in the AEA Group, but there was no statistical difference between the groups (p=0.065). Regarding hospitalization, ten patients in the AEA Group (25%) required hospital admission, while 80 patients in the AAP Group (100%) were hospitalized (p=0.02) (Table 1).

We revealed a significantly lower mean NLR in patients diagnosed with AEA than the AAPRS (mean NLR±standard deviation vs. NLR in the control group, p<0.001). The mean NLR for the AEA group was 3.463, the standard deviation was 2.34, and the cut-off value for NLR was 5.80. The mean NPR for the AEA group was 4.121, the standard deviation for NPR in the CT-positive group was 2.84, and the cut-off value for NPR was 6.96 (Table 2). The mean NLR for the AAPRS group was 9.341, the standard deviation was 3.48, and the cut-off value for NLR was 11.01. The mean NPR for the AAPRS group was 11.127, the standard deviation for NPR in the CT-positive group was 3.89, and the cut-off value for NPR was 13.9. This indicates that based on the given cut-off values, NLR and NPR have a sensitivity of 26.9% and 30.8% in correctly identifying AEA cases. The specificity is 92.0%, indicating a high ability to identify AEA cases correctly. The PPV was 77.8%, and the NPV was 52.4% for NLR and the PPV was 52.4 and the NPV was 52.4 for NPR.

Table 2. Mean and Standard Deviation of Neutrophil-to-Lymphocyte Ratios (NLR) and Platelet-to-Lymphocyte Ratios (NPR) in Acute Epiploic Appendagitis (AEA) and Abdominal Pain Requires Surgery (AAPRS) groups with Cut-off Values.

	Mean	Standard Deviation	Cut-off Value
AEA group NLR	3.463	2.34	5.8
AEA group NPR	4.121	2.84	6.96
AAPRS group NLR	9.341	3.48	11.01
AAPRS group NPR	11.127	3.89	13.9

Discussion

AEA is a rare condition characterized by inflammation or ischemia of fat-filled sacs around the colon. Ischemia develops due to torsion or spontaneous venous thrombosis of the relevant epiploic appendage. AEA is more prevalent in males and typically diagnosed in males between the ages of 40 and 50. It is usually linked to hernias, colonic diverticula, obesity, and intense exercise, most commonly seen in the rectosigmoid region. Its clinical symptoms overlap with other acute abdominal conditions, making its diagnosis challenging (1,7,14). However, accurate and timely diagnosis is essential to avoiding unnecessary surgical interventions and preventing high labor and costs for diagnosis and treatment. The CT findings of AEA, including the hyperattenuating ring sign and central dot sign, are specific and can aid in accurately diagnosing the condition. These findings were observed in a significant proportion of AEA patients in our study, supporting the importance of CT imaging in diagnosing suspected cases. CT allows for the visualization of characteristic features of AEA, such as the oval-shaped lesion with fat attenuation surrounded by a thin hyperdense rim and the central high-attenuation focus representing thrombosed veins within the fatty lesion (15,16).

In today's conditions, CT is a fast, easily accessible examination that provides remote evaluation. CT is very easily accessible in many parts of the world, but it is still not an examination that can be accessed as quickly and as early as it is thought in some parts of the world. In addition, since it is an examination involving radiation, the benefit and harm ratio should be considered when performing CT in emergency departments.

Since AEA presents with severe abdominal pain, it is a clinical condition that can easily be encountered with AAPRS. Misdiagnosis can result in unnecessary hospitalization, antibiotic use, and surgery.

Our results showed that the mean NLR and NPR values were significantly lower in patients diagnosed with AEA compared to the AAPRS group. These findings suggest that NLR and NPR could serve as diagnostic markers for AEA and help differentiate it from other causes of abdominal pain that result from surgery. NLR and NPR showed a moderate diagnostic performance in identifying AEA cases, with a sensitivity of 26.9% and a specificity of 92.0%. The PPV was 77.8%, with an NPV of 52.4%. While NLR and NPR can help identify AEA cases

with high specificity, their sensitivity was low, implying that they might not be accepted as independent diagnostic tools. However, they can provide further supportive information for diagnosing AEA when used with CT findings. With the results of our study, we think that the conservative approach can be made in a safer zone during the diagnosis, follow-up, and treatment stages of patients with low NLR and NPR levels in cases of acute abdominal pain presenting to the emergency department. NLR and NPR may indicate the presence of inflammation and indicate the severity of inflammation. In line with the results we obtained and those obtained in many studies in the literature, it was found that these two parameters were at lower levels in more localized and less severe inflammations (17).

When we looked at the results of our study, we found that the NLR and NPR cutoff values of the AEA and AAPNS groups differed significantly. In this way, we think we can use NLR and NPR as the first step to distinguish AEA cases from patients needing urgent surgery, as they are cheap, efficient, and quickly available, and changes during follow-up correlate with the prognosis of the disease.

The NLR has been shown to predict the severity of various conditions, including severe acute pancreatitis, acute appendicitis, COVID-19, and breast malignancies (18-21). NPR has also been investigated as a prognostic predictor, notably in individuals with metastatic colorectal cancer. Previous research has linked high NLR and NPR levels to esophageal, renal, and hepatocellular cancers (22-25).

Conservative management is the preferred approach for treating AEA. The main purpose of AEA treatment is pain control; anti-inflammatory drugs are prescribed for 4-7 days. Antibiotics are often not indicated. Close monitoring during treatment for AEA is not necessary. However, although very rare, some complications may develop during AEA follow-up. These complications are adhesion, abscess, peritonitis, bowel obstruction, and intussusception. In cases where pain persists or increases after diagnosis and conservative treatment, these complications should be considered. The literature recommends following the dynamic course of NLR and NPR for many clinical conditions, such as cancer and infection. Initial NLR and NPR monitoring and changes in these parameters before repeat imaging in these patients will be helpful to the clinician.

Despite the study's advantages, such as its relatively high sample size and evaluation of CT findings and hematologic markers, significant drawbacks should be noted. First, the study's retrospective approach brings limitations. Second, the study was conducted in a single center, which might limit the findings' generalizability. Future multicenter studies with larger patient populations must confirm our findings and explore the diagnostic value of NLR and NPR in AEA. Furthermore, in our study, while the specificity values for NLR and NPR were high, the sensitivity value was not as high as expected. It is important that sensitivity and specificity values are balanced and high in order to provide distinctive features. NLR and NPR may not be reliable in terms of discrimination and should not be generalized.

Conclusion

Our study highlights the potential contribution of CT findings and hematologic parameters, specifically NLR and NPR, in diagnosing AEA. While CT remains the gold standard imaging technique, NLR and NPR can serve as supportive markers in identifying AEA cases and differentiating them from other causes of AAPRS.

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Conflict of interest statement

The authors declared no potential conflicts of interest with respect to research, authorship, and publication of this article.

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The Relationship between Periostin Level and the Presence of Esophageal Varices in Patients with Decompensated Cirrhosis

Dekompanse Siroz Hastalarında Özofagus Varis Varlığı ile Periostin Düzeyleri Arasındaki İlişki

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Öz

Özofagus varisleri, dekompanse karaciğer sirozu hastalarında hastalığın şiddeti ile ilişkili olarak ortaya çıkan ve hayatı tehdit eden bir komplikasyondur. Bu çalışmada, dekompanse siroz hastalarında özofagus varis gelişimi ile serum periostin düzeyi arasında ilişki olup olmadığı incelenecektir. Dekompanse karaciğer sirozu tanısı olan ve üst GIS endoskopisi yapılan 18-70 yaş aralığındaki hastalar bu çalışmaya dâhil edildi. Hastaların serum periostin düzeyi ile özofagus varis gelişimi arasındaki ilişki incelendi. Özofagus varisi olan hastalar, varis evrelerine göre evre I, II ve III şeklinde üç gruba ayrılıp grupların periostin seviyeleri karşılaştırıldı. Hastaların 43'ü (%54.4) kadın, 36'sı (%45.6) erkekti ve yaş medyan değeri 62 (20-70) olarak hesaplandı. Hastaların 60'ında (%75.9) özofagus varisi mevcuttu (evre I; n=16, evre II; n=23, evre III; n=21). Özofagus varisi olan grubun serum periostin düzeyi, varisi olmayan gruba nazaran daha yüksekti ancak fark istatistiksel olarak anlamlı düzeyde değildi (p=0.222). Özofagus varisi olan hastalar varis evrelerine göre karşılaştırıldığında, gruplar arasında periostin seviyeleri açısından anlamlı fark yoktu (p=0.480). Korelasyon analizinde, periostin ile CHILD skoru (r=0.307, p=0.006), GPR (r=0.279, p=0.013), APRI (r=0.283, p=0.011), FIB-4 skoru (r=0.286, p=0.011) ve INR değeri (r=0.235, p=0.037) arasında pozitif korelasyon, P2/MS skoru (r=-0.275, p=0.014), trombosit (r=-0.282, p=0.012) ve albumin (r=0.356, p=0.001) arasında negatif korelasyon tespit edildi. Serum periostin düzeyi ile özofagus varisi varlığı ve varis evreleri arasında anlamlı ilişki bulunamadı. Periostin ile birçok prognostik belirteç, arasında korelasyon bulunması, periostinin siroz hastalarında potansiyel bir prognostik belirteç, olabileceğini düşündürdü.

Anahtar Kelimeler: Dekompanse Karaciğer Sirozu, Fibrozis, Özofagus Varisi, Periostin

Abstract

Esophageal varices are life-threatening complications of decompensated liver cirrhosis. Herein, it was aimed to explore the relationship between esophageal varices and serum periostin levels in decompensated cirrhosis patients. Decompensated liver cirrhosis patients (18-70 years) undergoing upper gastrointestinal (GIS) endoscopy were included in the study. The relationship between serum periostin and esophageal varices was investigated. Those with esophageal varices were divided into three groups: stages I, II, and III, and the periostin levels of the groups were compared. Forty-three (54.4%) patients were female, and the median age was 62 years (20-70 years). Sixty (75.9%) patients had esophageal varices (stage I, n=16; stage II, n=23; stage III, n=21). Although serum periostin level was higher in those with esophageal varices than those without, the difference was not statistically significant (p=0.222). Given the grades of esophageal varices, no significant difference was seen between the groups concerning periostin levels (p=0.480). In analyses, statistically significant positive correlations were found between periostin levels and Child-Pugh score (r=0.307, p=0.006), gamma-glutamyl transpeptidase to platelet ratio (GPR) (r=0.279, p=0.013), aminotransferase (AST)/platelet ratio index (APRI) (r=0.283, p=0.011), fibrosis-4 (FIB-4) score (r=0.286 p=0.011), and international normalized ratio (INR) value (r=0.235, p=0.037), and negative correlations between periostin levels and P2/MS scores (r=-0.275, p=0.014), platelet (r=-0.282, p=0.012) and albumin (r=0.356, p=0.001). There was no significant relationship between serum periostin levels and the presence and grade of esophageal varices. The correlation between periostin and other prognostic markers suggested that periostin might be a potential prognostic marker in cirrhosis patients.

Keywords: Decompensated Liver Cirrhosis, Fibrosis, Esophageal Varices, Periostin

Introduction

Liver fibrosis is a disease characterized by hepatic failure led by such factors as hepatitis B, hepatitis C, alcohol intake and autoimmunity, and the accumulation of collagen which is an extracellular matrix protein. In those having decompensated liver cirrhosis, esophageal varices are likely to develop secondary to portal hypertension because of liver fibrosis along with increased sinusoidal pressure (1).

Commonly found in such body parts as the stomach, placenta, uterus, breast tissue, aorta, lower gastrointestinal tract, and thyroid, periostin is a 90 kD extracellular matrix protein consisting of 836 amino acids and was named periostin since it was first identified in the periosteum of long bones. Various studies have shown that periostin is responsible for pathological processes such as atherosclerosis, fibrosis, metastasis, and tumorigenesis. Additionally, the chronic

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inflammation of the periostin has also been revealed to regulate the deposition of collagen by supporting the fibrosis process when secreted from fibroblasts and altering the mechanical features of the connective tissues (2).

Depending on the reasons behind liver damage, hepatic stellate cells (HSHs) or activated portal fibroblasts are the most important cells responsible for fibrosis. It has been recently demonstrated that integrins, having notable functions such as migration, proliferation, and maintenance of survival, are expressed by HSHs. Because of the way periostin and integrins interact, periostin is considered to control the progression of hepatic fibrosis by altering the activities of HSHs. The expression of periostin was found to be higher in liver biopsy tissue and HSHs in those with liver cirrhosis than in the controls (3). To our knowledge, however, no clinical study has been carried out, investigating the level of periostin in those having decompensated cirrhosis, especially those with esophageal varices.

Esophageal varices are life-threatening complications related to the severity of liver cirrhosis. Therefore, our study aimed to look at the relationship between the development of esophageal varices and serum periostin levels in those having decompensated cirrhosis.

Material and Method

Design of The Study and Patients' Selection

Seventy-nine patients diagnosed with decompensated liver cirrhosis through upper GIS endoscopy (18-70 years of age) were admitted to the departments of Gastroenterology and Internal Diseases in The Education and Research Hospital of Konya at Health Sciences University between January 2018 and 2019.

Our study was commenced after approval was obtained from the Non-Pharmaceutical and Medical Device Research Ethical Board of the Medical School of Karatay University of Konya Trade Chamber (Date: June 5, 2018, and number: 2018/015) under the World Medical Association (WMA) Declaration of Helsinki, later the October 2013 amendment of "Ethical Principles for Medical Research Involving Human Subjects". Our research was funded by Konya Training and Research Hospital of the University of Health Sciences Türkiye.

We did not include the women with pregnancy and such advanced co-morbid diseases as ulcerative colitis, asthma-chronic obstructive pulmonary disease, and malignancy, and those with non-cirrhotic portal hypertension; we also excluded the individuals not accepting to participate before and after the study.

The subjects in this cross-sectional research were enrolled voluntarily. The volunteers were comprehensively informed about the design of the study, and written consent was obtained from those accepting to take part in the study. Diagnosed with decompensated liver cirrhosis, the patients for whom endoscopy was decided made by their follow-up physician were evaluated for the study. Periostin levels were investigated with the blood samples obtained from these patients due to routine practice. The demographic, laboratory data and endoscopy findings of the participants were recorded on patients' files, and so the association of serum periostin with esophageal varices was investigated. In addition, the relationship between the prognostic models of liver cirrhosis calculated via the clinical and available laboratory parameters, and esophageal varices was also examined.

The Child-Pugh Classification

The Child-Pugh classification was created to evaluate cirrhosis risk in patients undergoing non-shunt surgery. This classification is the modified version of the 5-variable Child-Turcotte classification used for the risk assessment in patients who will undergo the portocaval shunt surgery. Five variables in the classification are serum albumin and bilirubin levels, ascites, encephalopathy, and nutrition. In the Child-Pugh classification, the status of nutrition has been modified by prothrombin time, and the scores range from five to 15. The patients with a score of five or six are considered class A (well-compensated cirrhosis), those with a score between seven and nine are considered class B (severe functional limitation), and those with a score ranging from 10 to 15 are considered class C (decompensated cirrhosis) (4).

The Model for End-Stage Liver Disease (MELD) Score

Another model used to prognose cirrhosis is the MELD score. In this scoring system, the levels of bilirubin, creatinine, and international normalized ratio (INR) are used for predicting the 3-month survival rate. The first version of this score has been created for predicting the 3-month mortality in the cases where elective transjugular portosystemic shunts are placed, and in this version, liver diseases (cholestatic, alcoholic, etc.) are also evaluated etiologically (5).

The Model for End-Stage Liver Disease-Sodium (MELDNa) Score

Kim et al. developed this model in 2008 to estimate the 90-day mortality in sufferers awaiting liver transplantation. MELDNa was suggested to predict the 90-day mortality better than the classical MELD score and is calculated by adding the serum sodium level to the score of classical MELD using the subsequent formula (6):

MELDNa = MELD – Na - [0.025 × MELD × (140 - Na)] + 140

However, MELDNa is usually calculated online, similar to the MELD score.

The Aspartate Aminotransferase/Alanine Aminotransferase Ratio (AAR)

AST-ALT ratio (AAR) is 0.8 in healthy individuals. In various studies, a ratio>1 has been shown to indicate the presence of cirrhosis (7). However, the results reported by different studies are generally inconsistent, and the clinical utility of AAR has yet to be clear in the diagnosis of cirrhosis (8).

P2/MS

The formula of P2/MS was described by Lee et al. in the research evaluating 556 sufferers with virus-associated chronic liver disease in 2009. In this research, a relationship has been shown between the P2/MS score, and the existence of esophageal varices and degree of liver fibrosis with the following formula (9):

(Thrombocyte count, 10^9/L)^2/monocyte fraction (%) x segmented neutrophil fraction (%)

The Forns Index (FI)

Such features as the patient's age, gamma-glutamyl transpeptidase (GGT), cholesterol, and thrombocyte count are used to calculate this index. In a study, FI was also investigated in individuals with hepatitis C virus (HCV) due to its similar performances to APRI, and its formula is as follows (10):

7.811-3.131× ln (thrombocyte count) + 0.781× ln (GGT) + 3.467 × ln (age) -0.014 × cholesterol

The gamma-glutamyl transpeptidase to platelet ratio (GPR)

As described by Lemoine et al. in a 2015 study investigating 135 sufferers with chronic hepatitis B undergoing liver biopsy, the model of the GPR score is calculated by the ratio of GGT to the thrombocyte count (11). In the study, the GPR score was found to be associated with the severity of liver fibrosis.

The aminotransferase (AST)/platelet ratio index (APRI)

The APRI is performed by using serum AST and thrombocyte count. To calculate the elevation of AST, the AST level is divided by the laboratory upper limit value, and the thrombocyte count is calculated by dividing the value in mm^3 by 1000 (12).

APRI = (elevation of AST/thrombocyte count) x 1000

APRI was first studied in individuals with HCV, the co-infection of HCV and human immunodeficiency virus (HIV), and those having alcoholic liver disease (12,13). In a meta-analysis evaluating a total of 40 studies, it was reported that the cut-off APRI value of 1.0 could predict cirrhosis with 76% sensitivity and 72% specificity (13).

The Neutrophil Lymphocyte Ratio (NLR)

As an inexpensive marker and an easily accessible and reproducible indicator, neutrophil-lymphocyte ratio (NLR) reflects the systemic inflammatory response. It has been shown that elevated NLR levels are linked to poor clinical results in most malignancies and cardiac diseases. While neutrophil count generally demonstrates inflammation, low lymphocyte count indicates malnutrition and inflammatory status. In the study performed by Biyik et al., an increased level of NLR was found to be related to early mortality in those with liver cirrhosis (14).

The fibrosis-4 (FIB-4) Index

In the system of FIB-4, the biochemical values of thrombocyte count, ALT and AST, and age are used in combination; FIB-4 was found to be successful in predicting progressed fibrosis in studies evaluating those having cirrhosis and non-alcoholic fatty liver disease (NAFLD) due to chronic HCV (15,16). The index is calculated as:

FIB-4 = (age x AST)/(thrombocyte count x √ALT)

In a retrospective research where 320 NAFLD sufferers were evaluated via the FIB-4 index, while a cut-off value of 0.81 was detected to be significant in predicting liver-related complications, a cut-off value of 0.67 was found significant for predicting mortality or liver transplantation (17).

The Measurement of Periostin

The sera of the patients were centrifuged and kept at -80°C until conducting the study. The serum samples of periostin were evaluated by the enzyme-linked immunosorbent assay (ELISA) method with Periostin ELISA kits (Elabscience, Houston, TX, USA). The sensitivity of periostin was found as 0.10 ng/mL, and for the serum periostin test, the intra- and inter-run CVs (CV%) were <10%.

Statistical Analyses

The SPSS statistical package for Windows, version 21.0, was utilized to perform the statistical analyses (IBM SPSS Inc., Chicago, IL, USA). The categorical variables were shown as numbers and percentages, while the numerical variables were presented as mean±standard deviation (SD) and median (min-max). The Kolmogorov-Smirnov test was used to determine if the data were normally distributed. To show if almost all parameters were not normally distributed, the Mann-Whitney U test was performed in the presence of two independent groups, and the Kruskal Wallis test was utilized in the presence of more than two independent groups in the comparison of the numerical data. The chi-square

test or Fischer's exact test was utilized in the comparison of the categorical data between the independent groups. Additionally, the Spearman test was conducted to analyze the correlation between the numerical data since the data showed no normal distribution. A p-value less than 0.05 was accepted to indicate significance.

Results

The demographic, clinical, and laboratory features of the whole study population were compared. Of 79 decompensated cirrhosis patients in the study, 43 (54.4%) were female, and the median age was found as 62 (20-70 years). Considering the etiology of the cirrhosis patients, it was seen that the distribution of the patients was as follows: 44 cryptogenic (idiopathic), 12 HBV-related, 10 HCV-related, seven autoimmune, two cardiac-related, two alcohol-related, one diagnosed with Wilson's, and one with non-alcoholic steatohepatitis. Given the endoscopy results, however, 60 (75.9%) of the patients were detected to have esophageal varices (stage I, n=16; stage II, n=23; stage III, n=21). There was also a history of ascites in 36 (45.5%) and a history of encephalopathy in 11 (14%) individuals. Patients' clinical and demographic features are presented in Table 1.

Table 1. The comparisons of demographic and clinical characteristics of the study group under the status of varices.

