EGE KLİNİKLERİ TIP DERGİSİ
MEDICAL JOURNAL OF AEGEAN CLINICS

Cilt /No: 62 **Sayı**/No: 1 **Nisan** /April 2024

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KLİNİK ÇALIŞMALAR/ CLINICAL TRIALS

EGE KLİNİKLERİ TIP DERGİSİ
THE MEDICAL JOURNAL OF AEGEAN CLINICS

«EGE KLİNİKLERİ TIP DERGİMİZ HAKEMLİ BİR DERGİDİR»

Dergimizin Amacı:
Akademik Çalışmaların Tüm Hekimlere Duyurulması
Dergimizin Kapsamı:
Tüm Klinik Ve Temel Tıp Bilimleri

Sahibi /Owner
İzmir Hastanelerine Yardım ve Bilimsel Araştırmaları Teşvik Derneği Adına
On behalf of the Society of Aid to Hospitals of İzmir and Fosterage of Scientific İnvestigations

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Chairman of the society

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Dökümantasyon ve Tasarım
Documentation and Design
Aslı GİRİT

4 ayda bir olmak üzere yılda 3 sayı yayınlanır.
Dergi basım ayları Nisan, Ağustos ve Aralık' tır.

The periodical is published three times in a year. The printing months are April, August and December

Dergimizin web adresi http://www.egeklinikleritipdergisi.com

Dergimizin Eski Adı: İzmir Atatürk Eğitim Hastanesi Tıp Dergisi' dir. (1963-2012)

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GENEL BİLGİLER

Ege Klinikleri Tıp Dergisi, İzmir Hastanelerine Yardım ve Bilimsel Araştırmaları Teşvik Derneği'nin süreli yayın organıdır. Yılda üç sayı olarak yayımlanır. Basım ayları Nisan, Ağustos ve Aralık'tır. Dergide, tıbbın her dalı ile ilgili prospektif, retrospektif ve deneysel araştırmalar, olgu sunumu, editöre mektuplar 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.

Dergiye gönderilen makale biçimsel esaslara uygun ise, baş editör ve en az yurt içi-yurt dışı iki danışman incelemesinden geçip gerek görüldüğü takdirde istenen değişiklikler yazarlar tarafından yapılıp hakemlerce kabul edildikten sonra yayımlanır.

BİLİMSEL SORUMLULUK

Tüm yazarlar çalışmaya direkt olarak katkıda bulunmalıdır. Yazar olarak tanımlanmış tüm kişiler çalışmayı planlamalı veya gerçekleştirmeli, çalışmanın yazılmasında, gözden geçirilmesinde ve son halin onaylanmasında rol almalıdır. Bilimsel kriterleri karşılayan bir metnin ortaya çıkması tüm yazarların sorumluluğudur.

ETİKSEL SORUMLULUK

İnsan çalışmaları ile ilgili tüm makalelerde 'yazılı onamım' alındığını, çalışmanın Helsinki Deklarasyonu'na

(World Medical Association Declaration of Helsinki http://www.wma.net/en/30/publications/10policies/b3/index.html) göre yapıldığı ve lokal etik komite tarafından onayın alındığını bildiren cümleler mutlaka yer almalıdır.

Etik Kurul Onamlarının kendisi (Etik Kurul Onam Belgesi) yayınla birlikte gönderilmelidir.

Hayvanlar üzerinde yapılan deneyleri bildirirken yazarlar; labaratuvar hayvanlarının bakım ve kullanımı konusunda kurumsal veya ulusal yönergelerin takip edilip edilmediğini mutlaka bildirmelidirler.

Ege Klinikleri Tıp Dergisi yazarların cümlelerinden sorumlu değildir. Makale bir kez kabul edildikten sonra derginin malı olur ve dergiden izinsiz olarak başka bir yerde yayınlanamaz.

İSTATİSTİKSEL DEĞERLENDİRME

Tüm retrospektif, prospektif ve deneysel çalışma makaleleri bioistatiksel olarak değerlendirilmeli ve uygun plan, analiz ve bildirimde bulunmalıdır. p değeri yazı içinde net olarak belirtilmelidir (örn, p=0.014).

YAZIM DİLİ

Derginin resmi dilleri Türkçe ve İngilizce'dir. Türkçe metinlerde Türk Dil Kurumu'nca (www.tdk.gov.tr)www.tdk.gov.tr yayınlanan Türkçe sözlük temel alınmalıdır. Gönderilmiş makalelerdeki tüm yazım ve gramer hataları sunulan verileri değiştirmeksizin editör tarafından düzeltilir. Yazım ve gramer kurallarına metin yazımı yazarların sorumluluğundadır.

TELİF HAKKI BİLDİRİMİ

Telif hakkı devrini bildirmek için kapak mektubunda 'Bu makalenin telif hakkı; çalışma, basım için kabul edilmesi koşuluyla Ege Klinikleri Tıp Dergisi'ne devredilir' şeklinde belirtilmelidir. Makaleler için yazarlara herhangi bir ücret ödenmez.

YAZI TİPLERİ

Derleme: Derlemeler yeni veya tartışmalı alanlara ışık tutar. Dergi editörü derleme yazımı için yazar veya yazarlardan istekte bulunur.