Parameters	Total (n=79)	Varices (+) (n=60)	Varices (-) (n=19)	*p*
Sex (F/M)	43/36	29/31	14/5	0.053
Age (years)	57.4±12.2	57.1±11.7	58.3±14.1	0.309
Ascites (+)	36 (45.5)	32 (53.3)	4 (21.1)	*0.014
Encephalopathy (+)	11 (14.0)	10 (16.7)	1 (5.3)	0.280
CKD (+)	5 (6.3)	4 (6.7)	1 (5.3)	0.653
DM (+)	30 (38)	22 (36.7)	8 (42.1)	0.670
Hypertension (+)	22 (27.8)	16 (26.7)	6 (31.6)	0.677
CAD (+)	9 (11.4)	8 (13.3)	1 (5.3)	0.308
Cerebrovascular event (+)	2 (2.5)	2 (3.3)	0 (0)	0.574
Hgb (gr/dL)	11±2.1	10.8±2.1	11.4±1.9	0.309
Hct (%)	33.9±5.4	33.7±5.5	34.7±5.1	0.492
Thrombocyte (10^3/mm^3)	123.9±91.6	118.4±88.1	141.4±102.4	0.338
WBC (10^3/mm^3)	4826.3±2243.1	4706.1±2154.6	5205.7±2527.4	0.473
Neutrophil (10^3/mm^3)	3117.9±1747.5	3080±1775.3	3237.8±1697.8	0.667
Lymphocyte (10^3/mm^3)	1079.7±531.8	1001.1±460.3	1327.8±667.3	*0.015
Monocyte (10^3/mm^3)	482.1±227.1	493.5±232.3	446.3±212	0.434
Creatinine (mg/dL)	0.86±0.32	0.88±0.30	0.82±0.37	0.100
Albumin (gr/dL)	3.1±0.6	3.1±0.5	3.1±0.6	0.878
Total bilirubin (mg/dL)	1.8±2.3	1.9±2.6	1.3±0.7	0.195
AST (IU/mL)	52.2±44.9	48.1±36.6	65.2±64.1	0.205
ALT (IU/mL)	32.1±37.1	29.5±34.2	40.1±45.6	0.085
GGT (IU/mL)	71.3±71.9	71.4±75.5	70.7±61.1	0.578
Total cholesterol (mg/dL)	146.2±59.4	149.1±64.1	137.1±41.2	0.562
INR	1.2±0.2	1.3±0.2	1.2±0.2	0.516
Sodium (mEq/mL)	137.7±3.2	137.5±2.8	138.3±4.1	0.256
Periostin (ng/mL)	4.45±2.52	4.64±2.55	3.85±2.41	0.222
Child-Pugh score	7.2±1.8	7.5±1.8	6.4±1.3	*0.022
Child class-n (%)				
A	31 (39.2)	20 (33.3)	11 (57.9)	0.062
B	38 (48.1)	30 (50)	8 (42.1)	
C	10 (12.7)	10 (16.7)	0 (0)	
MELD score	11.3±4.1	11.5±4	10.8±4.2	0.482
MELD mortality (%)	5±3.5	5.1±3.3	4.7±4.1	0.351
MELDNa score	13.4±4.2	13.7±4	12.5±5	0.126
AAR	1.8±0.7	1.9±0.8	1.7±0.7	0.147
P2/MS	266839.3±730189.4	260772.4±797477.3	285998.2±474713.6	0.318
FI	10.1±2.1	10.1±2	9.7±2.5	0.402
GPR	2.1±2.5	2.1±2.5	2±2.9	0.578
APRI	1.8±2.1	1.8±2.1	1.9±2	0.714
NLR	3.1±1.6	3.2±1.8	2.5±0.9	0.247
FIB-4 score	6.3±4.9	6.3±5	6.3±4.9	0.845

AAR: AST/ALT ratio; ALT: Alanine aminotransferase; APRI: Aminotransferase/platelet ratio index; AST: Aspartate aminotransferase; CAD: Coronary artery disease; CKD: Chronic Kidney Disease; DM: Diabetes mellitus; FI: Forns index; F/M: Female/Male; FIB-4: Fibrosis-4 score; GGT: Gamma-glutamyl transpeptidase; GPR: Gamma-glutamyl transpeptidase to platelet ratio; Hct: Hematocrit; Hgb: Hemoglobin; INR: International normalized ratio; MELD: Model for end-stage liver disease; NLR: Neutrophil lymphocyte ratio; WBC: White blood cell. Categorical variables are shown as n (%). *: Statistically significant.

When patients' laboratory findings were examined, it was found that the mean hemoglobin (Hgb) value, the median thrombocyte count, and the median lymphocyte value were 11±2.1 g/dL, 102 (24-539) $10^3/mm^3$, and 950 (290-3490) $10^3/mm^3$, respectively. However, the median periostin level of the patients was calculated as 4.25 (0.42-8.75) ng/mL, and other laboratory parameters of those in the study group have also been presented in Table 1.

Among the parameters used for prognosing liver cirrhosis patients, while the median score of Child-Pugh was calculated as 7 (5-12), the MELD and MELDNa scores were calculated as 10 (6-26) and 12 (6-28), respectively. The findings of all prognostic formulas calculated in the study are also presented in Table 1.

Given the comparisons of demographic, laboratory, and clinical features with patients' prognostic models as regards the status of varice, the participants were put into two groups: those with (+) and (-) esophageal varices. When the demographic and clinical parameters were compared, no difference was detected in both groups as regards age and gender (p=0.309 and p=0.053, respectively). Patients' rate with ascites (53.3%) was found to be significantly increased in those with varices, compared to those without (21.1%) (p=0.014). When it comes to other demographic and clinical parameters, there was no significant difference between both groups.

When the laboratory parameters of the study groups were compared, the level of serum periostin in those with esophageal varices was found to be 4.63 ng/mL (0.42-8.75) and higher than that of the group as 3.65 ng/mL (0.64-8.48) without varices, and the difference was not statistically significant (p=0.222). However, the levels of lymphocytes in esophageal varice group were determined to be significantly lower than those among the patients without esophageal varices (p=0.015). There was no significant difference was seen between both groups regarding other laboratory parameters evaluated in the study (Table 1).

In terms of prognostic factors in the study groups, the Child-Pugh score of the group with esophageal varices was found as 7 (5-12), and the outcome was significantly higher than the score found as 6 (5-9) in the group without esophageal varice (p=0.022). As regards other prognostic parameters, no difference was determined between both groups (Table 1).

Compared concerning the demographic, clinical, and laboratory characteristics via the prognostic models according to the stage of varices, esophageal varice patients were classified as stages I, II, and III. Given the comparisons of the demographic and clinical parameters of the groups, no significant difference was seen between the three stages I, II, and III in terms of the data evaluated (Table 2).

As to the comparisons of the three groups in terms of laboratory parameters, the levels of serum periostin were seen to increase as the levels progressed from stage I to stage III; however, the difference between stages I-III was observed not to be statistically significant (p=0.480). Considering periostin levels, in addition, the difference between those with stage III varice and non-varice groups was insignificant (p=0.069). A significant difference was also detected between the groups concerning Hgb levels. The post-hoc analysis revealed that this difference stemmed from the difference between stages I and II (p=0.010). Even so, no significant difference was found between the three groups related to other parameters evaluated in the study (Table 2). When the prognostic parameters of the groups were also compared, it was seen that no significant difference was seen between stages I, II, and III regarding the data evaluated (Table 2).

Correlation Analyses

In the correlation analyses carried out to investigate whether there were associations between serum periostin, age, and other numerical laboratory and prognostic parameters, it was found that there was a moderately negative correlation with albumin, a weakly negative correlation with thrombocytes, and a weakly positive and statistically significant correlation with INR. Additionally, a statistically significant weak positive correlation was also determined between the level of periostin and such prognostic parameters as the scores of Child-Pugh, GPR, APRI, and FIB-4. A statistically significant weak negative correlation was found between periostin level and P2/MS score, as well (Table 3).

Discussion

The level of periostin was found to be higher in patients with varice than in those without, albeit statistically insignificant, in the current study examining the association between the development of esophageal varice and the serum periostin level in the patients with decompensated liver cirrhosis. No differences in periostin levels were observed between the groups when the patients were compared according to the stages of esophageal varices. While the level of periostin and scores of Child-Pugh, GPR, APRI, FIB-4, and INR value were found to be positively correlated in the correlation analysis, the P2/MS score, platelet counts, and albumin values were detected to be negatively correlated.

Table 2. The comparisons of demographic and clinical characteristics of the study group under the stages of varices.

Parameters	Stage I (n=16)	Stage II (n=23)	Stage III (n=21)	*p*
Sex (F/M)	8/8	12/11	9/12	0.816
Age (years)	61.3±10.3	57.4±10.6	53.6±13.2	0.103
Ascites (+)	7 (43.8)	13 (56.5)	12 (57.1)	0.668
Encephalopathy (+)	4 (25)	1 (4.3)	5 (23.8)	0.130
CKD (+)	2 (12.5)	0 (0)	2 (9.5)	0.247
DM (+)	6 (37.5)	11 (47.8)	5 (23.8)	0.255
Hypertension (+)	5 (31.3)	6 (26.1)	5 (23.8)	0.877
CAD (+)	3 (18.8)	3(13)	2 (9.5)	0.715
Cerebrovascular event (+)	1 (6.3)	0 (0)	1 (4.8)	0.510
Hgb (gr/dl)	12.1±1.8	10.1±1.8	10.6±2.3	*0.013
Hct (%)	36.3±4.9	32.4±5	33.1±6.1	0.083
Thrombocyte (10^3/mm^3)	105.8±75.3	138.2±116.7	106.3±54.1	0.582
WBC (10^3/mm^3)	4709.3±1741.8	4584.7±2274.4	4836.6±2386.2	0.891
Neutrophil (10^3/mm^3)	2961.8±1458.6	3010.8±1924.5	3245.7±1892.7	0.818
Lymphocyte (10^3/mm^3)	1106.2±417.1	903±403.1	1028.5±543.3	0.180
Monocyte (10^3/mm^3)	557.5±245.6	480.4±259.8	459.5±187.1	0.424
Creatinine (mg/dL)	0.8±0.4	0.9±0.2	0.8±0.2	0.245
Albumin (gr/dL)	3±0.7	3.2±0.5	3.1±0.5	0.497
Total bilirubin (mg/dL)	2.7±4.8	1.5±1.1	1.8±1	0.437
AST (IU/mL)	43.3±24.4	48.4±43.7	51.2±37.2	0.583
ALT (IU/mL)	23.5±14.4	25.5±22.8	38.4±50.9	0.393
GGT (IU/mL)	47.8±37.1	74.2±84.1	86.3±85.4	0.466
Total cholesterol (mg/dL)	130.5±58.9	153±45.7	159±82.6	0.322
INR	1.2±0.1	1.2±0.2	1.2±0.2	0.522
Sodium (mEq/mL)	138.6±4.1	136.6±2.4	137.7±1.9	0.237
Periostin (ng/mL)	4.34±2.84	4.38±2.57	5.15±2.34	0.480
Child-Pugh score	7.6±2.3	7±1.2	8±2.1	0.337
Child class-n (%)				
A	6 (37.5)	8 (34.8)	6 (28.6)	*0.081
B	6 (37.5)	15 (65.2)	9 (42.9)	
C	4 (25)	0 (0)	6 (28.6)	
MELD score	12.5±4.8	10.6±3.4	11.8±3.9	0.328
MELD mortality (%)	5.7±4.1	4.2±2.1	5.4±3.7	0.313
MELDNa score	14.1±4.8	13.6±3.7	13.5±3.8	0.808
AAR	1.9±0.5	1.9±0.6	1.8±1.1	0.636
P2/MS	117643.1±184013.2	239450.6±479237.2	393175.2±1250101.8	0.434
FI	10.8±2.3	9.8±2.1	10.1±1.5	0.603
GPR	1.9±2.3	1.9±2.2	2.6±2.8	0.682
APRI	2.2±2.8	1.5±1.7	1.8±1.8	0.526
NLR	2.8±1.5	3.5±2.1	3.2±1.6	0.494
FIB-4 score	8.8±7.5	5.4±3.6	5.4±3.3	0.583

AAR: AST/ALT ratio; ALT: Alanine aminotransferase; APRI: Aminotransferase/platelet ratio index; AST: Aspartate aminotransferase; CAD: Coronary artery disease; CKD: Chronic Kidney Disease; DM: Diabetes mellitus; FI: Forns index; F/M: Female/Male; FIB-4: Fibrosis-4 score; GGT: Gamma-glutamyl transpeptidase; GPR: Gamma-glutamyl transpeptidase to platelet ratio; Hct: Hematocrit; Hgb: Hemoglobin; INR: International normalized ratio; MELD: Model for end-stage liver disease; NLR: Neutrophil lymphocyte ratio; WBC: White blood cell. Categorical variables are shown as n (%). *: Statistically significant.

Liver fibrosis is a condition marked by the accumulation of collagen, an extracellular matrix protein, and liver failure, which can be brought on by a variety of factors. Esophageal varices can arise as a secondary cause of portal hypertension in those with decompensated liver cirrhosis because of liver fibrosis and elevated sinusoidal pressure. Few studies have been conducted in the literature suggesting periostin is involved in the pathophysiology of liver fibrosis and could be a target for treatment. Additionally, periostin levels are higher in cirrhotic patients than in healthy individuals (3). To our knowledge, though, no research has been performed related to the association between cirrhosis complications, particularly esophageal varices, and serum periostin levels; so, our study is the first to look into the connection between varices and serum periostin levels.

For the first time, the impact of periostin on the progression of liver fibrosis was documented in an animal experiment conducted by Huang et al (18). The research findings indicate a significant increase in periostin expression in liver tissue in mice with both acute and chronic liver fibrosis caused by carbon tetrachloride or bile duct ligation. In periostin-deficient mice, no liver fibrosis was manifested. The levels of fibronectin, type I collagen, carbon tetrachloride, and smooth muscle actin were observed to be significantly elevated in

periostin+/+ mice, but not to change in periostin-/- mice.

The amount of collagen-stored area as well as the serum ALT and AST levels were found to be significantly lower in periostin-/- mice, compared to periostin+/+ mice following the two-week administration of carbon tetrachloride. The transforming growth factor-beta 1 (TGF-β1) markedly increased the expression of periostin in HSHs of the mice. Following the carbon tetrachloride administration, periostin-/- mice were found to have significantly lower levels of TGF-β1 and transforming growth factor-beta 2 (TGF-β) than periostin+/+ mice. Furthermore, in the identical investigation, the serum periostin, TGF-β1, and TGF-β2 levels were assessed in 32 patients with acute hepatitis, 20 patients with chronic hepatitis, and 28 healthy individuals. The results indicated that the serum periostin level was significantly higher in patients with acute or chronic hepatitis than in the controls ($p<0.001$). Additionally, a relationship was discovered between the patient groups' TGF-β1 and TGF-β2 levels and periostin levels. In the study by Huang et al., it was concluded that periostin might be a novel mediator in the development process of hepatic fibrosis (18).

Table 3. Results of the correlation analysis between periostin levels and other numerical parameters.

Parameters	rho	*p*
Age (years)	0.020	0.859
Thrombocyte	-0.282	*0.012
INR	0.235	*0.037
Albumin	-0.356	*0.001
Child-Pugh score	0.307	*0.006
MELD score	0.189	0.096
MELDNa score	0.201	0.076
AAR	0.066	0.565
P2/MS	-0.275	*0.014
GPR	0.279	*0.013
APRI	0.283	*0.011
NLR	-0.057	0.617
FIB-4 score	0.286	*0.011

AAR: Aspartate aminotransferase/alanine aminotransferase ratio; APRI: Aminotransferase/platelet ratio index; FIB-4: Fibrosis-4 score; GPR: Gamma-glutamyl transpeptidase to platelet ratio; INR: International normalized ratio; MELD: Model for end-stage liver disease; MELDNa: Model for end-stage liver disease-sodium; NLR: Neutrophil lymphocyte ratio; rho: Spearman's correlation coefficient. *: Statistically significant.

In another study examining the relationship between liver diseases and periostin, Lv et al. compared the serum periostin levels of 56 patients with hepatocellular carcinoma (HCC), 30 patients with cholelithiasis, 27 patients with cirrhosis, and 69 healthy controls. The periostin level in the HCC group was found to be significantly higher than that of the other three groups, and the increased periostin level was suggested to be an independent predictor of the prognosis and survival for HCC patients. In the study by Lv et al., although the level of serum periostin (27.3 ng/mL) was found to be higher in the cirrhosis patients than the controls (16.7 ng/mL), the data about whether the difference was statistically significant were not reported (19); such a comparison could not be performed in our study due to lack of a control group.

As the severity of cirrhosis increases, esophageal varice becomes more common in cirrhosis patients. About 9% of patients experience the development of new varices annually, and the size of these varices grows by 10-12% per annum (20,21). As a result, early detection of varices and carrying out the required interventions are directly linked to survival (22). Only 2% of cases where no varices are found at the initial endoscopy experience hemorrhages within two years, and the rate at which small varices grow into large ones has been reported as 12% in the first and 31% in the third years (23). The gold standard for diagnosing esophageal varices is endoscopy; according to the most recent guidelines, endoscopic screening programs should include patients with liver cirrhosis (24). However, because endoscopy is an invasive procedure, not all patients find it acceptable. Additionally, the procedure has several drawbacks, such as high cost-effectiveness and variations in reporting among doctors performing the procedure (1). Because of this, several non-invasive techniques have been suggested to identify the possibility of esophageal varices, particularly to minimize unnecessary endoscopic procedures.

Low thrombocyte count, enlarged spleen, elevated Child-Pugh score, and stiffness of the liver and spleen are among the most researched markers in this regard; however, none of these tests yield conclusive findings that can be substituted by endoscopy (25).

In the current study, our goal was to lower the number of unnecessary endoscopy procedures by predicting the presence of esophageal varices by measuring the serum periostin level, a marker linked to liver cirrhosis. As one of the laboratory parameters assessed in the study, the lymphocyte count was found to be lower in patients with esophageal varices than in those without; however, no statistically significant correlation was observed between the level of periostin and the presence of varices. Regarding the clinical parameters, it was discovered that varices and ascites were related. Upon reviewing the literature, we were unable to find any studies examining the association between lymphocyte count and esophageal varices. The presence of esophageal varices was found to be associated with splenomegaly, ascites, and spider angiomas, as well as with the values of thrombocyte and bilirubin in a study by Thomopoulos et al., where 184 patients with cirrhosis were investigated. In the study, Thomopoulos et al. found no association between the presence of varices and the presence of hepatic encephalopathy, serum albumin, AST, ALT, GGT, creatinine, and INR levels (26),

which is consistent with the results of our study. However, no correlation between the presence of varices and ascites was found in a different study conducted by Sarangapani et al., evaluating 106 patients with cirrhosis. The parameters that can predict the presence of esophageal varices were found to be thrombocytopenia, splenomegaly, portal vein diameter and the ratio of thrombocyte to spleen diameter (27).

We were unable to determine any correlation between prognostic scoring systems, other laboratory parameters, and the existence of esophageal varices in the current study. In general, the findings examining the issue reported by other researchers are also controversial. According to the study by Zhang et al. involving 153 cirrhosis patients, there was a correlation between esophageal varices and FIB-4 and APRI scores, but not with AAR (28).

Furthermore, a meta-analysis assessing the connection between prognostic models and esophageal varices was published in 2015 by Deng et al. In the analysis, 12 papers on the APRI score, four on the AAR score, five on the FIB-4 score, and three on the FI score were assessed. The values of area under the curve (AUC) for APRI, AAR, FIB-4, and FI were determined to be 0.67, 0.72, 0.77, and 0.75, respectively. Additionally, the values for sensitivity and specificity were found as 0.60 and 0.67 for APRI and 0.64 and 0.63 for AAR, respectively. In light of the available data, the researchers concluded that the scores APRI, AAR, FIB-4, and FI were not as effective as upper gastrointestinal endoscopy in predicting the presence of esophageal varices (29). The value of AUC was found to be 0.941 in the study by Kim et al., looking into the P2/MS score to predict the presence of varices in 318 cirrhosis patients related to hepatitis B. According to the researchers, the P2/MS scoring system is a low-cost and easy-to-use technique that may lessen the need for endoscopy in patients with HBV-related cirrhosis (30).

In our study, there was a correlation between the values of INR, thrombocyte, and albumin and the scores of Child-Pugh, GPR, APRI, FIB-4, and P2/MS, which are indicators of the severity of liver cirrhosis and associated with its prognosis. However, no relationship was found between the development and degree of esophageal varices and serum periostin levels. We propose that periostin could be a potential marker for predicting the clinical course of liver cirrhosis because of the correlation. To support such a finding, we believe that prospective studies assessing the prognosis and survival are necessary.

There are several limitations to our study. The most significant limitation is the absence of a control group and the cross-sectional design of the study. Periostin is a recently defined marker to evaluate fibrosis, and the cut-off values such as the laboratory upper limit have yet to be defined. In addition, since the prognostic models were added to the study later, some scores were found to be lower than expected according to the patient's clinical spectrum. Although the periostin level was found to be higher in patients with varicose veins, no statistical significance could be reached due to the small size of our patients, especially because of the presence of only 16 patients in the patient group without varicose veins.

Conclusion

There was no discernible relationship between the onset of esophageal varices in our study group and serum periostin levels. The existence of a correlation between periostin, and the Child-Pugh, GPR, APRI, FIB4, and P2/MS scores, and INR, platelet, and albumin values suggests that periostin may be a potential prognostic marker in cirrhosis sufferers. Further studies including larger populations will be beneficial to elucidate the entity better, which has yet to be investigated in the literature.

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Conflict of interest statement

The authors of this work have nothing to disclose.

Ethics Committee Approval: Non-Pharmaceutical and Medical Device Research Ethical Board of the Medical School of Karatay University of Konya Trade Chamber (Date: June 5, 2018, and number: 2018/015).

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The Evaluation of Basal Ganglia in Pediatric Patients with Cerebral Palsy Using Magnetic Resonance Histogram Analysis

Serebral Palsili Pediatrik Hastalarda Bazal Ganglionların Manyetik Rezonans Histogram Analizi Kullanılarak Değerlendirilmesi

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Öz

Konvansiyonel manyetik rezonans görüntüleme (MRG) görüntülerinde bazal ganglionlarda patolojik sinyal değişiklikleri olmayan serebral palsili (SP) hastalarda MRG histogramını kullanarak bazal ganglionlardaki değişiklikleri tespit etmeyi amaçladık. Serebral palsili 40 çocuk ve beyin MRG incelemesinde anlamlı intrakraniyal bulgusu olmayan 60 çocuğun görüntüleri retrospektif olarak değerlendirildi. Ortalama, varyans, çarpıklık, basıklık, 1. yüzdelik (P), 10. P, 50. P, 90. P ve 99. P histogram parametreleri her hasta ve kontrol grubu için talamus, lentiform ve kaudat nukleuslardan tanımlanan alanlarda hesaplandı ve her vaka için ayrı ayrı değerlendirildi. Talamustan elde edilen histogram parametrelerinin ortalama, basıklık ve 50. P değerleri açısından gruplar arasında anlamlı fark bulundu (sırasıyla p=0.001, p=0.002, p=0.025). Lentiform çekirdeklerden elde edilen histogram parametrelerinin ortalama, çarpıklık, basıklık ve 1. P değerleri arasında anlamlı bir fark bulunmuştur (sırasıyla p=0.021, p=0.005, p=0.015, p=0.035). Nukleus kaudatustan elde edilen histogram parametrelerinin ortalama, basıklık, 90. P ve 99. P değerleri arasında anlamlı farklılık tespit edildi (sırasıyla p=0.002, p=0.03, p=0.004, p=0.042). Doku analizi, serebral palsili hastalarda bazal ganglionlar ve talamustaki farklılıkları gösterebilecek objektif özellikler üretebilir. Doku analizi, konvansiyonel MRG görüntülerinde patolojik sinyal değişikliği olmayan SP'li hastalarda bazal ganglionlardaki değişiklikleri tanımlayabilir.

Anahtar Kelimeler: Bazal Ganglionlar, Doku Analizi, Serebral Palsi, Talamus

Abstract

The aim of this study is to detect changes in the basal ganglia using magnetic resonance imaging (MRI) histogram in patients with cerebral palsy (CP) who do not have pathological signal changes in the basal ganglia on conventional MRI images. A retrospective evaluation was made of the images of 40 children with CP and 60 children with no significant intracranial findings on brain MRI examination. The histogram parameters of mean, variance, skewness, kurtosis, 1st percentile (P), 10th P, 50th P, 90th P and 99th P were calculated for each patient and control group on the areas identified in the head of the thalamus, lentiform nucleus and nucleus caudatus and these were evaluated separately for each case. A significant difference was found between the groups in terms of the mean, kurtosis and 50th P values of histogram parameters obtained from the thalamus (p=0.001, p=0.002, p=0.025, respectively). A significant difference was found between the mean, skewness, kurtosis and 1st P values of histogram parameters obtained from the lentiform nuclei (p=0.021, p=0.005, p=0.015, p=0.035, respectively). A significant difference was found between the mean, kurtosis, 90th P and 99th P values of the histogram parameters obtained from the head section of the nucleus caudatus (p=0.002, p=0.03, p=0.004, p=0.042, respectively). Texture analysis can produce objective features that may indicate differences in the basal ganglia and thalamus in patients with CP. Texture analysis can identify changes in the basal ganglia in patients with CP who do not have pathological signal changes on conventional MRI images.

Keywords: Basal ganglia, Texture analysis, Cerebral palsy, Thalamus

Introduction

Cerebral palsy (CP) is a condition that occurs with permanent disorders in motor functions, mostly in infants with very low birth weight (<1500 g), resulting from damage to the immature brain (1). Although the prevalence of CP varies with different birth weights and gestational ages, it is approximately 2 to 3 per 1,000 live births (2). CP is considered a clinical condition rather than an etiological diagnosis (3), and may present with many problems such as hearing, vision, learning disorders and epilepsy (4,5).

Different cerebral abnormalities have been observed on magnetic resonance imaging (MRI) in children with CP. Deep gray nuclei and the cortex may be affected. Gray matter damage occurs in approximately 14% to 22% of children with CP (6). Gray matter damage is associated with perinatal hypoxia-ischemia/hypotension, and in some etiological cases, it may also occur in infection, kernicterus, bleeding and hypoglycemia (7).

The importance of MRI as neuroimaging in the diagnosis of CP is increasing (8). The MRI classification system for children with CP has been used qualitatively to indicate maldevelopments, predominant white matter injuries, predominant gray matter injuries, miscellaneous and normal findings (9).

The aim of this study was to detect changes in the basal ganglia using MRI histogram in patients with CP who do not have pathological signal changes in the basal ganglia on conventional MRI images.

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Material and Method

The study population included children who were admitted to Sanliurfa Training and Research Hospital Pediatric Neurology Outpatient Clinic and had clinical features compatible with CP, such as sensory disorders accompanied by movement and posture disorders between January 2022 and June 2023. CP is a neurological disease that develops in the childhood age group and involves movement control, posture disorders, disorder of cognition, communication, perception, behavior and seizures secondary to developing brain damage. In our study, 40 patients and 60 control groups were included. When post hoc power analysis was performed, power=0.99 was found when alpha=0.05 and effect size 1.157 were taken. (Gpower 3.1 software was used.)

Inclusion criteria

Children aged>2 years with non-progressive posture or movement disorders due to a lesion in the brain during the prenatal, perinatal, or postnatal period, who were diagnosed with CP. A group of patients with normal basal ganglia and thalamus despite white matter involvement on conventional MRI was included.

Exclusion criteria

Cases with neurodegenerative disease, brain tumor, psychomotor retardation due to genetic causes, movement disorders caused by muscle or peripheral motor neuron disease, brain abscess, hydrocephalus, meningitis (both septic and tuberculous), and encephalitis.

MRI examination and histogram analysis

All patients participating in the study underwent brain MRI. All the brain MRI scans were performed on a 3T unit (Siemens Magnetom Skyra, Erlangen, Germany) using a head coil. T1, T2, T2 tirm TRA dark-fluid sequences were acquired. The T1 se tra sequence was TR: 370 ms and TE: 11 ms. The T2 se tra sequence was TR: 4540 ms and TE: 109 ms. The T2 tirm TRA dark fluid sequence was TR: 9140 ms and TE: 81 ms.

The images of 40 children with CP and 60 children with no significant intracranial findings on brain MRI examination were retrospectively evaluated. The collected MRI images were then reviewed using “Radiant DICOM Viewer 2020.2.3” software.

For image analysis, a single observer, (M.D.) with 10 years of experience in radiology, evaluated the axial slice brain MRI images of each case using the same window settings (window level 20 and window width 380). The axial image showing the basal ganglia was identified and registered. The registered images were then opened using “qMaZda v4.6” software.

The histogram parameters of mean, variance, skewness, kurtosis, 1st percentile (P), 10th P, 50th P, 90th P and 99th P were calculated for each patient and control group over the areas identified in the head of the thalamus, lentiform nucleus and nucleus caudatus and these were evaluated separately for each case (Figure 1).

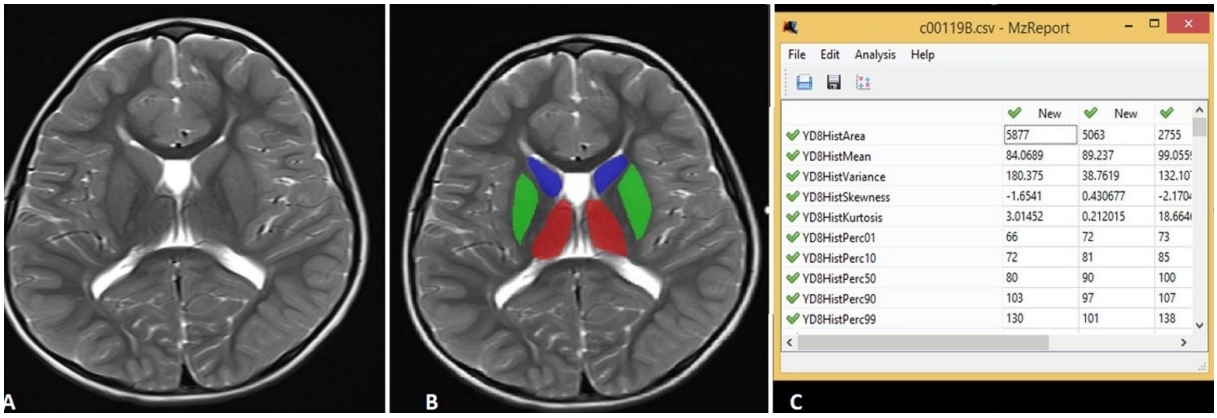

Figure 1. 5-year-old male patient with cerebral palsy. (A) Ventricular level on T2-weighted axial brain MRI image. (B) Two-dimensional segmentation of the thalamus (RED), lentiform nucleus (GREEN) and head of the nucleus caudatus (BLUE) from the same level using qMazda V.6 software. (C) Quantitative values of the histogram parameters of the area determined in image B.

Approval for this study was granted by the Harran University Medical Ethics Committee (decision no: 23.23.32, dated: 11.12.2023). All the study procedures were in compliance with the Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed using SPSS version 22.0 software (IBM Inc, Armonk, NY, USA). The conformity of numerical data to normal distribution was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics were stated as mean±standard deviation

values for numerical data showing normal distribution, and as median with minimum-maximum values for numerical data not showing normal distribution. The Independent Student's t-test and Mann Whitney U-test were used for intergroup comparisons. A value of $p<0.05$ was considered statistically significant.

Results

The images of 40 children with CP and 60 children in the control group were evaluated. The CP group comprised 22 boys and 18 girls with a mean age of 7.58±3.45 years, and the control group comprised 35 boys and 25 girls with a mean age of 8.1±2.48 years. No significant difference was found between the patient and control groups in terms of age and gender (p=0.410, p=0.742, respectively) (Table 1).

In the brain MRI images of the patient and control groups, histogram analyses were performed from the thalamus, lentiform nucleus and nucleus caudatus. A significant difference was determined between the groups in respect of the mean, kurtosis and 50th P values of the histogram parameters obtained from thalamus (p=0.001, p=0.002, p=0.025, respectively) (Table 2). In the measurements made in the thalamus, mean and 50th p values were found to be low and kurtosis value was found to be high in CP patients.

Table 1. Age and gender distribution of the patient and control groups.

	CP (n=40)	Control (n=60)	p
Age	7.58±3.45	8.1±2.48	0.410[a]
Sex			
Male, n (%)	22 (55)	35 (58.3)	0.742[b]
Female, n (%)	18 (45)	25 (41.6)	

[a]Independent samples T Test. [b]Pearson Chi square test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or number (%).

Table 2. Histogram parameters and comparison of images obtained from Thalamus in patients and control group.

	CP (n=40)	Control (n=60)	p
Mean	78.7±10.2	89.4±10.1	**0.001[a]**
Variance	39.1±11.2	41.1±12.1	0.195[a]
Skewness	-0.15 (-1.1 - 0.13)	-0.11 (-1 - 0.16)	0.085[b]
Kurtosis	-0.388 (-0.12 - 0.62)	-0.50 (-0.32 - 0.81)	**0.002[b]**
1th P	60.2±9.5	62.2±9.41	0.123[a]
10th P	68.9±10.5	74.2±9.1	0.069[a]
50th P	79.8±10.2	88.5±9.5	**0.025[a]**
90th P	91.2±11.5	96.5±10.1	0.065[a]
99th P	97.2±10.1	101±11.2	0.089[a]

[a]Independent samples T Test. [b]Mann-Whitney U test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or median (minimum - maximum).

A significant difference was found between the mean, skewness, kurtosis and 1st P values of the histogram parameters obtained from the lentiform nuclei (p=0.021, p=0.005, p=0.015, p=0.035, respectively) (Table 3). In the measurements performed in the lentiform nuclei, mean, skewness and 1st p values were found to be low and kurtosis value was found to be high in CP patients.

A significant difference was found between the mean, kurtosis, 90th P and 99th P values of the histogram parameters obtained from the head section of the nucleus caudatus (p=0.002, p=0.03, p=0.004, p=0.042, respectively) (Table 4). In the head section of the Nucleus Caudatus mean, 90th P and 99th P values were found to be low and kurtosis value was found to be high in CP patients.

Table 3. Histogram parameters and comparison of images obtained from Lentiform Nucleus in patients and control group.

	CP (n=40)	Control (n=60)	p
Mean	75.6±9.8	84.5±10	**0.021[a]**
Variance	45.2±12.2	40.5±11.8	0.320[a]
Skewness	-0.3 (-0.51 - 0.21)	-0.11 (-0.31 - 0.8)	**0.005[b]**
Kurtosis	-0.3 (-0.4 - -0.11)	-0.45 (-0.78 - -0.25)	**0.015[b]**
1th P	61±8.5	69±9.2	**0.035[a]**
10th P	66.2±10.1	74.2±8.9	0.089[a]
50th P	75.2±8.2	83.1±8.8	0.075[a]
90th P	88.9±10.2	96±10.3	0.065[a]
99th P	100±9.8	101±11.2	0.165[a]

[a]Independent samples T Test. [b]Mann-Whitney U test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or median (minimum - maximum).

Table 4. Histogram parameters and comparison of the images obtained from the head section of the Nucleus Caudatus in the patient and control groups.

	CP (n=40)	Control (n=60)	p
Mean	77.6±9.6	88±10.1	**0.002**[a]
Variance	42.4±11.8	39.4±10.1	0.252[a]
Skewness	-0.15 (-0.31 – 0.1)	-0.14 (-0.28 – 0.11)	0.075[b]
Kurtosis	-0.49 (-0.82 – -0.12)	-0.72 (-1.1 – -0.32)	**0.030**[b]
1th P	63±7.7	66±8.1	0.082[a]
10th P	67.1±9.9	72.1±8.9	0.078[a]
50th P	78.1±7.9	8.2±7.2	0.120[a]
90th P	82.2±12.1	97.2±11.2	**0.004**[a]
99th P	95.4±9.7	103±13.1	**0.042**[a]

[a]Independent samples T Test. [b]Mann-Whitney U test. CP: Cerebral Palsy. Data are presented as mean±standard deviation or median (minimum - maximum).

Discussion

This study, using tissue analysis, also revealed effects at the lentiform, caudate nucleus and thalamus levels of patients with CP, which cannot be visually detected with conventional MRI.

Genetic and metabolic causes should be investigated in CP patients whose history is not clear or in whom atypical clinical features are observed. In cases where etiology cannot be determined, MRI, which is considered the most predictive tool, is used to detect risk (10).

Traditional and advanced techniques have been described regarding brain MRI findings in children with CP (11). Histogram-based statistics, an advanced technique, measure the global distribution of pixels/voxels of gray level tones (12–14). The MRI findings have been reported to be abnormal in 86% of CP cases. Periventricular white matter damage is the most common finding at the rate of 56%, followed by deep gray matter damage at 18% (9). This study is the first to have investigated whether the basal ganglia are involved in CP patients with white matter involvement using MRI histogram analysis.

Quantitative imaging features can be derived from MRI-based texture analysis (TA), encompassing a variety of characteristics. The first-order statistical feature, often referred to as a histogram, involves the distribution of voxel densities within the region of interest. This distribution is based on fundamental properties such as skewness, kurtosis, entropy, and energy of grey level density. Based on the TA results of the patient and control groups in the current study, these differences were thought to be an indicator of heterogeneity in the brain parenchyma of CP patients (15). Statistical calculations can be made from the histogram. The mean gives the average intensity level of the image, variance gives the roughness of the image, skewness defines the symmetry of the histogram, and kurtosis defines its flatness (16).

Sarıoglu et al. (15) made this possible by using MRI-based TA of the basal ganglia and thalamus for the accurate diagnosis of moderate to severe hypoxic ischemic encephalopathy in newborns. TA may provide objective features that can reveal visually undetectable MRI differences in the basal ganglia and thalamus of perinatal asphyxiated newborns. Wang et al. (17) reported that histogram analysis would be useful in the demonstration of hypoglycemic encephalopathy in the neonatal period. Suoranta et al. (16) performed 3D TA of bilateral thalamus, amygdala, hippocampus, caudate nucleus and putamen of 16 patients with progressive myoclonic epilepsy type 1 and 16 healthy control subjects. There were reported to be significant textural differences in progressive myoclonic epilepsy type 1 patients compared to the control group, especially in the thalamus and right putamen. Valdés et al. (18) suggested that basal ganglia TA can be used to evaluate blood-brain integrity in small vessel disease. The results of the current study showed that patients with CP had lower mean values in the thalamus, lentiform and caudate nuclei than the control group. This demonstrated lower tissue density in the thalamus, lentiform and caudate nuclei in patients with CP than in healthy control subjects.

The current study patients with CP had higher kurtosis values in the thalamus, lentiform and caudate nuclei than the control group. This showed that the flatness of the thalamus, lentiform and caudate nucleus tissue in patients with CP was greater than in the healthy control subjects.

The patients with CP were found to have lower skewness values in the lentiform nucleus than the control group, thereby demonstrating lesser histogram symmetry of the tissue in the lentiform nucleus in patients with CP than in the healthy control group.

Baykara et al. (19) demonstrated significant differences between patients with functional neurological disorder and healthy control subjects using histogram analysis of the amygdala. Johns et al. (20) found that basal ganglia tissue properties differ significantly in patients with amyotrophic lateral sclerosis. Bhattacharya et al. (21) compared the changes in corpus callosum in progressive supranuclear palsy using three different tissue analyses using T2-weighted MRI. These were gray level co-occurrence matrix, local binary pattern, and oriented Gaussian derivative filter-bank. It was hypothesized that progressive supranuclear palsy may cause non-selectable loss of tissue structure of

the corpus callosum. The results of that study revealed that local binary pattern TA was superior to other TA methods.

The primary limitation of this study was the retrospective design. A second limitation was that sequences may have variability in non-normalizable parameters, such as TR and TE values. There is a need for further studies to be conducted with different protocols to confirm these results. However, as there has been no similar study before, the results of this study can be considered of value in contributing to the literature. In addition, TA application is both simple and applicable to many imaging modalities.

Conclusion

Texture analysis can produce objective features that may indicate differences in the basal ganglia and thalamus in patients with CP with white matter involvement. The results of this study showed many statistically significant tissue parameters between the healthy control group and the patients with CP in the lentiform, caudate nucleus and thalamus.

Conflict of interest statement

There is no conflict of interest in our study.

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Examining the Effect of the COVID-19 Pandemic on Cases of Violence Against Women: An Evaluation Through Media News

COVID 19 Pandemisinin Kadına Yönelik Şiddet Olgularına Etkisinin İncelenmesi: Medya Haberleri Üzerinden Bir Değerlendirme

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Öz

Bu çalışmada ülkemizde COVİD-19 pandemisinin kadına yönelik şiddet olgularının sıklığına etkisinin medya haberleri üzerinden değerlendirilmesi amaçlanmıştır. Retrospektif tanımlayıcı bir çalışmadır. Anahtar sözcükler kullanılarak tirajı en yüksek beş ulusal gazetenin haberleri pandemi öncesi iki yıl ve pandemi dönemi iki yılı kapsayacak şekilde retrospektif olarak incelenmiştir. Veri toplama formunda ki bilgiler her medya haberi için ulaşılabildiği kadarı ile SPSS dosyasına kaydedilmiştir. Veriler 1-31 Ağustos 2022 tarihleri arasında toplanmıştır. Etik kurul izni alınmıştır. Veri analizinde SPSS 22.0 paket programı kullanılmış, tanımlayıcı istatistikler; sayı, yüzde, ortalama, standart sapma olarak verilmiştir. İncelenen şiddet haberlerinin %29.5'i pandemi öncesinde, %70.5'i pandemi döneminde meydana gelmiştir. Şiddet mağduru kadınların yaş ortalaması 33.67±12.25, uygulayıcılarının yaş ortalaması 38.11±11.94'dür. Pandemi döneminde Marmara bölgesinde, kış mevsiminde, gündüz saatlerinde, ev ortamında ve evli olanlarda şiddet sıklığı artmıştır. Ayrıca darp, boğma şeklinde gerçekleşen şiddet olgularının sıklığının arttığı, şiddet sonrası ölüm sıklığının ise azaldığı görülmüştür. Kadına yönelik şiddetin önlenmesi için toplumsal düzeyde farkındalık çalışmaları yapılması, ulusal çapta düzenli kayıtların tutulması, yakın partner şiddeti için risk gruplarını tanımlayan (risk odaklı yaklaşım), sosyal ve demografik faktörleri sorgulayan ayrıntılı çalışmalar yapılarak daha etkili ve çözüm odaklı önlemler planlanması önerilebilir.

Anahtar Kelimeler: COVID-19 Pandemisi, Fiziksel Şiddet, Haberler, Kadına Yönelik Şiddet, Yakın Partner Şiddeti

Abstract

This study aims to evaluate the impact of the COVID-19 pandemic on the frequency of violence against women cases in our country through media news. It is a retrospective descriptive study. Using keywords, the news of the five national newspapers with the highest circulation were examined retrospectively, covering two years before and during the pandemic. The information in the data collection form was recorded in the SPSS file as much as available for each media news. Data were collected between August 1-31, 2022. Ethics committee permission was obtained. SPSS 22.0 package program was used in data analysis, and descriptive statistics were given as frequency, percentage, mean, and standard deviation. Of the violence news examined, 29.5% occurred before the pandemic, and 70.5% occurred during the pandemic. The mean age of the victims of violence was 33.67±12.25 years, and the mean age of the perpetrators was 38.11±11.94 years. During the pandemic, the frequency of violence increased in the Marmara region, in the winter season, during daylight hours, in the home environment and among married women. In addition, it was observed that the frequency of violent cases in the form of beating and strangulation was increased while the frequency of death following violence was decreased. In order to prevent violence against women, it may be recommended to conduct awareness-raising activities at the societal level, keep regular records on a national scale, identify risk groups for intimate partner violence (risk-oriented approach), and plan more effective and solution-oriented measures by conducting detailed studies questioning social and demographic factors.

Keywords: COVID-19 Pandemic, Physical Violence, News, Violence Against Women, Intimate Partner Violence

Introduction

In the Declaration on the Elimination of Violence against Women issued by the United Nations Organization in 1993, violence against women is defined as any act of gender-based violence that results in or is likely to result in, physical, sexual or psychological harm or suffering to women, including threats of such acts, coercion or arbitrary deprivation of liberty, whether occurring in public or in private life (1). Violence against women is classified as physical, sexual, psychological, economic, cyber violence and unilateral persistent following (2).

Violence is an essential public health problem that adversely affects women's physical, mental, sexual and reproductive health, continues to exist as a reflection of gender inequality and is a violation of women's human rights. Its frequency and appearance vary between countries. Estimates published by the World Health Organization (WHO) show that approximately one in three (30%) of women worldwide have been exposed to physical and/or sexual intimate partner violence or non-partner sexual violence throughout their lives (3). According to the results of the "Research on Domestic Violence against Women in Turkey" conducted in 2014, the proportion of women who stated that they had been subjected to physical and/or sexual violence at any time in their lives was 38% and 11% in the last 12 months. It was stated that 68% of married women were subjected to physical or sexual violence by their husbands or intimate partners (4).

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WHO recognized the Coronavirus Disease (COVID-19), which emerged in China and affected the whole world, as a pandemic on March 11, 2020, and announced on May 5, 2023, that the pandemic is no longer a global emergency. The COVID-19 pandemic has not only caused a health crisis but also had significant social and economic impacts. During the pandemic, restrictions, isolation measures and economic uncertainties have been faced worldwide. There is information in the current literature that the public health measures implemented globally to control the spread of COVID-19 have created conditions that can have a profound impact on crime trends and have increased violence against women as well as in many areas of social life (5,6). Challenging conditions such as quarantine measures, economic uncertainties, difficulties in health systems and social isolation have been defined as situations that pave the way for an increase in violence against women (7). In these cases, spending more time in close contact with family members, spending less time with family and friends who can provide support and protection against violence, the stress caused by the burden of care work, which increased with the closure of schools during the pandemic, decreased livelihoods, decreased access to basic needs and services, decreased access to health services and psychosocial support services with restrictions are the factors that increase violence (3,8). In the report published by U.N. Women in 2021, there was an increase in the risk factors of violence against women with the COVID-19 pandemic, and it was reported that 45% of women had been exposed to violence themselves or a woman they know since the beginning of the pandemic (9).

The media is a mirror of social events, problems and changes. Although physical violence against women is mainly covered in the media news, our study will provide a perspective to develop effective combating strategies for measures that can be taken to protect women and prevent violence by reflecting on the dynamics of violence before and during the pandemic, revealing descriptive characteristics such as the characteristics of victims of violence, perpetrators of violence and cases of violence, and the consequences of violence. This study aims to evaluate the impact of the COVID-19 pandemic on the frequency of violence against women cases in our country through media news.

Material and Method

In this retrospective descriptive study, the news of the five national newspapers with the highest circulation were retrospectively examined for two years before the pandemic (11.03.2018-10.03.2020) and two years during the pandemic period (11.03.2020-10.03.2022) by using the keywords "kadına yönelik şiddet", "kadına yönelik aile içi şiddet", "kadın cinayeti", "öldürülen kadınlar", "namus ve töre cinayeti", "kadın kurban", "kadın istismarı", "darp edilen kadın", "şüpheli kadın ölümü", "kadın intiharı" in the news section of the Google search engine. 343 news links were accessed before the pandemic and 525 news links were accessed during the pandemic. The news about the same event found with different keywords used, the news about the same event in different newspapers, the news of the same event published on different days of the week were handled once and the re-evaluation of the news about the same event was prevented. There are no other inclusion or exclusion criteria. Ultimately, 156 news before the pandemic and 373 news during the pandemic period constituted the study population and was included in the analysis (Figure 1).

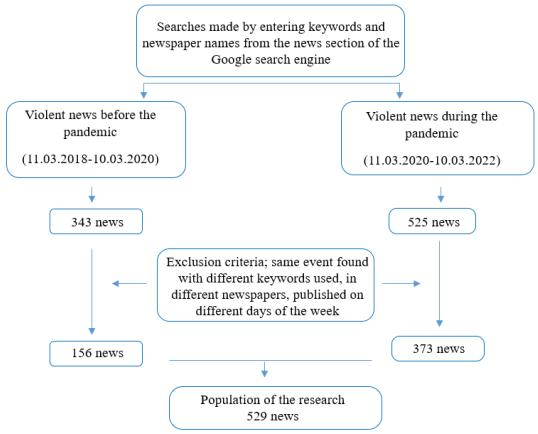

Figure 1. Selection of Media News

The information in the data collection form, created by reviewing the existing literature on the subject during the research planning phase, was recorded in the SPSS file as much as available for each media news. The data collection form includes information about the age and marital status of the victim of violence, previous exposure to violence by the same person, age and gender of the perpetrator of violence, proximity to the victim, previous criminal record, date of violence, region, province, season, time, place, cause, type, patterns of occurance, result of violence, people affected by violence, and the status of the perpetrator after violence. Data were collected between August 1 and 31, 2022. The variables of the study were age, gender, marital status, proximity status, previous experience of violence by the same person, the criminal record of the perpetrator, region, province, season, time, place, causes, types, ways of violence, the outcome of violence, people affected, and the status of the perpetrator after the violence. Ethics committee permission was obtained from The Medical and Health Sciences Ethics Committee of the Muğla Sıtkı Koçman University (Date:19.07.2022, No:52).

Statistical analysis

SPSS 22.0 package program was used in data analysis, and descriptive statistics were given as frequency, percentage, mean, and standard deviation.

Results

Of the examined violent news, 29.5% (n=156) occurred before the pandemic, and 70.5% (n=373) occurred during the pandemic period. The average age of female victims of violence was 33.67±12.25 (32.83±11.71 before the pandemic, 34.05±12.50 during the pandemic). When age groups were examined, it was determined that the victims were 19 years of age or younger in 6.8% of the news articles, between the ages of 20-29 in 37.2%, between the ages of 30-39 in 31.4%, between the ages of 40-49 in 15.6% and 50 years and older in 9.0%. The mean age of the perpetrators was 38.11±11.94 (37.40±11.22 before the pandemic, 38.72±12.26 during the pandemic). When age groups were examined, it was determined that the perpetrators were 19 years of age or younger in 1.9% of the news articles, between 20-29 years of age in 23.2%, between 30-39 years of age in 31.8%, between 40-49 years of age in 26.4% and 50 years of age or older in 16.7%. Considering the marital status of women victims of violence, more than half of them were married (60.5%) (98.6% before the pandemic, 98.3% during the pandemic). 98.4% of the perpetrators of violence were male (56.1% before the pandemic, 62.5% during the pandemic), and 70.3% of them were husbands, lovers, fiancés (71.8% before the pandemic, 69.7% during the pandemic). 17.2% of women victims of violence had previously experienced violence perpetrated by the same person (12.8% before the pandemic, 19.0% during the pandemic). In 15.1% of the examined newspaper articles, it was stated that the perpetrator had a previous criminal record (16.7% before the pandemic, 14.5% during the pandemic). Information on the occupation of the victim (15.7%), the educational level of the victim (5.5%), the occupation of the perpetrator (15.3%), and the educational level of the perpetrator (2.3%) could be reached at low rates in the violence news (Table 1).

Table 1. Characteristics of victims and perpetrators of violence

Characteristics	Before the pandemic		During the pandemic		Total	
	N	%	N	%	N	%
Age groups of women victims of violence (N=411)						
≤19 age	10	7.7	18	6.4	28	6.8
20-29 age	52	40.0	101	35.9	153	37.2
30-39 age	40	30.8	89	31.7	129	31.4
40-49 age	20	15.4	44	15.7	64	15.6
≥50 age	8	6.1	29	10.3	37	9.0
Age groups of perpetrators of violence (N=311)						
≤19 age	2	2.1	4	1.9	6	1.9
20-29 age	25	25.8	47	22.0	72	23.2
30-39 age	27	27.8	72	33.6	99	31.8
40-49 age	29	29.9	53	24.8	82	26.4
≥50 age	14	14.4	38	17.8	52	16.7
Marital status of women victims of violence (N=387)						
Married	69	56.1	165	62.5	234	60.5
Single	49	39.8	83	31.4	132	34.1
Religiously married	5	4.1	16	6.1	21	5.4
Gender of perpetrators of violence (N=492)						
Male	144	98.6	340	98.3	484	98.4
Female	2	1.4	6	1.7	8	1.6
Proximity of perpetrators of violence to the victim (N=529)						
Husband, Lovers, Fiancé	112	71.8	260	69.7	372	70.3
Relatives	14	9.0	19	5.1	33	6.2
Friends	5	3.2	14	3.8	19	3.6
Other	25	16.0	80	21.4	105	19.9
Previous exposure to violence by the same person (N=529)						
Exposure	20	12.8	71	19.0	91	17.2
No information	136	87.2	302	81.0	438	82.8
Violence perpetrators' criminal record (N=529)						
Yes	26	16.7	54	14.5	80	15.1
No information	130	83.3	319	85.5	449	84.9

Table 2. Characteristics of violence cases

Characteristics	Before the pandemic		During the pandemic		Total	
	N	%	N	%	N	%
Period of violence (N=529)	156	29.5	373	70.5	529	100.0
Regions where violence occurred (N=529)						
Marmara Region	41	26.3	136	36.5	177	33.5
Mediterranean Region	30	19.2	66	17.7	96	18.1
Central Anatolia Region	36	23.1	55	14.7	91	17.2
Aegean Region	31	19.9	44	11.8	75	14.2
Black Sea Region	5	3.2	33	8.9	38	7.2
Southeastern Anatolia Region	7	4.5	24	6.4	31	5.8
Eastern Anatolia Region	6	3.8	15	4.0	21	4.0
Provinces where violence occurred (N=529)						
İstanbul	22	14.1	89	23.9	111	21.0
Ankara	13	8.3	24	6.4	37	7.0
İzmir	12	7.7	21	5.6	33	6.2
Adana	6	3.8	24	6.4	30	5.7
Other	103	66.1	215	57.7	318	60.1
Season in which cases of violence occurred (N=529)						
Winter	40	25.6	144	38.6	184	34.8
Autumn	44	28.2	90	24.1	134	25.3
Spring	32	20.6	85	22.8	117	22.1
Summer	40	25.6	54	14.5	94	17.8
Time of occurrence of violence (N=145)						
Daytime	15	53.6	66	56.4	81	55.9
Night	13	46.4	51	43.6	64	44.1
Place of occurrence of violence (N=520)						
At home	79	51.3	204	55.7	283	54.4
Out of home	75	48.7	162	44.3	237	45.6

The top two regions with the highest number of violence against women news are the Marmara region 33.5% (26.3% before the pandemic, 36.5% during the pandemic) and the Mediterranean region 18.1% (19.2% before the pandemic, 17.7% during the pandemic). At the same time, the city is Istanbul 21.0% (14.1% before the pandemic, 23.9% during the pandemic), Ankara 7.0% (8.3% before the pandemic, 6.4% during the pandemic) and Izmir 6.2% (7.7% before the pandemic, 5.6% during the pandemic). Violence against women was most common in winter 34.8% (25.6% before the pandemic, 38.6% during the pandemic), daytime 55.9% (53.6% before the pandemic, 56.4% during the pandemic) and home 54.4% (51.3% before the pandemic, 55.7% during the pandemic) (Table 2). The most common causes of violence against women were jealousy 15.2% (13.9% before the pandemic, 15.6% during the pandemic), 15.0% of the victim's desire for divorce (24.1% before the pandemic, 12.2% during the pandemic) and 6.7% of the victim's desire to separate from her lover (10.1% before the pandemic, 5.7% during the pandemic). Among the types of violence reflected in newspaper news, physical violence ranks first with 93.6% (96.1% during the pandemic period, 92.6% during the pandemic). Considering the way violence occurred, it was determined that it was most common with firearms 34.5% (42.1% before the pandemic, 31.3% during the pandemic) and 30.1% with cutting, piercing and crushing tools (35.5% before the pandemic, 27.8% during the pandemic) (Table 3).

Considering the results of violence cases, 85.2% of women lost their lives (93.3% before the pandemic, 81.3% during the pandemic). Approximately one-third (31.8%) of the violence cases contained information about the affected persons, and it was determined that the children of the victims were affected in approximately half (48.8%) of these news reports (53.2% before the pandemic, 47.1% during the pandemic). In addition, 8.3% of them were informed that the victim was pregnant (8.5% before the pandemic, 8.3% during the pandemic). It was observed that 38.4% of the perpetrators of violence were under arrest (48.7% before the pandemic, 33.9% during the pandemic), 36.8% were under investigation (33.1% before the pandemic, 38.4% during the pandemic), 8.5% were free (3.2% before the pandemic, 10.7% during the pandemic) (Table 4).

Discussion

This study aims to analyze the relationship between violence against women and the COVID-19 pandemic through media news. In order to control the spread of the disease during the pandemic, various measures such as social distancing and isolation and, in some cases, quarantine have been implemented in our country and the world. With these challenging conditions that emerged during the

COVID-19 pandemic, how the frequency of violence against women, the characteristics of victims, perpetrators and cases of violence, and the consequences of violence are affected constitute the main focus of our study.

First of all, the number of media reports on violence against women during the pandemic was found to be approximately 2.5 times higher than before the pandemic. The We Will Stop the Femicide Platform reported that the number of violence in March, April and May 2020, when women stayed at home due to the pandemic, increased by 44%, 55.4% and 78%, respectively (10). According to the results of a survey conducted by the Socio-Political Field Research Center with the participation of 1873 women living in 28 cities between April 3-8, 2020, violence against women increased by 27.8% (approximately three times) during the pandemic (11). United Nations Office on Drugs and Crime (UNODC) reported that the number of murders of women and girls occurring globally in 2022 was the highest recorded in the last twenty years (12). This information is consistent with the results of our study, and it is known that violence against women increases in pandemics and emergencies.

When we look at the average age of victims and perpetrators of violence, it has been observed that the average age of the perpetrators is approximately five years more than before and during the pandemic. Violence was mostly experienced by women between the ages of 20-29. This feature has not changed before and during the pandemic. When we look at the age groups of the perpetrators, it is seen that men in the 30-39 age group have committed violence the most. Centers for Disease Control and Prevention (CDC) has identified individual risk factors, such as young age, low education, and income status, as factors that contribute to the occurrence and persistence of intimate partner violence (13). In the Research on Domestic Violence against Women in Turkey, violence in the last 12 months was found to be higher among young women, and it was stated that young and married women were the most disadvantaged group in terms of the risk of exposure to violence (4).

Table 3. Causes, types and occurrence patterns of violence cases

Characteristics	Before the pandemic		During the pandemic		Total	
	N	%	N	%	N	%
Causes of violence (N=341)						
Jealousy	11	13.9	41	15.6	52	15.2
Victim's request for divorce	19	24.1	32	12.2	51	15.0
Victim's desire to break up with her lover	8	10.1	15	5.7	23	6.7
Other	41	51.9	174	66.5	215	63.1
Types of violence cases (N=517)						
Physical violence	146	96.1	338	92.6	484	93.6
Physical and psychological violence	2	1.3	17	4.6	19	3.6
Psychological violence	2	1.3	6	1.7	8	1.6
Sexual violence	2	1.3	4	1.1	6	1.2
Patterns of occurrence of violence (N=519)						
Firearms	64	42.1	115	31.3	179	34.5
Cutting, piercing, crushing tool	54	35.5	102	27.8	156	30.1
Beating attempts	21	13.8	77	21.0	98	18.9
Strangulation attempts	7	4.6	29	7.9	36	6.9
Other	6	4.0	44	12.0	50	9.6

Table 4. Results of violence cases

Characteristics	Before the pandemic		During the pandemic		Total	
	N	%	N	%	N	%
Outcome of violence (N=418)						
Death	125	93.3	231	81.3	356	85.2
Injury	9	6.7	53	18.7	62	14.8
Affected people as a result of violence (N=168)						
The baby in the victim's womb	4	8.5	10	8.3	14	8.3
Children of the victim	25	53.2	57	47.1	82	48.8
Victim's friends	3	6.4	10	8.3	13	7.7
Relatives of the victim	9	19.1	22	18.2	31	18.5
Victim's spouse	1	2.1	3	2.5	4	2.4
Other	5	10.6	19	15.7	24	14.3
Status of the perpetrator after the violence (N=508)						
Under arrest	75	48.7	120	33.9	195	38.4
Under investigation	51	33.1	136	38.4	187	36.8
Release	5	3.2	38	10.7	43	8.5
Fugitive	9	5.9	27	7.6	36	7.1
Dead	14	9.1	16	4.5	30	5.9
Other	0	0.0	17	4.9	17	3.3

When the marital status of women who are victims of violence is examined, it has been determined that they are mostly married. The news during the pandemic is more than the news before the pandemic among married women. When the proximity of the perpetrators of violence to the victim was examined, it was determined that in seven out of ten news reports, the victim was his wife, lover or fiancée, and this situation did not change much with the pandemic. Hande Şahin et al. also reported that women were similarly subjected to violence by their husbands and intimate partners (14). CDC, regarding the prevalence of intimate partner violence, found that approximately 41% of women have experienced sexual violence, physical violence, and/or stalking by an intimate partner and have reported an impact of intimate partner violence throughout their lives. More than half of femicide victims in the United States have been killed by a current or former male intimate partner (15). According to the WHO, globally, 38% of all femicides are committed by intimate partners (3). In the report of the UNODC, it has been reported that 55% of murders of women and girls are committed by intimate partners or family members (12). In foreign literature, individual, relationship structure, social risk factors and protective factors related to intimate partner violence have been identified (13). In our country, data on this subject are incomplete. More effective and solution-oriented measures can be planned by keeping regular records on a national scale, defining risk groups for intimate partner violence (risk-oriented approach) and conducting detailed studies questioning social and demographic factors.

It was found that in approximately one-fifth of the violence news examined, women who were victims of violence had previously been exposed to violence by the same person. This rate has emerged more clearly during the pandemic period. At the same time, it was determined that in 15.1% of the news, the practitioner had a previous criminal record. According to the data of The We Will Stop the Femicide Platform, in 280 femicides committed in 2021, it was reported that 33 of the murdered women had previously complained to the police or prosecutor's office or had a protection order (16). In our country, the penal execution law was enacted to ensure prison infection control during the pandemic. The fact that many criminals were released from prisons without taking measures in favor of women, children and disadvantaged groups may also have an impact on the increase in violence. Considering that violence against women is preventable, the importance of imposing deterrent punishments, especially for people who have committed violence and have a criminal record, draws attention.

In the violence news examined, information about the victim's profession (15.7%), the education level of the victim (5.5%), the perpetrator's profession (15.3%), and the education level of the perpetrator (2.3%) could be accessed at a low rate. The information obtained belongs to the working group with a high level of education. In this respect, our study in defining risk groups for violence against women has not been sufficient. Gülsen Erden et al. (2018) also accessed this information at a low rate in their research with the news of femicides. They commented that the perpetrators and victims may not be working, their income and education level may be low in parallel, and these situations may pose a risk for violence (17).

In our study, violence against women was primarily experienced in the Marmara region and Istanbul. During the pandemic, it was observed that there was a decrease in violent incidents in Central Anatolia and the Aegean region and an increase in the Black Sea Region. In the study of Serpil Dündar et al, the Marmara region and in the study of Ayşegül Akgül et al, Istanbul were stated as the places where violence was experienced in the first place (18,19). The multinational structure of Istanbul and the Marmara Region may be related to this situation, as the population constitutes the majority of Turkey's population and receives much immigration.

Violence against women was most common in the winter season, during daylight hours and in the home environment. During the pandemic, there has been an increase in the news of violence in the winter season and the home environment. According to the report of The We Will Stop the Femicide Platform, 65% of the women killed in 2023 were killed in their homes. Homes, which are the places where individuals should feel safest, have become unsafe spaces for women (20). Long-term close contact within the family during events such as natural disasters and pandemics can increase domestic violence by reducing safe time (e.g., because a person goes to work), increasing interactions as more time is spent together, and uncovering various habits that may not be compatible with each other (21).

When the causes of violence were examined, while the victim's desire for divorce was at the forefront (24.1%) before the pandemic, jealousy (15.6%) was found to be at the forefront during the pandemic. In many studies in the literature, jealousy, request for divorce, or desire to break up have been stated as the cause of violence. In the study conducted by Gülsen Erden et al. on femicides, the top three reasons were arguing, jealousy and the woman's desire for divorce (17). During the pandemic, jealousy may have come to the fore due to increased close contact between family members and economic problems.

Looking at the types of violence cases, it was observed that physical violence was at the forefront of the news during the pandemic, and psychological violence was also reflected in the news, albeit at a low rate. The We Will Stop the Femicides Platform revealed that 37% of women were subjected to

psychological violence during the pandemic in the May 2020 Applicant Reception Report and that the applications for psychological violence increased by 51% compared to the previous month (10). Serpil Dündar et al, in their study conducted before the pandemic, found that physical violence ranked first and was accompanied by sexual and psychological violence (18). According to the Research on Domestic Violence against Women in Turkey (2014), one in every two women in Turkey is exposed to psychological violence (4). Psychological violence may lead to physical, economic and sexual violence and may be the beginning of a pathological process leading to femicide (22). The fact that physical violence is more frequently covered in the news is because it is the concrete, visible face of violence. Making psychological violence visible and raising awareness at the social level that it is a form of violence that can have serious consequences may be necessary in terms of a proactive approach to violence.

Considering how violence occurs, it has been observed that while the use of firearms and cutting-piercing-crushing tools decreased during the pandemic period, battering and strangulation attempts increased. In the study conducted by Erden et al. (2018) investigating femicides, firearms (51.9%), sharp/striking tools (35.8%), strangulation (6.9%), and beating (4.2%) were given as the tools used (17). As a result of the challenging conditions experienced during the pandemic period, the sudden increase in stress levels and the inability to control anger, battering and strangulation attempts may have increased.

When evaluated according to the results of the cases of violence, the news of violence resulting in death decreased during the pandemic. In contrast, the news of violence resulting in injury increased approximately three times. According to the data of The We Will Stop the Femicide Platform, while the number of femicides was 360 in 2019, it was 300 in 2020 and 280 in 2021 (20). In a study examining records between 2015 and 2020 in Spain, it was reported that women's deaths decreased during the pandemic period (23). We think that this decrease may be a relative decrease secondary to the decrease in homicides caused by reasons such as divorce/separation due to the closure measures taken during the pandemic period and the increase in violence resulting in fewer deaths in the home environment. In the news of violence recorded during the pandemic period, the arrest status of the perpetrators of violence decreased while the release status increased. In the study, which examined the applications made to a police station in the USA, while domestic violence service calls increased with the stay-at-home measures during the pandemic, the arrest rates did not change. They explained this situation because the calls for service included non-violent domestic unrest (24). Similarly, in our study, crimes such as battering and strangulation attempts may have been considered lesser crimes during the pandemic period, and the perpetrators may have been released. However, considering that such crimes as psychological violence may be a harbinger of violence that will result in death, it is crucial to give deterrent punishments to the perpetrators, investigate the causes of violence and take precautions.

In approximately one-third (31.8%) of the news reports on violence, there was information about the people affected. In approximately half (48.8%) of these news reports, it was determined that the victim's children were affected. In addition, 8.3% of the news items contained information that the victim was pregnant. Violence against women negatively affects not only the women who are subjected to it but also their children. Studies reveal the link between domestic violence against women and physical abuse of children and the trauma and behavioural and emotional disorders caused by witnessing domestic violence in children. Research also reveals the intergenerational transmission of violence as one of the critical consequences of violence. In this framework, it is known that maternal exposure to violence in the family has an impact on the normalization of violence or exposure to violence by women and men in their future lives. According to research results, there is a positive correlation between women's exposure to violence by their mothers and their exposure to violence (2,3,13).

Conclusion

The most important result of our study is that violence against women news increased significantly during the COVID-19 pandemic. During the pandemic, the frequency of violence news increased in the Marmara region, in the winter season, during daylight hours, in the home environment and among married women. In addition, it was observed that the frequency of violent cases in the form of beating and strangulation was increased while the frequency of death following violence was decreased. The complex relationship between the COVID-19 pandemic and violence against women should be an essential focus for both communities and policymakers. In order to prevent violence against women, it is necessary to carry out awareness studies at the social level, to keep regular records on a national scale, to plan more effective and solution-oriented measures by conducting detailed studies that define risk groups for intimate partner violence (risk-oriented approach) and question social and demographic factors. In addition, international regulations on violence against women should be adopted and necessary studies should be carried out for the implementation and supervision of these regulations.

Limitations: The limitations of our study include the possibility that not all news about violence against women could be reached, not all incidents of violence against women may have been reported in the press, social, economic and cultural risk factors that were not given in newspaper news could not be evaluated, and risk factors could only be obtained as much as they were reported in newspaper news. In addition, it is noteworthy that more information about victims of violence is included in media reports, and less information about perpetrators of violence is included. Although the analysis of media reports does not provide a complete picture of the cases of violence against women, it can be a guide for further studies.

Conflict of interest statement

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

Ethics Committee Approval: The study was approved by the Medical and Health Sciences Ethics Committee of the Muğla Sıtkı Koçman University (Date:19.07.2022, No:52).

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Age-Related Diffusion Changes in The Corpus Vitreum And Aqueous Humor of The Ocular Bulb

Bulbus Okulinin Korpus Vitreumu ve Hümör Aközünde Yaşa Bağlı Difüzyon Değişiklikleri

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Öz

Bulbus okuli, anteriorda hümör aköz (HA) ve posteriorda vitröz hümör (VH) olmak üzere iki ana sıvı içerikli anatomik yapıdan oluşur. Bu çalışmada, farklı biyokimyasal içeriğe sahip bu iki yapıda yaşlanmaya bağlı olarak oluşan difüzyon değişikliklerini manyetik rezonans görüntüleme kullanarak araştırdık Yaşlarına göre 8 farklı gruba ayrılan toplam 128 hastanın gözünde VH ve HA difüzyon değerleri hesaplandı. Elde edilen sonuçlar yaş, cinsiyet ve sağ-sol ayrımına göre karşılaştırıldı. Hem VH hem de HA için elde edilen difüzyon değerlerinde cinsiyetler arasında ($p=0.397$, $p=0.383$) ve sağ ve sol gözler arasında ($p>0.568$, $p>0.717$) istatistiksel olarak anlamlı fark saptanmadı. Ancak ilk dekat yaş grubu her iki yapı için de en düşük difüzyon değerlerine sahipti ($p<0.001$). Yaşlanmaya bağlı olarak gözün VH ve HA'de difüzyon değerlerinde meydana gelen değişiklikler, her iki yapının biyokimyasal içeriğinin yaşlanmayla birlikte değiştiğini göstermektedir.

Anahtar Kelimeler: 3 Tesla, ADC, Difüzyon MR, Hümör Aköz, Vitröz Hümör

Abstract

The bulbus oculi consists of two main fluid-containing anatomical structures: the aqueous humor (AH) at the anterior and the vitreous humor (VH) at the posterior. In this study, we investigated the diffusion changes that occur due to aging in these two structures with different biochemical contents using magnetic resonance imaging. VH and HA diffusion values were calculated in the eyes of a total of 128 patients divided into 8 different groups according to their ages. The results obtained were compared according to age, gender and right-left distinction. There was no statistically significant difference in the diffusion values obtained for both VH and HA between genders ($p=0.397$, $p=0.383$) and between right and left eyes ($p>0.568$, $p>0.717$). However, the first decade age group had the lowest diffusion values for both structures ($p<0.001$). Changes in the diffusion values of the eye in VH and HA due to aging show that the biochemical contents of both structures change with aging.

Keywords: 3 Tesla, ADC, Diffusion MRI, Aqueous Humor, Vitreous Humor

Introduction

The ocular bulb contains two fluids that are anatomically distinct and have different chemical compositions (1). Humor aqueous (HA), which fills the anterior and posterior chambers anterior to the bulbus oculi, has a transparent, low-viscosity structure consisting of ions, carbohydrates, amino acids, urea, oxygen, carbon dioxide, glutathione and water (2-4). In the posterior part of the bulbus oculi, just behind the lens, there is the vitreous humor (VH), which has a gel-like form and is surrounded by the chorioretinal complex and constitutes approximately 80 percent of the eye (1). VH, the largest structure of the eye, consists of water, collagen and hyaluronic acid groups, and its viscosity is higher than HA (5). Deterioration of homogeneity in VH due to aging is called liquefaction, and liquefaction may result in vitreous detachment and retinal tear and/or detachment (6). Although the chemical content of both HA and VH and changes due to aging can be evaluated by invasive methods (such as VH or HA fluid sampling), these methods also bring complications such as infection, hemorrhage and detachment (6-8). The chemical content of both structures and changes due to aging can be evaluated with magnetic resonance imaging (MRI), a non-invasive method (9-11). Diffusion-weighted imaging (DWI), one of the advanced MRI methods, is an imaging method that evaluates the random microscopic movement of water protons and depends on the biophysical properties of the examined tissue (12,13). Aging changes water content, microcirculation, microstructure and perfusion in tissues, and these changes can be evaluated with DWI (13,14). In the literature, there are studies on diffusion changes in VH due to aging in normal cases and diffusion changes in pathological conditions (9,15). However, according to our limited knowledge, there are not enough studies on the diffusion properties of HA. The aim of this study is to reveal age-related diffusion changes in HA and VH, which have different chemical contents.

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Material and Method

Patient Selection

This retrospective study was approved by the local Ethics Committee (21.12.2023 date / 118 no). Patient information was kept confidential throughout the study and patient privacy was taken into

consideration. Among the cases who underwent brain MRI examination including a diffusion sequence using a standard head coil for different reasons between September 2022 and November 2023, those without pathological imaging findings were included in our study. Cases with glaucoma, uncontrolled hypertension and/or diabetes in the file scan were excluded from the study. In addition, cases with previous retinal detachment, posterior vitreous detachment, intraocular bleeding, trauma, infection clinics and cases with artificial images were excluded from the study.

Review and Evaluation of MRI Images

All MRI examinations were performed with a 3 Tesla (Magnetom Skyra, Siemens, Erlangen, Germany) scanner. DWI consisted of axial slices (b-values of 0 and 1000 s/mm2 for calculation of ADC, TR/TE 6400/98 ms, FOV 220 x 220 mm, slice thickness 4 mm). Average apparent diffusion coefficient (ADC) values were measured by placing a region of interest (ROI) in front and behind the lens using an axial section passing through the middle point of the lens on the axial ADC map (Figure 1). All radiological measurements were made on a Siemens workstation (syngo via) with the consensus decision of two radiologists with over 10 years of experience. A total of 8 groups were created considering age and gender (according to decades, the first group is 1-10 years old and the eighth group is over 70 years old).

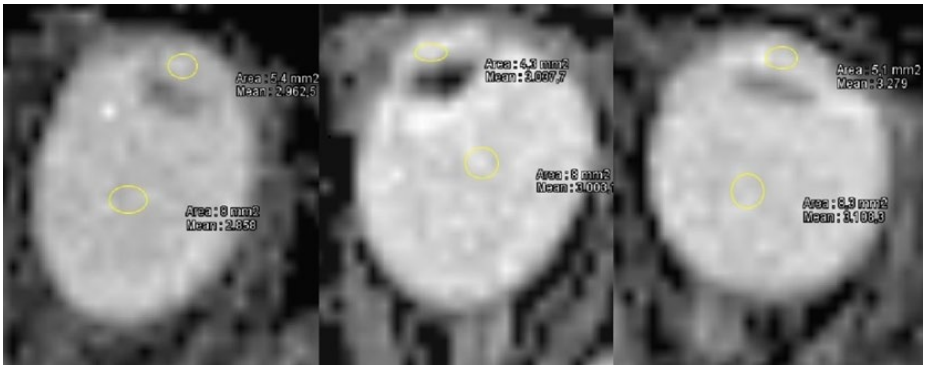

Figure 1. Axial ADC images. Average ADC values measured in normal cases aged 8 years (Figure A), 17 years (Figure B) and 55 years (Figure C). HA measurement in the anterior ROI and VH measurement in the posterior ROI.

Statistical Analyses

IBM SPSS version 20.0 software (IBM Corp, Armonk, NY, USA) was used for statistical evaluation and normal distribution was checked using Kolmogorov-Smirnov test. Data are presented as mean±standard error of mean or mean±standard deviation. Comparison of right and left VH and HA ADC values and VH and HA ADC values was performed by paired samples t-test. Comparison of VH and HA according to gender was performed with Independent T-test. One-way ANOVA test was used to evaluate the statistical differences between groups formed according to age. Multiple comparisons were made with the Tukey test and a p value of 0.05 was considered statistically significant.

Results

A total of 128 patients (59 males, 69 females) were included in the study. The mean age was 40.84±23.04 (range 4-94). The mean ADC value (x 10^{-6} mm^2/sn) for VH was 3147±165 (range 2800-3599) on the right side and 3143±160 (range 2765-3552) on the left side. There was no statistical difference between right and left side VH (p=0.568). There was no statistical difference between the genders for mean, right and left VH (p=0.397, p=0.487 and p=0.261, respectively**) (**Table 1). Mean ADC values for HA were 3239±205 on the right and 3243±216 on the left. There was no statistical difference between right and left in terms of HA (p=0.717). There was no statistical difference between the genders for mean, right and left HA (p=0.383, p=0.494 and p=0.449, respectively) (Table 1). Additionally, according to Table 1, the ages of men and women are similar (p=0.715).

The distribution of mean VH and HA according to age groups are given in Table 2. Among the age groups, the values of the first group in terms of mean, right and left VH were lower than the other groups (Table 2) (p<0.001). Among the age groups, the values of the first group in terms of mean, right and left HA were lower than the other groups (Table 2) (p<0.001). The values of the second group in terms of mean, right and left VH were lower than the 5th and 7th groups (Table 2) (p<0.01). The values of the second group in terms of mean, right and left HA were lower than the 5th and 7th groups (Table 2) (p<0.01). The values of the 3th group in terms of mean, right and left HA were lower than the 5th group (Table 2) (p<0.01).

In Table 2, the effect size obtained as a result of the posterior power analysis performed according to the descriptive statistics of the average VH variable was calculated as 1.038 and the achieved power was calculated as 99%.

Table 1. The distribution of age, mean and both sides vitreous humor and aqueous humor in according to sexes.

	Group A (n=59)	Group B (n=69)	p value
Age	40.03±3.01	41.54±2.79	0.715
Mean VH	3142±22.5	3147±17.7	0.871
Right VH	3134±22.6	3158±19.2	0.414
Left VH	3151±23.1	3136±17.6	0.602
Mean HA	3250±27.3	3233±23.2	0.628
Right HA	3251±26.7	3227±24.9	0.515
Left HA	3249±30.1	3238±24.7	0.780

Descriptive statistics are shown as mean±standard error. VH: Vitreous humor, HA: Aqueous humor

Discussion

According to the results of our study, there was no statistically significant difference between the mean ADC values of VH and HA as well as between the right and left eyes, when gender is taken into account. However, the mean ADC value of HA was higher than that of VH in both the right and left eyes. Additionally, in the first decade, ADC values of both HA and VH were lower than other age groups.

DWI is a radiological modality that creates imaging through the microscopic random movement of water molecules in tissues. In general, relatively increased diffusion is encountered in cystic tissues with high water content, necrotic tissues with impaired membrane integrity, and tissues with low number of nuclei (containing fewer cells) (16,17). The diffusion property of the tissue is measured quantitatively via ADC images, and tissues with high water content and low cell content have higher ADC values (17,18).

MRI is successfully used in diagnosis and follow-up treatment for many orbital pathologies (19-22). Regarding the use of diffusion-weighted MRI in orbital pathologies, the ADC values of normal cases and ocular adnexal lymphoma (OAL) cases were compared in the study conducted by Politi et al. (23). In this study, it was found that the average ADC values in orbital tissues with OAL were lower than the ADC values in orbital tissues in normal cases, and the ADC values of tissues that responded to treatment increased. As a result, DWI was found to be useful in estimating the correct diagnosis and post-treatment therapeutic response in OAL cases.

A study by Itakura et al. showed a decrease in the amount of hyaluronic acid in VH due to aging (24). In the study conducted by Meral et al., it was found that ADC values in VH increased with aging in normal cases (9). According to the results of both studies, the decrease in eye VH in hyaluronic acid groups due to aging and the increased ADC values due to the increase in water content in VH (liquefaction) with age are parallel to the values we found in our study. However, unlike the study conducted by Meral et al., in our study, the average VH ADC values measured in the 2nd decade were found to be lower than the 5th and 7th decade age groups.

In one of the studies showing the changes in the content of the aqueous humor that occur with aging, it was shown that the immunological environment of the anterior chamber becomes more pro-inflammatory and pro-angiogenic from childhood to adulthood (25). Although there are studies in the literature showing changes in the content and dynamics of the aqueous humor due to aging and glaucoma, there are not yet sufficient studies on DWI features (26-29). According to our study, HA mean ADC values increase with age, similar to VH ADC values, and the lowest was measured in the first decade.

Our study has some limitations, the first of which is that interobserver variability was not taken into account. Moreover, the area measured for HA is small and although the measurement is avoided as much as possible, the ADC values of the surrounding tissues may have contributed to the calculated ADC value. However, we think that these age-related normal data for VH and HA in normal cases have the potential to be used in the evaluation of eye diseases.

Table 2. The distribution of age, mean and both sides vitreous humor and aqueous humor in according to age groups.

	0-10 y (n=16)	11-20 y (n=16)	21-30 y (n=14)	31-40 y (n=19)	41-50 y (n=14)	51-60 y (n=17)	61-70 y (n=15)	>70 y (n=17)
Age (years)	7.3±0.4	14.9±0.7	25.8±0.8	35.8±0.7	44.5±0.8	54.7±0.7	65.9±0.7	75.7±1.5
Mean VH	2928±91*	3072±93£	3149±119	3171±101	3245±136	3203±182	3183±136	3210±158
Right VH	2923±90*	3074±97£	3157±138	3156±110	3244±132	3202±180	3183±142	3238±43££
Left VH	2933±97**	3070±94£	3140±108	3186±99	3247±143	3204±192	3183±147	3182±164
Mean HA	2966±116	3145±91***	3217±127	3279±139	3427±171	3269±190	3345±173	3290±213
Right HA	2970±121**	3143±96***	3216±131£££	3259±106	3412±177	3287±189	3348±219	3289±205
Left HA	2962±115*	3147±95***	3218±127	3299±208	3443±212	3252±210	3342±157	3292±217

Data are n of participants, mean±SD. VH: Vitreous humor, HA: Aqueous humor. *: Group 1 is different from other age groups ($p<0.05$). **: Group 1 is different from other age groups except group 2. ***: Group 2 is different from groups 5 and 7. £: Group 2 and group 5 are different from each other. ££: Group 8 is different from group 2. £££: Group 3 is different from group 5.

Conclusion

In order to obtain better results in the diagnosis and treatment of eye diseases, it is necessary to understand the changes that occur with aging in the two main fluids of the bulbus oculi. According to our study, the lowest mean ADC values of both HA and VH were detected in the first decade and increased with age. For both structures, the values obtained in the 2nd decade were found to be lower than those in the 5th and 7th decades. Although these findings show that there are changes in HA and VH content depending on age, we believe that larger studies should be conducted on this subject.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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Assessment of Factors Affecting the Management of Chronic Diseases in Patients with Type 2 Diabetes: A Community-Based Cross-Sectional Study

Tip 2 Diyabetli Hastalarda Kronik Hastalıklarının Yönetimine Etki Eden Faktörlerin Değerlendirilmesi: Toplum Tabanlı Kesitsel Bir Çalışma

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Öz

Çalışmamız Manisa merkez ilçede yaşayan tip 2 diyabetli hastalarda kronik hastalıklarının yönetimlerini etkileyen faktörleri değerlendirmek amaçlanmıştır. Kesitsel tipteki araştırmamıza çok aşamalı, tabakalı rastgele örnekleme yöntemiyle 505 tip 2 diyabetli hasta katılmıştır. Katılımcılara yüz yüze anket uygulanmıştır. Anket literatür taraması ile hazırlanmış yarı yapılandırılmış sorular ve hastaların kronik hastalık bakımlarını kendilerinin değerlendirdiği Patient Assessment of Chronic İllness Care (PACIC) Türkçe ölçeğinden oluşmaktadır. Çok değişkenli çözümlemelerde regresyon analizi uygulanmıştır. Katılımcıların HbA1c düzeyi ortalaması 6.9±1.7 mg/dl'dir. HbA1c'ye göre %61.7'sinin metabolik kontrolü iyi ve sadece %69.5'i evde kendi kendine kan şekeri takiplerini yapmaktadır. Katılımcıların toplam PACIC skor ortalaması 2.59±0.62'dir. Tek değişkenli analiz sonuçlarına göre; kent merkezinde yaşayanların, erkeklerin, 45 yaş altındakilerin, yüksek gelirlilerin, yüksek eğitimlilerin ve evde kendi kendine şeker takibi yapanların, HbA1c, kan lipid düzeyleri kontrol altında olanların, rutin izlemlerini düzenli yaptıranların ve diyabete bağlı sağlık problemi olmayanların toplam PACIC skorları anlamlı olarak daha yüksektir ($p<0.05$). Çok değişkenli modelde; karar verme becerisinin toplam PACIC skorlarındaki değişimin %52.5'ini, düzenli rutin izlemleri yaptıranların ise %19.0'ını açıkladığı bulunmuştur. Bu, hastaların kendi sağlık yönetimlerinde aktif roller alması ve düzenli sağlık kontrolü yaptırmasının, hasta merkezli bakımın kalitesini önemli ölçüde etkileyebileceğini gösterir. Diyabet eğitiminin nicel ve nitel kalitesinin artırılması, hastaların karar verme becerilerini geliştirmesi kronik hastalık yönetimini kolaylaştırabilir.

Anahtar Kelimeler: HbA1c, Kronik Bakım Modeli, Kronik Hastalık Bakımının Hasta Değerlendirmesi Ölçeği (PACIC), Metabolik Kontrol, Tip 2 Diyabet

Abstract

Our study aimed to evaluate the factors affecting the management of chronic diseases in patients with type 2 diabetes living in Manisa central district. In our cross-sectional study, 505 type 2 diabetic patients participated in a multi-stage, stratified random sampling method. A face-to-face questionnaire was applied to the participants. The questionnaire consisted of semi-structured questions prepared with a literature review and the Patient Assessment of Chronic Illness Care (PACIC) Turkish scale in which patients self-assessed their chronic disease care. Regression analysis was applied in multivariate analysis. The mean HbA1c level of the participants was 6.9±1.7 mg/dl. According to HbA1c, 61.7% had good metabolic control and only 69.5% of the participants self-monitored their blood glucose at home. The mean total PACIC score of the participants was 2.59±0.62. According to the results of univariate analysis, the total PACIC scores of those living in urban centers, males, those under the age of 45, those with higher income, those with higher education, those who self-monitor glucose at home, those with controlled HbA1c and blood lipid levels, those who have regular routine follow-ups and those who do not have diabetes-related health problems are significantly higher ($p<0.05$). In the multivariate model; decision-making ability was found to explain 52.5% of the change in total PACIC scores and 19.0% of those who had regular routine follow-ups. This indicates that patients taking active roles in their own health management and having regular health check-ups can significantly impact the quality of patient-centered care. Increasing the quantitative and qualitative quality of diabetes education and improving patients' decision-making skills can facilitate chronic disease management.

Keywords: HbA1c, Chronic Care Model, Patient Assessment of Chronic Illness Care Scale (PACIC), Metabolic Control, Type 2 Diabetes

Introduction

Noncommunicable diseases (NCDs) are the result of a combination of genetic, physiological, environmental, and behavioral factors that are usually long-lasting. The main types of NCDs are cardiovascular diseases, cancer, chronic respiratory diseases, and diabetes. They continue to be an important public health challenge in all countries, including low- and middle income countries where more than three quarters of NCDs deaths occur (1). Diabetes mellitus (DM) describes a group of metabolic disorders characterized by high blood glucose levels. Type 2 diabetes mellitus (T2DM) is the most common type of diabetes, accounting for over 90% of all diabetes worldwide. In T2DM, the response to insulin is diminished, and this is defined as insulin resistance. Thus, insulin secretion is unable to maintain glucose homeostasis, producing hyperglycemia (2).

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The Global Picture (burden of disease and health effect)

Globally, more than one in 10 adults are now living with diabetes. The distribution of diabetes prevalence is estimated to increase due to aging populations. A systematic literature review was

estimated 537 million adults aged 20–79 years are currently living with diabetes. This represents 10.5% of the world's population in this age group. The total number is predicted to rise to 643 million (11.3%) by 2030 and to 783 million (12.2%) by 2045 (3). According to the International Diabetes Federation (IDF)'s project, that there are 61.4 million (9.2%) diabetics in the European region, where our country is located, according to 2021 data, and this number will increase to 69.2 million (10.4%) in 2045 and an increase of 13% is expected in the estimated number of diabetics. Turkey ranks first with 14.5% among the five countries with the highest prevalence of age-standardized diabetes among 20-79 adults, according to 2021 estimates (2).

It is estimated that approximately 6.7 million adults between the ages of 20-79 have died due to diabetes or complications in 2021. This corresponds to 12.2% of global deaths for all reasons in this age group (3). Persistent hyperglycemia can cause several complications such as cardiovascular disease (CVD), blindness, kidney failure, and amputation of lower limbs. Acute complications include hypoglycemia and hyperglycaemic diabetic coma. Chronic microvascular complications include nephropathy, neuropathy, and retinopathy, whereas chronic macrovascular complications include coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease.

Strategies for improving care management and promoting health

Diabetic patients must assume an active role in their care, in order to learn self-management skills and follow-up systems. Patients must be educated to take responsibility for their diabetes management including diet control, physical exercise, self-monitoring of blood glucose, regular screening for the development of early diabetic complications, such as kidney disease, retinopathy, neuropathy, peripheral artery disease, and foot ulceration to avoid complications associated with DM. With regular check-ups and effective lifestyle management, as well as medication if required, people with type 2 diabetes can lead long and healthy lives (4). Thus, The Chronic Care Model (CCM) was developed for improving the quality of diabetes care. The CCM is a patient-centered approach to care that requires a close working relationship between the patient and clinicians involved in treatment planning. The CCM consists of 6 basic elements in providing high-quality chronic disease care services in health systems. These elements are respectively self-management support, decision support, redesign of the health service delivery system, clinical information systems, links with community resources, and organization of health services. Many studies indicate that the CCM can be applied in diabetes patients, is beneficial, and has achieved clinical and behavioral effective results. Patients who were enrolled in the CCM experienced the cumulative incidence of diabetes-related complications and all-cause mortality reduced (5). Patient assessment of Chronic Illness Care (PACIC) originated from the chronic care model and was developed by Glasgow et al. in 2005. It has been found that a scale is an appropriate tool for evaluating the quality of care in diabetes, as it is in various chronic diseases (6,7). The Turkish version of the Chronic Disease Care Assessment Scale (Turkish PACIC), which allows it to be used in our country for those with chronic diseases (8).

Our results will be guiding in terms of ensuring that health professionals participate in their patients' own health management is an effective strategy in chronic disease management. This study aims to improve the quality of care of individuals with chronic diseases by evaluating the follow-up and care services of people with type 2 diabetes living in the central district of Manisa, quantitatively and qualitatively.

Material and Method

Study design and Sample selection

The population of the cross-sectional study consists of 30,518 with diabetes patients living in the central district of Manisa, according to the standardized prevalence rate of 13.7%, which is expected to be approximately 222,766 people over the age of 20 in the region. The sample size was calculated as 95% confidence, when the prevalence of inadequate service/care was taken as 35% according to The Turkish Epidemiology Survey of Diabetes, Hypertension, Obesity and Endocrine Disease (Turdep 2) study, it was calculated as a minimum of 384 people with a deviation of 5% (9).

Step 1: Twenty-four primary health care center (PHC) (58 urban; 28 semi-urban and 12 rural), were selected proportionally from ninety-eight family physicians to each stratum using a multi-stage, stratified, simple random sampling method. It was planned to reach 480 people in total, with a sample size of 20 patients for each primary health care physicians (PHPs).

In primary care, patients with suspected diabetes should be screened with the acceptance of a preliminary diagnosis. It was understood that 98 of them did not actually have diabetes, and only 330 of the remaining ones were surveyed. These 98 people, whose pre-diagnosis of diabetes was entered into the system by the physician, did not actually have diabetes.

The accessibility rate was calculated to be 68.75%, and a new reserve list of 240 people in total was created from 10 patients with type 2 diabetes for each PHPs.

Step 2: It was understood that 35 people from the new reserve list did not actually have diabetes, and a questionnaire was applied to 175 patients from the

remaining ones. As a result, the rate of participation in the research (505/587) was 86.1%. The questionnaires were filled in by face-to-face interview method at patients' home through their addresses registered to the PHPs in 2014.

Properties of the Participants

The independent variables are grouped into four main clusters:

1. Sociodemographic variables (age, gender, marital status, job, educational status, family type, etc.)
2. Positive Health Behaviors (alcohol, smoking status, physical activity, nutrition, diabetes education)
3. Variables of accessibility to health services, health service utilization
4. Other variables related to the disease (laboratory tests results, acute and chronic diabetes complications, regular follow-up visits (10).

Dependent variables (quantitative and qualitative):

1. The quantitative indicator: HbA1c was chosen to assessment of the metabolic control. In patients diagnosed with type 2 diabetes, the first single oral antidiabetic drug therapy is started simultaneously with lifestyle adjustments. If glycated hemoglobin A1c (HbA1C) >7% despite lifestyle adjustments, adjustments are made by adding new additional drugs in the treatment. If the patient's HbA1C is >7% despite the new treatment, the treatment is rearranged by adding new drugs. HbA1C was chosen because it is the parameter that changes the treatment regimen in evaluating the achievement of glycemic targets of type 2 diabetes patients with poor metabolic control (11).

2. The qualitative indicator: Patient Assessment of Chronic Illness Care (PACIC), which was adapted to Turkish society and validated was used. PACIC is a scale developed in English by Glasgow et al., based on the chronic care model, that allows patients to evaluate the health care services offered to chronic diseases, and consists of 20 items and 5 sub-dimensions, and each item consists of five-point Likert-type response options. These sub-dimensions are (Questions 1-3) Patient Activation, (Questions 4-6) Decision support, (Questions 7-11) Goal setting (Questions 12-15) Problem-Solving, (16-20 Questions) Follow-up/Coordination. The total score of the scale and the mean score of each sub-dimension are obtained by summing the scores in a five-point Likert-type rating such as 1 = never, 2 = rarely, 3 = sometimes, 4 = often, and 5 = always in each item and then dividing by the number of items. Total scale score and sub-dimension scores can get a minimum of 1 and a maximum of 5. An increase in scale scores indicates that individuals with chronic disease are satisfied with the care/service they receive, and that chronic disease management is sufficient (12).

Statistical Analysis

Statistical analyses were performed by using IBM SPSS version 15 package program. The dataset was prepared for analysis with checked for missing data and outliers. In the study, we used both descriptive and inferential statistics to analyze our results. Descriptive statistics were used to summarise background characteristics of the study population. Qualitative parameters were presented by percentages and frequencies. Continuous data were analyzed using mean, median, standard deviation, and min-max values. In univariate analyses, we checked the goodness of fit using by Kolmogorov-Smirnov test which determines the normal distribution of continuous data. Student's t-test was used to compare the means between two groups, and one-way ANOVA was used to compare the means among three or more groups. Where parametric test assumptions could not be met, non-parametric methods were used to compare the groups. Chi-square test was used to evaluate the differences between the ratios.

Multiple linear regression analysis was performed to explain the effect on the total PACIC score, which is one of the independent variables that are significant in univariate analysis. The total PACIC score was taken as the dependent variable. In order for multiple linear regression analysis to give reliable results, the linear relationship between the independent and dependent variables was examined with a scatter graph, extreme values were checked with case wise diagnostics, randomness of errors was verified with the Durbin-Watson test, and multilinearity was evaluated through VIF and Tolerance values.

In all statistical analysis p-values of <0.05 were considered statistically significant.

Results

Descriptive statistics

In our study, a questionnaire was applied to 505 patients. The mean age of the patients was 57.9±12.3 years, 65.7% were female, 17.4% had high school education or higher, and 39.8% had income less than expenses.

The mean diagnosis of diabetes in the study group was 7.9±6.7 years and 64.2% had diabetes for less than ten years. In terms of metabolic control parameters, hemoglobin A1C (HbA1C) 61.7%, fasting plasma glucose (FBG) 41.3%, Triglycerides (TG) 47.7%, LDL 34.4%, cholesterol 59.2%, and systolic blood pressure (SBP) 65.2% of the diabetics were found to be at desired levels. Only 56.8% of the diabetics who participated in our study had HbA1c results. The mean HbA1c level was 6.9±1.7 mg/dl. We achieved follow-up controls of diabetic patients

such as 81.8% for electrocardiogram (ECG), 71.7% for fundoscopic examination, 78.4% for glucosuria, 57.2% for ketonuria, 17.4% for microalbuminuria and 28.5% for neurological sensory examination. These results are shown in table 1.

Distribution of Turkish PACIC and Sub-Dimensional Scores

Patient Activation (items 1-3) subscale mean score is 2.60±0.89, Decision/Support (items 4-6) subscale mean score is 2.58±0.91, Goal Setting (items 7-11) subscale mean score is 2.59±0.77, Problem Solving (items 12-15) subscale mean score is 2.58±0.75, Monitoring\Coordination (items 16-20) subscale mean score is 2.59±0.77 and total scale mean score is 2.59±0.77. items) sub-dimension was 2.58±0.75, the mean of the Monitoring\Coordination (items 16-20) sub-dimension was 2.59±0.77 and the mean of the total scale score was 2.59±0.62, the lowest score was 1.24 and the highest score was 4.36.

Univariate analysis

The qualitative indicator

Total (Turkish PACIC) scale and subscale scores were analyzed with independent variables using univariate analysis. The PACIC scores of diabetics were statistically significantly higher those living in urban areas than those living in rural areas ($p<0.001$), those under 45 years of age than those aged 45 and over ($p<0.001$), those male than those female ($p=0.043$), those with higher education than those lower educated ($p<0.001$), those with good perceived income those with poor perceived income ($p<0.001$), those had a family history of diabetes than those had not ($p=0.012$). The findings are shown in table 2.

Table 1. Distribution of Socio-demographic and Chronic Disease Management Skills of Patients with Type 2 Diabetes.

Variables		N	%
PCC Region*	Urban	285	56.4
	Semi-urban	156	30.9
	Rural	64	12.7
Age	45 ≤	436	86.3
Gender	Female	332	65.7
Educational Status	High school & higher	88	17.4
Diabetes diagnosis time	≤ 9 years	324	64.2
Diabetes treatment method	Diet and OAD Drug	365	72.3
Diabetes treatment satisfaction	Good and higher	343	67.9
Using medication regularly	Good and higher	192	38.0
Self-monitoring blood glucose	+	351	69.5
Flu vaccination	Regular (once per 1 year)	70	13.9
Pneumonia vaccination	Regular (once per 5 year)	35	6.9
Hospitalization or emergency	+ (last 6 months)	75	14.8
Low blood glucose (less than 50 mg/lt)	+ (last 6 months)	80	17.6
High blood glucose (over 250 mg/dl)	+ (last 6 months)	212	42.0
Diabetes complications	Hypertension	245	48.5
	Loss of sensation in the feet	149	29.5
	Retinopathy	139	27.5
	Cataract	95	18.8
	Heart Disease	61	12.1
	Wound in the feet	49	9.7
	Renal Failure	12	2.4
	Foot or finger amputation	6	1.2
Diabetes education	Never	82	16.2
	Once when diagnosed	180	35.6
HbA1c (n:287); M±Sd: 6.9±1.7	<7,00 mg/dl	177	61.7
FBG (n:392); M±Sd: 144.5±59.1	70 – 120 mg/dl	162	41.3
TG (n:381); M±Sd: 176.5±115.3	<149 mg/dl	182	47.8
LDL (n:366); M±Sd: 116.8±41.3	<99 mg/dl	126	34.4
SBP (n:374); M±Sd: 132.6±19.3	≤139 mmHg	244	65.2
DBP (n:374); M±Sd: 81.4±11.8	≤89 mmHg	249	66.6
Cholesterol (n:380); M±Sd: 195.3±47.0	≤199 mg/dl	225	59.2
Microalbuminuria (n:16); M±Sd: 63.9±128.8	≤29 mg/day	7	43.8
ECG (n:413)	≤1 year	322	78.0
Fundoscopic examination (n:362)	≤1 year	295	81.5
Glucose urine test (n:396)	≤ 6 months	269	67.9
Ketones in urine test(n:289)	≤ 6 months	195	67.5
Microalbuminuria test (n:88)	≤1 year	77	87.5
Neurological examination (n:144)	≤1 year	108	75.0

N: numbers, %: Percent, M±Sd: Mean±standard Deviation, *PCC: Primary Care Center, OAD: oral antidiabetic drug, HbA1c: glycated hemoglobin, FBG: fasting blood glucose, TG: Triglyceride, LDL: low-density lipoprotein, SBP: Systolic blood pressure, DBP: diastolic blood pressure, ECG: electrocardiogram

Table 2. The relationship between the sociodemographic characteristics of the participants and the Turkish PACIC scale scores.

Variables	Patient Activation Mean±SD	Decision Support Mean±SD	Goal Setting Mean±SD	Problem Solving Mean±SD	Follow-up Mean±SD	Total Scale Mean±SD
PCC Region*						
Urban	2.75±0.88†	2.69±0.90†	2.69±0.76†	2.65±0.78†	2.72±0.81†	2.70±0.63†
Semi-urban	2.42±0.91	2.45±0.95	2.48±0.80	2.51±0.74	2.45±0.73	2.46±0.60
Rural	2.41±0.78	2.39±0.88	2.48±0.74	2.48±0.69	2.38±0.65	2.43±0.54
P	**0.000**	**0.006**	**0.009**	0.104	**0.000**	**0.000**
Age						
<45	2.93±0.82	2.92±0.89	3.00±0.73	2.92±0.78	2.85±0.67	2.92±0.57
≥45	2.55±0.89	2.53±0.90	2.54±.076	2.53±0.73	2.55±0.78	2.54±0.61
P	**0.001**	**0.001**	**0.000**	**0.000**	**0.004**	**0.000**
Gender						
Male	2.71±0.82	2.71±0.89	2.65±0.76	2.65±0.72	2.63±0.79	2.67±0.61
Female	2.55±0.92	2.52±0.93	2.57±0.79	2.55±0.77	2.58±0.77	2.55±0.63
P	**0.045**	**0.028**	0.260	0.174	0.458	**0.043**
Educational Status*						
Un-educated	2.26±0.85	2.25±0.81	2.35±0.74	2.37±0.72	2.28±0.72	2.30±0.55
Primary & Middle school	2.65±0.85	2.65±0.92	2.61±0.74	2.58±0.69	2.64±0.75	2.62±0.57
High school and above	3.00±0.91†	2.89±0.90†	2.95±0.83†	2.94±0.87†	2.94±0.79†	2.95±0.67†
P	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
Perceived Income*						
Less	2.47±0.87	2.52±0.92	2.48±0.77	2.44±0.76†	2.39±0.76	2.46±0.61
Equal	2.64±0.88	2.58±0.90	2.64±0.78	2.67±0.74	2.70±0.77	2.65±0.62
Much	3.03±0.93†	2.91±0.98†	2.96±0.63†	2.76±0.69	2.93±0.65	2.92±0.55†
P	**0.001**	**0.046**	**0.001**	**0.001**	**0.000**	**0.000**
Perception of educational competency*						
Bad	2.35±0.90	2.35±0.81	2.34±0.74	2.37±0.71	2.26±0.69	2.33±0.56
Moderate	2.57±0.85	2.56±0.91	2.65±0.74	2.58±0.74	2.68±0.79	2.61±0.60
Good	2.95±0.83†	2.87±0.96†	2.84±0.78†	2.84±0.75†	2.88±0.71†	2.88±0.59†
P	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
Current perception of health						
Bad	2.40±0.88	2.41±0.99	2.37±0.69	2.34±0.72	2.47±0.81	2.40±0.61
Moderate	2.52±0.84	2.57±0.86	2.54±0.78	2.49±0.76	2.55±0.72	2.53±0.58
Good	2.69±0.91	2.62±0.93	2.68±0.78	2.68±0.74	2.64±0.80	2.66±0.64
P	**0.029**	0.278	**0.014**	**0.002**	0.210	**0.005**
Presence of Physician						
+(a)	2.67±0.91†	2.64±0.93†	2.64±0.78†	2.63±0.77†	2.66±0.78†	2.65±0.63†
- (b)	2.18±0.64	2.17±0.68	2.23±0.61	2.23±0.56	2.14±0.56	2.19±0.41
Not Sure(c)	2.23±0.64	2.25±0.70	2.41±0.75	2.38±0.62	2.17±0.67	2.29±0.45
P	**0.000** a>(b=c) *	**0.001** a>(b=c) *	**0.003** a>(b=c) *	**0.003** a>(b=c) *	**0.000** a>(b=c) *	**0.000** a>(b=c) *
Family History of Diabetes						
+	2.69±0.90	2.64±0.91	2.65±0.81	2.64±0.73	2.62±0.77	2.65±0.61
-	2.47±0.86	2.50±0.93	2.52±0.73	2.50±0.78	2.55±0.79	2.51±0.63
P	**0.006**	0.089	0.072	**0.034**	0.301	**0.012**

PCC: Primary Care Center; *One-way analysis of variance; †Post hoc Tukey b (the group that makes the difference)

The PACIC scores of diabetics were statistically significantly higher those who self-measure glucose at home compared to those who did not (p=0.005), those who did not visited to the emergency room in the last 6 months compared to those who have (p=0.002), those who did not experienced an episode of hypoglycemia (p=0.012) or hyperglycemia (p=0.001) in the last 6 months compared to those who have (p=0.001), those who have regular flu (p=0.001) or pneumonia vaccination (p=0.003) than those who did not have regular vaccinations, those who were satisfied with their diabetes treatment (p=0.001) than those who were not satisfied with their treatment, those who knew the symptoms associated with diabetes than those who did not (p=0.005). The findings are shown in table 3.

Total (Turkish PACIC Scale) scores of those whose HbA1c value, fasting and postprandial blood glucose levels, and blood lipid (TG, HDL, LDL and cholesterol) values were under control and who have routine health checks such as fundus examination, neurological examination, glucose and ketone examination in the urine on time, was found to be statistically significantly higher than those with poor values and those who did not have regular follow-ups (p<0.005). The relationship between total PACIC score and other metabolic control indicators such as routine follow-up and laboratory parameters of diabetic patients are shown in table 4.

The quantitative indicator

The HbA1c measurement was used to assess the patients' glycemic management who have diabetes. The HbA1c value was cut from <7.00 mg/dl and the metabolic control target was categorized as binary. According to the test results, the significance relationship between the two variables was evaluated by Chi-Square test.HbA1c levels in diabetic patients were found to be statistically significant in terms of glycemic control; these included those diagnosed in year ≤9 (p=0.003), those receiving diet-only treatment (p=0.003), those who were physically active (p=0.012), those who checked their blood glucose levels self-monitoring (p=0.012), those who received a routine flu vaccination (p=0.044), those who did not experience an episode of hyperglycemia (p=0.027), and those without peripheral neuropathy (p=0.002).

Table 3. The relationship between the disease management characteristics of patients and the Turkish PACIC scale scores.

Variables	Patient Activation Mean±SD	Decision Support Mean±SD	Goal Setting Mean±SD	Problem Solving Mean±SD	Follow-up Mean±SD	Total Scale Mean±SD
Self-monitoring at home (n:351)						
+	2.68±0.90	2.62±0.93	2.62±0.78	2.64±0.77	2.66±0.76	2.64±0.64
-	2.43±0.85	2.49±0.89	2.54±0.76	2.46±0.71	2.44±0.80	2.47±0.56
P	**0.005**	0.127	0.301	**0.017**	**0.004**	**0.005**
Emergency admission in the last 6 months						
+ (n: 42)	2.29±0.87	2.37±0.80	2.35±0.79	2.26±0.72	2.26±0.67	2.31±0.53
-	2.63±0.89	2.60±0.92	2.62±0.77	2.61±0.75	2.62±0.78	2.62±0.62
P	**0.019**	0.132	**0.033**	**0.004**	**0.004**	**0.002**
Hypoglycemia in the last 6 months*						
-	2.67±0.91†	2.66±0.92†	2.67±0.79†	2.65±0.78†	2.67±0.78†	2.66±0.62†
+ (n: 89)	2.46±0.79	2.41±0.90	2.42±0.67	2.43±0.62	2.44±0.67	2.43±0.56
-	2.37±0.91	2.28±0.83	2.35±0.77	2.37±0.68	2.26±0.88	2.32±0.60
P	**0.029**	**0.006**	**0.002**	**0.007**	**0.001**	**0.000**
Hyperglycemia in the last 6 months*						
-	2.74±0.86†	2.69±0.96†	2.75±0.77†	2.69±0.77†	2.71±0.79†	2.72±0.62†
+ (n: 212)	2.47±0.89	2.49±0.85	2.45±0.76	2.49±0.75	2.51±0.72	2.48±0.59
-	2.40±1.05	2.29±0.89	2.39±0.76	2.36±0.56	2.24±0.90	2.34±0.64
P	**0.002**	**0.010**	**0.000**	**0.003**	**0.000**	**0.000**
Flu vaccination						
No	2.56±0.90	2.50±0.92	2.55±0.78	2.55±0.76	2.54±0.78	2.54±0.61
Yes(n:117)	2.75±0.84	2.85±0.87	2.77±0.75	2.68±0.72	2.77±0.75	2.77±0.62
P	**0.041**	**0.000**	**0.006**	0.111	**0.005**	**0.001**
Pneumonia vaccination						
No	2.58±0.89	2.56±0.92	2.59±0.79	2.59±0.76	2.55±0.78	2.57±0.62
Yes (n: 35)	2.94±0.88	3.05±0.98	2.87±0.79	2.75±0.78	2.91±0.82	2.90±0.64
P	**0.020**	**0.003**	**0.044**	0.250	**0.010**	**0.003**
Perception of disease management compliance *						
Never-Little	2.41±0.86	2.43±0.92	2.44±0.76	2.55±0.76	2.38±0.73	2.44±0.62
Moderate	2.66±0.89	2.63±0.92	2.60±0.74	2.55±0.75	2.54±0.73	2.59±0.58
Good and higher	2.68±0.90†	2.63±0.90†	2.70±0.81†	2.64±0.76†	2.79±0.81†	2.69±0.64†
P	**0.020**	0.099	**0.011**	0.420	**0.000**	**0.002**
Diabetes treatment satisfaction*						
Never-Little	2.31±0.70	2.33±0.86	2.33±0.66	2.28±0.63	2.30±0.63	2.31±0.50
Moderate	2.53±0.91	2.55±0.90	2.50±0.79	2.45±0.76	2.37±0.71	2.48±0.61
Good and higher	2.67±0.90†	2.63±0.92†	2.67±0.78†	2.67±0.75†	2.71±0.79†	2.67±0.63†
P	**0.021**	0.104	**0.005**	**0.000**	**0.000**	**0.000**
Diabetes Education						
Never	2.28±0.84	2.39±0.91	2.32±0.70	2.41±0.70	2.39±0.76	2.36±0.57
At least once	2.67±0.89	2.62±0.91	2.65±0.78	2.62±0.76	2.63±0.78	2.64±0.62
P	**0.000**	**0.039**	**0.000**	**0.024**	**0.008**	**0.000**
Knowing the symptoms of hypoglycemia						
-	2.40±0.82	2.25±0.88	2.18±0.76	2.33±0.77	2.43±0.79	2.32±0.60
+	2.62±0.90	2.61±0.92	2.63±0.77	2.60±0.75	2.61±0.78	2.61±0.62
P	0.149	**0.022**	**0.000**	**0.030**	0.179	**0.005**
Diabetes related health problems						
- (n:298)	2.97±0.92	2.83±0.92	2.88±0.74	2.81±0.75	2.80±0.73	2.86±0.62
+ (n:207)	2.52±0.87	2.53±0.91	2.54±0.77	2.54±0.75	2.55±0.78	2.53±0.61
P	**0.000**	**0.004**	**0.000**	**0.002**	**0.005**	**0.000**

*One-way analysis of variance; †Post hoc (group that makes the difference): Tukey b

Table 4. The relationship between total Turkish PACIC scale and subscale scores with metabolic control and routine follow-ups

Variables	Patient Activation Mean±SD	Decision Support Mean±SD	Goal Setting Mean±SD	Problem Solving Mean±SD	Follow-up Mean±SD	Total Scale Mean±SD
HbA1c value (mg/dl) (n:287)						
≤ 6.99	2.76±0.92	2.75±0.90	2.70±0.80	2.70±0.80	2.72±0.82	2.73±0.64
≥ 7.00	2.40±0.91	2.38±0.85	2.44±0.70	2.42±0.71	2.49±0.75	2.42±0.56
P	**0.001**	**0.001**	**0.004**	**0.002**	**0.016**	**0.000**
FBG (mg/dl) (n:392)						
70 -120	2.71±0.87	2.81±0.91	2.73±0.76	2.76±0.76	2.75±0.79	2.75±0.61
≥ 121	2.51±0.89	2.43±0.88	2.50±0.74	2.42±0.72	2.51±0.75	2.48±0.58
P	**0.027**	**0.000**	**0.003**	**0.000**	**0.003**	**0.000**
PBG (mg/dl) (n:113)						
≤139	2.97±0.89	2.89±1.18	2.73±0.92	2.87±1.03	3.09±0.96	2.91±0.83
≥140	2.57±0.90	2.57±0.88	2.59±0.65	2.53±0.60	2.57±0.67	2.56±0.51
P	0.065	0.156	0.393	**0.049**	**0.029**	**0.016**
Total Cholesterol / HDL						
≤ 3.99	2.65±0.87	2.77±0.94	2.73±0.79	2.69±0.82	2.76±0.77	2.72±0.64
≥ 4.00	2.58±0.89	2.53±0.88	2.53±0.73	2.51±0.72	2.55±0.78	2.54±0.58
P	0.463	**0.016**	**0.015**	**0.025**	**0.011**	**0.006**
SBP (mmHg) (n:374)						
≤ 139	2.67±0.91	2.63±0.95	2.69±0.83	2.65±0.79	2.67±0.80	2.66±0.66
≥140	2.50±0.76	2.49±0.85	2.44±0.63	2.50±0.73	2.47±0.75	2.48±0.51
P	0.052	0.159	**0.003**	0.068	**0.019**	**0.003**
DBP (mmHg) (n:374)						
≤ 89	2.67±0.89	2.62±0.94	2.69±0.80	2.70±0.79	2.66±0.78	2.67±0.65
≥ 90	2.50±0.79	2.50±0.86	2.44±0.71	2.39±0.68	2.48±0.79	2.46±0.54
P	0.058	0.233	**0.003**	**0.000**	**0.034**	**0.002**
LDL* (mg/dl) (n:366)						
≤ 99	2.72±0.89	2.81±0.96†	2.79±0.79†	2.68±0.83†	2.74±0.85†	2.75±0.67†
100- 129	2.61±0.85	2.53±0.87	2.59±0.74	2.66±0.76	2.71±0.78	2.62±0.56
≥130	2.50±0.88	2.48±0.88	2.41±0.69	2.41±0.64	2.41±0.67	2.44±0.55
P	0.153	**0.008**	**0.000**	**0.009**	**0.001**	**0.000**
Routine Follow ups of diabetic patients						
Fundoscopic examination (n:362)						
≤1 year	2.71±0.91	2.72±0.93	2.63±0.80	2.65±0.77	2.68±0.78	2.68±0.63
>1 year	2.47±0.86	2.39±0.85	2.50±0.75	2.43±0.70	2.46±0.76	2.45±0.60
P	**0.045**	**0.008**	0.233	**0.031**	**0.038**	**0.007**
Glucose analysis in the urine (n:396)						
≤6 months	2.75±0.91	2.69±0.94	2.68±0.79	2.69±0.80	2.70±0.79	2.70±0.66
>6 months	2.50±0.84	2.45±0.87	2.58±0.73	2.49±0.71	2.54±0.74	2.51±0.56
P	**0.010**	**0.015**	0.212	**0.020**	**0.050**	**0.005**
Ketone analysis in the urine (n:289)						
≤6 months	2.76±0.94	2.67±0.98	2.65±0.79	2.68±0.83	2.76±0.81	2.70±0.68
>6 months	2.55±0.79	2.53±0.87	2.65±0.70	2.47±0.66	2.57±0.72	2.55±0.53
P	0.051	0.226	0.933	**0.019**	**0.048**	**0.043**
Neurological examination (n:144)						
≤1 year	2.73±0.91	2.75±0.94	2.69±0.75	2.76±0.81	2.81±0.75	2.75±0.63
>1 year	2.36±0.81	2.46±0.84	2.33±0.75	2.25±0.65	2.46±0.81	2.37±0.53
P	**0.034**	0.108	**0.014**	**0.001**	**0.018**	**0.002**

*One-way analysis of variance; †Post hoc (group that makes the difference): Tukey b HbA1c: glycated hemoglobin, FBG: fasting blood glucose, PBG: postprandial blood glucose, TG: Triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, SBP: Systolic blood pressure, DBP: diastolic blood pressure, ECG: electrocardiogram.

Multiple Linear Regression Analysis Results

The total PACIC score was taken as the dependent variable. Factors such as age, gender, education level, duration of diabetes diagnosis, presence of diabetes-related complications, status of measuring blood glucose at home, status of receiving diabetes education, knowledge of diabetes-related problems, continuous physician follow-up, regular follow-up, flu vaccination, ability to recognize complications and go to the doctor, and the latest HbA1c value were taken into account as independent variables to the model.

When the significance level corresponding to the F value was examined, it was seen that the established model was statistically significant ($F=191.90$; $p<0.05$). In the last model, those who have the ability to make decisions in visited to their physician, have regular follow-ups, are university graduates, and when the t-value and significance levels of the Beta coefficients of HbA1c variables are examined; It appears to have a statistically

significant effect on total PACIC scores ($p<0.05$). It is seen that the change in total PACIC scores was explained by 52.5% of those who had decision-making skills and 19.0% of those who had regular routine follow-ups. The findings are shown in table 5.

Discussion

HbA1c (Quantitative Approach)

Socioeconomic status variables such as age, gender, education, income, occupation, health insurance, and ownership of the house are strong indicators of the development of diabetes complications and diabetes management (13,14). Our study showed same findings in literature that those with poor socioeconomic diabetics were had poor glycemic control, then those with good socioeconomic status. In addition, poor socioeconomic diabetics were less pay attention to checking their laboratory tests, vaccination, access to a physician, compliance diabetes treatment, and screening exams.

In the quantitative examination, which we consider as an indicator of metabolic control in diabetes management, HbA1c data of only 56.8% of type 2 diabetes patients diagnosed in the region were obtained. The mean HbA1c level is 6.9±1.7 mg/dl, and 61.7% of the patients have good metabolic control. The mean time after diagnosis of diabetes is 7.4±6.9 years, and 35.5% of patients have diabetes for ten years or more. According to the duration of diabetes, 50.9% of diabetics for ten years or more have good metabolic control. Metabolic control worsens significantly as time passes after the diagnosis of diabetes. We can interpret this as the lack of self-responsibility of the patients as well as the lack of continuity of service. When a model which consists of blood pressure control, blood lipids levels, and smoking status for the patients that HbA1c levels unknown (43.2%) and calculated for diabetics who meet all 3criteria at the same time and then customized for the whole group, the good metabolic control drops to 40.4%. When metabolic control was evaluated simultaneously for a total of four variables together with the HbA1c value, it was seen that only 22.7% of the patients had good metabolic control.

According to the National Diabetes Statistics 2021 Report prepared by the Centers for Disease Control (CDC) in the USA, 49.4 % of have poor metabolic control and just 18.2% of diabetics was good metabolic control level which were evaluated with HbA1c, blood pressure, cholesterol, and smoking (15).

Table 5. The final model of multiple linear regression analysis results for Turkish PACIC total score

Final model*									
Dependent Variable	**Independent Variable**	**ß**	**t**	**p**	**VIF**	**F**	**Model (p)**	**Adjusted R2**	**DW**
	Constant	1.56	14.46	<0.001					
Total	Decision-making skills	0.375	15.91	<0.001	1.19			52.5	
PACIC	Regular monitoring	0.597	13.68	<0.001	1.16	191.90	<0.001	71.5	1.93
Score	University of Education	0.162	3.38	<0.001	1.02			72.5	
	HbA1c	-0,024	-2.13	0.034	1.04			72.8	

*Stepwise, VIF: (Variance Inflation Factor), DW (Durbin-Watson), F: Overall significance of the model

When HbA1C<7% mg/dl cut-off value of metabolic control is taken as a criterion in other international studies: 50.6% in Spain (15), 54.6% in Italy (16), 18.0% in Bangladesh (17) and 24.1% in Saudi Arabia (18) had adequate glycemic control. The condition of our diabetic patients in our study is better in terms of both the average HbA1c and the rates of patients with metabolic control compared to many international study examples. Some study samples of our country findings were same when compared metabolic control ratios to international examples. For example; 40.2% of diabetics in Turkish Endocrine Metabolism Society (TEMD) study (19), 28.1% of diabetics in Turkey's 5th wave results study (20) and 25% of Prospective Urban Rural Epidemiology (PURE) study (21) had good metabolic control.

Our findings, evaluated HbA1c value for good metabolic control, is better than in many other studies. Diabetes management should be evaluated together with the level of control of risk factors (HbA1c, blood pressures, LDL cholesterol, smoking) that may lead to complications. Only in National Diabetes Statistics 2021 Report (15) provides all four condition and we found same good metabolic control levels. We avoid interpreting results while we were aware of how other studies evaluated good metabolic control.

On the other hand, the level of availability of HbA1c data may affect the validity of quantitative results. When the differences between the sociodemographic variables between the 43.2% group without HbA1c data and the 56.8% group with HbA1c recorded data were examined, it was seen that the group without HbA1c data was statistically significantly older and belonged to the lower socioeconomic strata. Accordingly, it can be assumed that the group with missing HbA1c data has more disadvantaged social class characteristics and, as mentioned in the literature, the group's HbA1c glycemic control is poor. This shows that the level of

good glycemic control we obtained in our study may have been lesser than it was.

PACIC (Qualitative approach)

In our study, the PACIC total score, which was evaluated as indicator of metabolic control, was (2.59). Our total score was found to be similar or better than Aung's study (2.20) (22), Simonsen's study (2.32) (23), Anne's study (2.44) (24) and Aghili's study (2.52) (25). A systematic meta-analysis that used PACIC to evaluate diabetes care, which included 25,942 diabetics from 34 studies in 13 different countries, showed the overall total PACIC score ranged from 1.7 to 4.3 (26). We thought that the cause of the wide range of total PACIC scores might be affected by cultural norms and local languages.

Congruent with some studies; regarding demographic variable, our study showed gender of men, higher education (28), younger patients (29,30) had significantly had higher PACIC score while some other studies showed not significantly results (26,31). Contrary to our study some investigations in which with lower level of education had higher PACIC score (26,30). We thought that diabetics with higher education had better awareness and ability to search for information about their treatment.

In our study showed crucial results on self-management of diabetes care to the health care providers. Higher Turkish PACIC scores were associated with self-care behaviors (self-monitoring blood glucose levels, regular vaccinated, satisfied treatments, treatment compliance, received diabetes education, checked follow up exams, routine physical activity, healthy eating), under control HbA1c, FBG, PBG, blood pressure and LDL cholesterol, and diabetes-related health problems such as applied to the emergency department, hyperglycemia and hypoglycemia attacks.

There were some studies in which the chronic care model was applied that demonstrate significant association between self-care behaviors, laboratory results such as HbA1c and PACIC scores (32,33).

In addition, the intervention study by Piatt et al. (34), the 5-year study by Griffin et al. (35) showed that an increase in PACIC scores, diabetes education, patient participation in goal setting and decision making significantly improvement in HbA1c, LDL cholesterol, blood pressure and also reduced diabetes-related complications. Similarly, to our findings, some studies found positive association between PACIC scores and increasing health literacy and ensuring patient-centered decision-making in diabetes management (36-38). Finally, in multivariate regression analysis showed advanced age, being uneducated, could not reach physician at any time were negatively associated with PACIC scores. We also noticed that only one-third of diabetics were able to reach their glycemic control target. We concluded that the perception of blood glucose control in the Turkish population cannot be in harmony with quantitative assessments, and metabolic control cannot be measured only with patient reporting.

Conclusion

One of the most striking findings was that one in five diabetic patients seen in the family physician information system records did not actually have diabetes. We noticed that family physicians had to enter a preliminary diagnosis to request tests from their patients. It is recommended to ensure the integration of patient records and results in the continuity of primary and secondary health care services in disease management.

In terms of HbA1c, the quantitative metabolic control variable of diabetes, approximately three-fifths are under control. We found that the contribution of primary health care services in the follow-up of diabetes was very limited. About one in seven didn't have a constant physician for diabetes and half of them didn't self-monitor their blood glucose levels. However, we demonstrated that self-monitoring blood glucose is one of the main variables affecting the HbA1c level. There was a statistically significant relation between higher Turkish PACIC scores and social determinants such as younger age, high education, and diabetes education. Besides, diabetics who had higher Turkish PACIC scores had good metabolic control parameters such as HbA1c levels, total cholesterol, and blood pressure.

It is important to note that diabetes care management should not be taken lightly and requires a collaborative effort from both the healthcare team and the patient. A comprehensive approach is necessary to ensure long-term success. Adequate lifestyle modifications, such as improved diet, exercise and regular monitoring of blood glucose levels, are essential for successful diabetes management. Furthermore, access to health services, presence of a regular follow-up physician, medications used and comprehensive diabetes education regarding diabetes self-management is also important in providing effective treatment and preventing further complications. Healthcare providers should also consider the individual's cultural and social aspects when designing patient education programs. Finally, supporting patients' self-management efforts in diabetes management, including training in the choice of treatment method and decision-making skills of the diabetic, will play a facilitating role in providing metabolic control.

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Conflict of interest statement

Authors declare no conflict of interest.

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The Quality of Life in Children with Congenital Heart Disease Who Underwent an Intervention

Konjenital Kalp Hastalığı Tanılı ve Girişim Uygulanmış Olan Çocuklarda Hayat Kalitesi

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Öz

Konjenital kalp hastalıkları çocukların ve ailelerin hayatlarını etkileyen en yaygın kronik çocukluk çağı hastalıklarından birisidir. Çocukların hayat kalitesinin değerlendirilmesi 1980'lerde kullanılmaya başlanmış olup son zamanlarda tedavi seçeneklerinin karşılaştırılmasında ve etkinliklerinin değerlendirilmesinde ve klinik uygulamada yaygın olarak kullanılmaktadır. Çalışmamızda Dr. Behçet Uz Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesi Çocuk Kardiyoloji Biriminde konjenital kalp hastalığı tanılı ve girişim uygulanmış olan 8-16 yaşları arasındaki 52 hastaya yaş grubuna özgü ve sağlıkla ilgili yaşam kalitesi ölçeği olan Konjenital Kalp Hastalıkları Yaşam Kalitesi (ConQol) anketi uygulanmıştır. 8-11 yaş grubu 27 hasta ve 26 sağlıklı kontrolden oluşuyordu. 12-16 yaş grubunda 25 hasta ve 26 sağlıklı kontrol vardı. 8–11 yaş grubunda koşuşturabilme, spor ve egzersiz yapılmasına izin verilmesi ve arkadaşlara ayak uydurabilme sorularında kontrol grubuna göre anlamlı bir fark olduğu saptanmıştır. 12–16 yaş grubunda spor ve egzersiz yapılmasına izin verilmesi, arkadaşlara ayak uydurabilme ve kulübe gitme veya okul dışında aktivitelere katılma sorularında kontrol grubuna göre anlamlı bir fark olduğu saptanmıştır. Konjenital kalp hastalıklı çocuklarda yaşam kalitesi özellikle fiziksel aktivite kısıtlanmasından etkilenmektedir.

Anahtar Kelimeler: Çocuk, ConQol, Konjenital Kalp Hastalığı, Yaşam Kalitesi

Abstract

Congenital heart disease (CHD) is one of the most common chronic pediatric conditions, exerting a substantial impact on the lives of children and families. The assessment of children's quality of life gained prominence in the 1980s and is now widely used in clinical practice for comparing treatment options and evaluating their efficacy. We applied the Congenital Heart Disease Quality of Life (ConQol) questionnaire, age-appropriate and disease-specific, to 52 children aged 8–16 years with CHD who underwent intervention at the Pediatric Cardiology Unit of Dr. Behcet Uz Children's Diseases and Surgery Training and Research Hospital. A control group of 52 healthy individuals without CHD was also included. The 8–11 age group consisted of 27 patients and 26 healthy controls. There were 25 patients and 26 healthy controls in the 12–16 age group. There were significant differences in specific areas such as being able to run about, being allowed to do sports and exercise, and being able to do keep up with friends in 8–11-year-old patient group compared to the control group. The ConQol Index Score was statistically significantly different between 12–16-year-old patient and control groups, about being allowed to do sports and exercise, being able to do keep up with friends, and being able to take part in clubs / do activities outside of school. Our findings underscore the impact of CHD on the quality of life in children with CHD, particularly manifesting in reduced physical activity.

Keywords: Child, ConQol, Congenital Heart Disease, Quality of Life

Introduction

Congenital heart diseases (CHD) are among the most common major congenital anomalies (1). Despite advances in interventional and surgical techniques, CHD is still an important cause of morbidity and mortality in the pediatric age group. Approximately one-third of children with CHD are critically ill in the first year of life, during which these children either die or require an urgent surgical intervention (2).

In general, "quality" refers to a degree of well-being. Quality of life (QoL) is a broader concept that includes personal well-being beyond personal health status. It comprises various components such as life satisfaction, subjective well-being, happiness, functional competence, and social well-being, considering culture, value judgments, an individual's position and aspirations, and reflecting personal responses to diseases as well as the physical, mental, and social effects of daily life that affect the level of personal satisfaction achievable in living conditions (3,4). Therefore, the QoL assessment extends beyond the parameters of health-related measures (5-7). Health-related quality of life (HRQoL) is the patient's subjective perception of their satisfaction with their health, with their subjective perceptions directly tied to the individual's psychosocial well-being. Health-related QoL components were first incorporated into the definition of health in the Constitution of the World Health Organization (WHO) in 1948 (8). In recent years, the HRQoL approach has been widely used in adult and child psychiatry as an approach that examines the psychosocial consequences of physical health problems.

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Health-related Quality-of-life Scales and Their Use

The scales designed to assess QoL quantify an individual's physical, mental, and social well-being

based on the assumption that the individual engages in dynamic interactions with their environment. These QoL scales standardize the concept of QoL, rendering the collected data comparable (5). QoL assessment instruments are divided into two categories: generic and disease-specific scales. While generic QoL scales are superior to disease-specific QoL scales in social norm development studies, a significant drawback is their limited sensitivity to subtle changes. In treatment-specific evaluations, it is recommended to use disease-specific QoL scales instead of generic QoL scales. Conversely, disease-specific QoL scales, frequently chosen for their high sensitivity in obtaining information have a notable disadvantage – they do not address the individual as a whole (9-11).

Quality of Life in Children and Adolescents and Scales Used

The initial investigations into HRQoL in children commenced in the 1980s. Despite their relatively basic nature, these early assessments in children were deemed significant as they played a pioneering role in the development of both generic and disease-specific QoL scales (11).

The evaluation of QoL in children varies from those in adults. According to the literature, only 13% of approximately 20,000 studies related to HRQoL across all fields are focused on children. Awareness of these differences concerning the developmental periods of children is crucial for researchers involved in developing and utilizing QoL scales. In children, the evaluations consider activities such as eating, going to the toilet on their own, bathing, performing small daily tasks, and playing. When evaluating social functioning in adults, areas such as the school environment or friendships are not highly significant, however, in the evaluation of social functioning in children, meeting with friends, playing games with them, and the level of adaptation to school hold considerable importance.

When conducting QoL assessments in children, determining whether objective or subjective evaluations should take precedence is a topic of debate. Despite differing opinions on whether parents or children themselves should perform QoL assessments, the prevailing idea in recent years is that children should assess their QoL by themselves as much as possible (10-12). In situations where a child or an adolescent is too ill or too young to respond to the scale questions or do not want to answer the questions, it is recommended to use parent forms for QoL assessment.

Despite CHD's widespread impact, there is a limited number of studies on the QoL of children with CHD in the world. This study aims to investigate the QoL in children who underwent open-heart surgery or cardiac catheterization for CHD via Congenital Heart Disease Quality-of-Life Questionnaire (ConQol) Scale.

Material and Method

ConQol Scale

The ConQol is a disease-specific QoL measurement tool developed specifically for children and adolescents. It was designed to explore the subjective perception of QoL in children or young people or pinpoint areas where assistance can be provided in clinic settings. Unlike similar scales, ConQol adopts a child-centered approach, deriving from interviews with children and adolescents rather than relying solely on opinions of experts or parents. The questionnaire asks questions about the impact of events rather than just the frequency of events or symptoms because this approach recognizes that an event may occur frequently, but may not necessarily be perceived by the child as affecting their HRQoL.

ConQol has two age-specific versions: one for children aged 8-11 years and another for those aged 12-16 years. The version for 8-11 age group consists of 29 questions, with 13 related to symptoms, 6 to activities, and 10 to relationships. The version for 12-16 age group consists of 35 questions, with 13 relating to symptoms, 7 to activities, 10 to relationships and 5 to controlling and coping with the illness. Recognizing that symptoms reported by children may not always align with their perceived importance, ConQol incorporates a separate scoring for symptoms. ConQol generates 3 scores:

1. A QoL score derived from questions describing the frequency of symptoms experienced by the child in the past week related to activities, relationships and controlling and coping with the illness
2. A descriptive profile detailing the symptoms experienced by the child in the last week
3. A weighed symptom index score summarizing how these symptoms make life difficult for respondents

Participants

This case-control study included a cohort of 52 patients with CHD and 52 healthy volunteers between April 2011 and June 2011. The study was conducted at Pediatric Cardiology Unit of Dr. Behcet Uz Children's Diseases and Surgery Training and Research Hospital. The age-appropriate ConQol scale items were administered to participants. They were allowed to answer the survey questions in a calm environment with no external intervention within an average of 15 minutes.

Convenience sampling was used in the study. Eligible cases who met all of the following inclusion criteria participated in the study:

1. Diagnosis of CHD
2. Males and females, from 8 to 16 years of age
3. Had undergone open-heart surgery or interventional treatment at least 2 months before
4. Did not have any neurological problems preventing communication

5. They were allowed to answer the questions without parental influence

We categorized the patients into two subgroups according to the age-specific version of ConQol questionnaire: 8-11 years old and 12-16 years old groups. The primary aim was to compare ConQol index score and ConQol symptom score between case and control groups. The Standard Effect Size was determined as 0.8 with a 5% Margin of Error (95% confidence interval), 80% Power. With the power analysis performed with G-power, we aimed to include at least 25 patients in both groups.

Ethical Approval

The research related to human use complied with all the relevant national regulations and institutional policies, in accordance the tenets of the Helsinki Declaration. The study was approved by the Clinical Trials Ethics Committee of İzmir Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital (Number: 2012/11). All patients or their legal guardians provided written informed consent.

Statistical Analysis

The Microsoft Excel program that automatically calculates the quality-of-life item (ConQol Index Score) and symptom item (ConQol Symptom Score) was used for scoring. The program calculates the score, with 100 points being the best QoL and 0 points being the worst. The program cannot calculate the score if there are more than 3 unanswered questions.

Median and first quartile (Q1) and third quartile (Q3) value frequency were used for descriptive statistics. The distribution of variables was checked with the Kolmogorov-Simirnov test. The Mann-Whitney U test was used to compare quantitative data. SPSS 28.0 was used for statistical analyses. The statistical significance level was accepted as $p<0.05$ for all tests.

Results

The age-appropriate ConQol questionnaire was administered to 52 patients aged between 8 and 16 years who had undergone surgery or interventional procedures to treat CHD and 52 healthy volunteers aged between 8 and 16 years.

Table 1 and 2 demonstrate that no significant difference was found in ConQol Index Score and Symptom Score between the case patient and control groups in the 8-11 age group (p=0.155 and p=0.581) and 12-16 age group (p=0.055 and p=0.169).

Table 1. ConQol Index Score / Symptom Score in 8-11 years old case and control groups.

	Control Group (n=26)		**Case Group (n=27)**		**p**
	Q1-Q3	Median	Q1-Q3	Median	
Symptom Score	73.3-93.4	82.2	59.4-93.4	83.1	0.581[m]
ConQol Index Score	61.5-82.4	70.7	50.2-75.6	69.1	0.155[m]

[m]Mann-Whitney U test

Table 2. ConQol Index Score / Symptom Score in 12-16 years old case and control groups.

	Control Group (n=26)		**Case Group (n=25)**		**p**
	Q1-Q3	Median	Q1-Q3	Median	
Symptom Score	64.8-93.3	78.2	59.4-93.4	83.1	0.169[m]
ConQol Index Score	64.6-86.3	71.8	55.3-72.6	64.8	0.055[m]

[m]Mann-Whitney U test

The responses by 8-11 age group regarding the activities, as shown in Table 3, indicate that there was a significant difference in being able to run about (p=0.048), being allowed to do sports and exercise (p=0.031) and being able to keep up with friends (p=0.018) between the case and control groups. No significant difference was found in the responses by the 8-11 age group in questions related to the relationships between the patient and control groups. Likewise, there was no significant difference between the patient and control groups in their responses to questions related to symptoms (Table 3).

As shown in Table 4, there was a significant difference in the responses to questions related to symptoms between the 12-16-year-old case and control groups in terms of slowed-down thoughts (p=0.030). There was also another significant difference in the responses to questions related to activities between the 12–16 years old case and control groups in terms of being allowed to do sports and exercise (p=0.001), being able to keep up with friends (p=0.023), and being able to take part in clubs/do activities outside of school (p=0.009). In contrast, responses by the 12-16 age group to questions on relationships showed no significant differences between the case and control groups. Similarly, there was no significant difference between the patient and control groups of 12-16-year-olds in their responses to questions on control over health or body (Table 4).

Discussion

In the 8-11 age group, the age-appropriate ConQol questionnaire was administered to 27 patients and 26 controls and no statistically significant difference was observed between the patient and control groups in terms of ConQol Index Score and Symptom Score. In the 12-16 age group,

the relevant ConQol QoL questionnaire was given to a group of 25 patients and a group of 26 controls, and no significant difference were found between the patient and control groups in the Symptom Score and ConQol Index Score.

A study conducted at the Children's Hospital of Wisconsin assessed the QoL in 21 children aged 8 to 18 years with repaired tetralogy of Fallot (TOF), administering the Pediatric Quality of Life Inventory (PedsQL) to compare with normative data for children considered healthy, chronically ill, and with CHD. The same questionnaire was also administered to the parents of these children. The self-reported HRQoL in the clinically well group of patients with repaired TOF was similar to that in healthy children, although parental scores were lower. The QoL in the patient group was superior to that of the group with chronic diseases. The PedsQL questionnaire assesses physical health, social functioning, emotional functioning, and school functioning. Among these dimensions, only emotional functioning exhibited no significant difference between the patient group and the control group with chronic diseases. In parental scores, the scores were significantly lower in parents of children with repaired TOF compared to the scores of parents of healthy children in all dimensions except emotional functioning (13).

In a study conducted in Poland, the QoL of 67 children aged between 8 and 18 years with mitral valve prolapse was assessed by administering KIDSCREEN-27, a HRQoL questionnaire, to the patient and healthy control groups, and no significant differences were observed in children with mitral valve prolapse compared to healthy children. KIDSCREEN measures five dimensions including physical well-being, psychological well-being, parents and autonomy, peers and social support, and school environment. Of these dimensions, only physical well-being exhibited statistically significant difference in the patient group (14).

A study conducted by Uzark et al. (15) evaluated the QoL in 347 children with cardiovascular disease, primarily consisting of those with CHD, between the ages of 5 and 18 years using PedsQL, and found that the QoL was lower in the patient group. A significant difference was found in the patient group compared to the control group in physical and psychosocial functioning among the dimensions of PedsQL outlined above.

Table 3. Comparison of responses by 8-11 years old case and control groups

Age 8-11	**Control Group (n=26)**		**Case Group (n=27)**		**p**
	Q1-Q3	Median	Q1-Q3	Median	
Standardized Symptom Score	73.3-93.4	82.2	59.4-93.4	83.1	0.581[m]
Standardized ConQol Score	61.5-82.4	70.7	50.2-75.6	69.1	0.155[m]
Symptoms					
Short of breath	0.0-2.0	0.0	0.0-5.0	1.0	0.196[m]
Too tired	1.0-4.0	2.0	0.0-5.0	3.0	0.330[m]
Aches and pains	0.0-4.0	2.0	0.0-5.0	2.0	0.883[m]
Dizzy or faint	0.0-1.0	0.0	0.0-3.0	0.0	0.425[m]
Unable to keep up with schoolwork or homework	0.0-5.0	0.5	0.0-5.0	0.0	0.809[m]
Difficulty concentrating	0.0-3.0	0.5	0.0-2.5	0.0	0.656[m]
Forgetful	0.0-4.0	2.0	0.0-5.0	1.0	0.906[m]
Slowed-down thoughts	0.0-2.0	0.0	0.0-5.0	1.0	0.210[m]
Sad or fed up	0.0-2.0	1.0	0.0-5.0	2.5	0.190[m]
Worried or nervous	0.0-4.0	1.5	0.0-8.0	3.0	0.098[m]
Feeling different to others	0.0-3.0	1.0	0.0-5.0	3.0	0.328[m]
Feel like treated differently to others	0.0-3.3	1.0	0.0-4.0	2.0	0.655[m]
Uncomfortable with looks	0.0-2.0	0.0	0.0-2.0	0.0	0.876[m]
Activities					
Able to run about	0.0-3.0	0.0	0.0-10.0	3.0	***0.048[m]***
Allowed to do sports and exercise	0.0-2.3	0.0	0.0-10.0	4.0	***0.031[m]***
Able to spend time with friends	0.0-3.3	1.0	0.0-3.0	0.0	0.450[m]
Able to keep up with friends	0.0-2.0	0.0	0.0-7.0	3.0	***0.018[m]***
Allowed to do things friends do	0.0-5.0	2.0	0.0-8.5	4.0	0.256[m]
Able to go to clubs/do activities outside of school	0.0-3.5	0.0	0.0-3.0	0.0	0.947[m]
Relationships					
My relationships with my friends were harmonious	0.0-2.0	0.0	0.0-4.5	1.0	0.160[m]
My friends pay attention to me	0.0-3.5	0.0	0.0-2.3	0.0	0.856[m]
Finding it difficult to make friends	0.0-10.0	3.0	0.0-10.0	1.5	0.722[m]
They get unnecessarily worried about me too often.	0.0-10.0	2.5	0.0-10.0	4.0	0.851[m]
They make fun of me, they tease me	1.0-10.0	7.5	2.0-10.0	8.0	0.751[m]
I feel lonely	4.0-10.0	9.0	2.0-10.0	7.0	0.651[m]
I'm allowed to do the things I can do	0.0-5.0	3.0	0.0-5.0	1.0	0.831[m]
I think people understand what I can do	0.0-5.3	0.5	0.0-6.0	3.0	0.350[m]
I think people expect me to do too much	0.0-8.3	3.0	0.8-10.0	6.0	0.155[m]
I can do more than people think	0.0-5.0	1.0	0.0-5.0	3.0	0.391[m]

[m]Mann-Whitney U test

Table 4. Comparison of responses by 12-16 years old case and control groups

Age 12-16	Control Group (n=26)		Case Group (n=25)		p
	Q1-Q3	Median	Q1-Q3	Median	
Standardized Symptom Score	64.8-93.3	78.2	52.9-82.4	73.4	0.169[m]
Standardized ConQol Score	64.6-86.3	71.8	55.3-72.6	64.8	0.055[m]
Symptoms					
Short of breath	0.0-5.0	1.0	0.0-4.5	3.0	0.604[m]
Too tired	1.0-6.0	3.0	1.0-6.5	4.0	0.481[m]
Aches and pains	1.0-6.0	3.0	2.0-5.0	3.0	0.887[m]
Dizzy or faint	0.0-4.3	0.5	0.0-4.5	1.0	0.788[m]
Unable to keep up with schoolwork or homework	0.0-3.0	0.5	0.0-4.8	1.5	0.217[m]
Difficulty concentrating	0.0-5.0	2.0	0.0-7.0	4.0	0.227[m]
Forgetful	0.0-6.3	3.0	0.0-4.5	2.0	0.802[m]
Slowed-down thoughts	0.0-2.3	0.0	0.5-5.0	3.0	***0.030[m]***
Sad or fed up	0.0-5.5	2.0	1.5-6.0	3.0	0.172[m]
Worried or nervous	0.0-5.5	2.0	1.3-6.8	3.0	0.280[m]
Feeling different to others	0.0-5.0	0.0	0.0-7.5	4.0	0.060[m]
Feel like treated differently to others	0.0-4.3	0.0	0.0-6.5	3.0	0.137[m]
Uncomfortable with looks	0.0-3.3	0.0	0.0-4.0	2.0	0.117[m]
Activities					
Able to run about	0.0-5.0	1.5	0.0-6.5	3.0	0.506[m]
Allowed to do sports and exercise	0.0-4.0	0.5	1.0-10.0	6.0	***0.001[m]***
Able to spend time with friends	0.0-5.0	1.0	0.0-5.0	3.0	0.383[m]
Able to keep up with friends	0.0-5.0	1.0	1.0-8.5	5.0	***0.023[m]***
Able to go sightseeing or shopping with my friends	0.0-6.3	1.5	0.5-8.0	3.0	0.306[m]
Allowed to do things friends do	0.0-5.5	2.0	1.0-7.0	3.0	0.463[m]
Able to go to clubs/do activities outside of school	0.0-2.0	0.0	0.3-8.8	4.0	***0.009[m]***
Relationships					
My relationships with my friends were harmonious	0.0-7.0	0.0	0.0-5.0	1.0	0.670[m]
My friends pay attention to me	0.0-5.5	1.0	1.0-6.5	2.0	0.297[m]
Finding it difficult to make friends	5.0-10.0	10.0	3.0-10.0	9.0	0.314[m]
They get unnecessarily worried about me too often.	1.8-10.0	6.0	1.0-6.0	5.0	0.148[m]
They make fun of me, they tease me	6.5-10.0	10.0	4.0-10.0	10.0	0.500[m]
I feel lonely	4.0-10.0	8.5	4.0-10.0	9.0	0.889[m]
I'm allowed to do the things I can do	0.0-5.0	1.5	0.0-6.0	2.0	0.477[m]
I think people expect me to do too much	2.0-9.3	5.0	3.0-9.5	6.0	0.906[m]
I can do more than people think	0.0-6.0	1.5	0.0-6.0	3.0	0.822[m]
I think people understand what I can do	0.0-5.3	3.0	0.0-5.0	3.0	0.795[m]
Control of Disease					
I feel like my body doesn't belong to me	9.8-10.0	10.0	6.5-10.0	10.0	0.332[m]
I feel like my health is out of my control	4.0-10.0	9.0	6.0-10.0	9.0	0.790[m]
I'm tired of talking to people about my health	4.0-10.0	10.0	4.0-9.5	8.0	0.134[m]
I think about my heart	0.0-9.5	3.0	1.0-9.0	4.0	0.561[m]
My life is good	0.0-5.0	2.0	0.0-5.5	1.0	0.628[m]

[m]Mann-Whitney U test

In the three aforementioned studies (13-15), the age ranges were broader than in our study; therefore, the difference in the ConQol Index Score evaluating the QoL between two age groups in our study was not observed in these studies. While the QoL results in two of the three studies (13,14) mentioned above overlap with the QoL results of our 8-11 age group, the results of one study align with the QoL results of our 12-16 age group (15). As children age, their comprehension of the disease and their knowledge about it tend to increase. Therefore, in our study, while the QoL of the 8-11 age group did not appear to be significantly affected, it seems that the QoL of the 12-16 age group was affected.

Regarding questions related to activities, there was a statistically significant difference in the 8-11 age group for being able to run about, allowed to do sports and exercise, and able to keep up with friends. In the 12-16 age group, a statistically significant difference was found in being allowed to do sports and exercise, able to keep up with friends, and allowed to participate in clubs/do activities outside of school. Previous similar studies (16-18) have demonstrated that restrictions in physical activities due to physical conditions or lack of parental permission can significantly impact the QoL in children. Scientific evidence indicates that physical activities should not be restricted even in moderate heart diseases (19).

In another study from Turkey, the effect of psychosocial factors and disease-related variables on QoL of children with CHD was evaluated by Sertçelik et al. (20). They included a total of 80 children, 40 of whom had cyanotic CHD and 40 had acyanotic CHD and their mothers. They evaluated them using the Parental Attitude Research Instrument and the KINDer Lebensqualitätsfragebogen – (KINDL) Quality-of-

Life Questionnaire for Children. They reported that symptoms of CHD affected the psychosocial quality-of-life subscales rather than the physical subscales. However, as observed in our study and other studies, families often adopt an overprotective attitude, leading to a negative impact on QoL in children (19-22).

There was no significant difference in questions related to the relationship between the two groups. However, in studies focusing on more specific patient groups, such as those with cyanosis, cardiac surgery, and manifestation of symptoms in physical appearance, significant differences were observed in questions related to relationships (16,21-23). We did not differentiate patients based on cyanosis status or the type of intervention (cardiac catheterization or open-heart surgery).

No significant difference was found between the patient and control groups in the questions related to control of health/body in the 12-16 age group. In studies conducted in the United Kingdom during the development of ConQol, clinicians gave low scores in the weighted score of the questions related to control of health/body, while children with and without CHD self-reported higher scores in the weight of impact on QoL (24). Other studies assessing the QoL in children with CHD have not focused on assessing health/body control (25-27).

This study had some limitations. Firstly, the study was conducted in a single center, and secondly, had a small study group. In parallel with these limitations, a comparison could not be made between subgroups that had undergone correction with surgical intervention or angiographic intervention, since a sufficient sample size could not be reached.

Conclusion

Physical activity restrictions significantly impact children with CHD, for which overprotective attitudes of families play an important role. It is crucial to educate parents that there should be no limitations on physical activity for these children unless there is a medical necessity during follow-up.

Conflict of interest statement

The authors state no conflict of interest.

Ethics Committee Approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration and has been approved by the local İzmir Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital Ethics Committee (Number: 2012/11).

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