Orijinal makaleler: Orijinal makaleler temel veya klinik çalışmalar veya klinik denemelerin sonuçlarını bildirir". Orijinal makaleler 2500 kelime ve 25 kaynaktan fazla olmamalıdır.

Olgu Sunumları: Dergi, tıbbın her alanındaki belirgin öneme haiz olgu sunumlarını yayınlar. Yazar sayısı 6'yı, kaynak sayısı ise 5'i geçmemelidir.

Editör'e Mektup: Metin 400 kelimeyi geçmemeli ve kaynak sayısı ise en fazla 3 olmalıdır (kaynaklardan biri hakkında değerlendirme yapılan yayın olmalıdır)

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Tüm yazılar elektronik ortamda idhdergi@yahoo.com adresine gönderilmelidir.

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 içermelidir.

Başlık sayfası: Bu sayfada çalışmanın tam ismi ve kısa başlığı (karakter sayısı ve boşluklar toplamı 55'i geçmemelidir) olmalıdır. Katkıda bulunanların adlarını ve çalıştıkları kurumları listeleyin. Yazışmaların yapılacağı yazar (yazışma yazarı) belirtilmelidir. Bu yazar yayının basım sürecinde dergi editörü ile iletişimde bulunacaktır. Öte yandan tüm yazarların ORCID numarası da eklenilmeli, ORCID numarası olmayan yazarlar en kısa zamanda edinmelidir. http://orcid.org adresinden bireysel ORCID için **ücretsiz** kayıt oluşturulabilinir.

Öz ve Anahtar Kelimeler: Özet 250 kelimeyi geçmemelidir. Çalışmanın amacını, yöntemi, bulgu ve sonuçları özetlemelidir. İlaveten 3 adet anahtar kelime alfabetik sırayla verilmelidir.

Giriş: Giriş bölümü kısa ve açık olarak çalışmanın amaçlarını tartışmalı, çalışmanın neden yapıldığına yönelik temel bilgileri içermeli ve hangi hipotezlerin sınandığını bildirmelidir.

Gereç ve yöntemler: Okuyucunun sonuçları yeniden elde edebilmesi için açık ve net olarak yöntem ve gereçleri açıklayın. İlk vurgulamada kullanılan araç ve cihazların model numaralarını, firma ismini ve adresini (şehir, ülke) belirtin. Tüm ölçümleri metrik birim olarak verin. İlaçların jenerik adlarını kullanın.

Bulgular: Sonuçlar mantıklı bir sırayla metin, tablo ve görüntüler kullanılarak sunulmalıdır. Çok önemli gözlemlerin altını çizin veya özetleyin. Tablo ve metinleri tekrarlamayın.

Tartışma: Çalışmanın yeni ve çok önemli yönlerine, sonuçlarına vurgu yapın. Tartışma bölümü çalışmanın en önemli bulgusunu kısa ve net bir şekilde içermeli, gözlemlerin geçerliliği tartışılmalı, aynı veya benzer konulardaki yayınların ışığında bulgular yorumlanmalı ve yapılan çalışmanın olası önemi belirtilmelidir. Yazarlara, çalışmanın esas bulgularını kısa ve özlü bir paragrafla vurgu yapmaları önerilir.

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

Kısaltmalar: Kelime veya söz dizinini ilk geçtiği yerde parantez içinde verilir. Tüm metin boyunca o kısaltma kullanılır.

Tablolar: Metin içinde tablolar ardışık olarak numaralandırılmalıdır. Her bir tabloya bir numara ve başlık yazın. Tablolar fotoğraf veya grafik dosyası olarak gönderilmemelidir.

Kaynaklar: Kaynaklar metin içinde alıntılanma sırasına uygun olarak doğal sayılar kullanılarak numaralandırılmalı ve cümlenin sonunda parantez içinde verilmelidir. " Uniform Requirements for Manuscript Submitted to Biomedical Journals" formatını kullanın. Yazar sayısı altı veya daha az ise hepsini, yedi veya daha fazla ise sadece ilk üç ismi yazın ve 've ark.'ı ilave edin. Dergi isimleri tam olarak verilmelidir. Kaynak ve kısaltılmış dergi adları yazımları Cumulated Index Medicus'a veya aşağıda verilen örneklere uygun olmalıdır.

Dergi makaleleri için örnek

Sigel B, Machi J, Beitler JC, Justin JR. Red cell aggregation as a cause of blood-flow echogenicity. Radiology 1983;148(2):799-802.

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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• Makaleniz tek dosyada olmalıdır. Çalışma tasarımı sırası şu şekilde olmalıdır: Türkçe Başlık, İngilizce Başlık, Türkçe Özet ve Türkçe Anahtar Kelimeler, İngilizce Özet ve İngilizce anahtar kelimeler. Tablo/tablolar ve resim/resimler belirtilen yerde olmalıdır.

• Kapak sayfası ekteki örnekte olduğu gibi tasarlanılmalıdır.

EGE KLİNİKLERİ TIP DERGİSİ

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Yazının Başlığı:

Sorumlu Yazarlar:

Yazarların sorumlulukları:

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Yazar Adı Soyadı **İmza** **Tarih**

Determinant Role of Magnetic Resonanceİmaging in Transition of Clinical Isolated Syndrome to Multiple Sclerosis

Klinik İzole Sendromda Multipl Skleroza Dönüşümde Manyetik Rezonans Görüntülemenin Belirleyici Rolü

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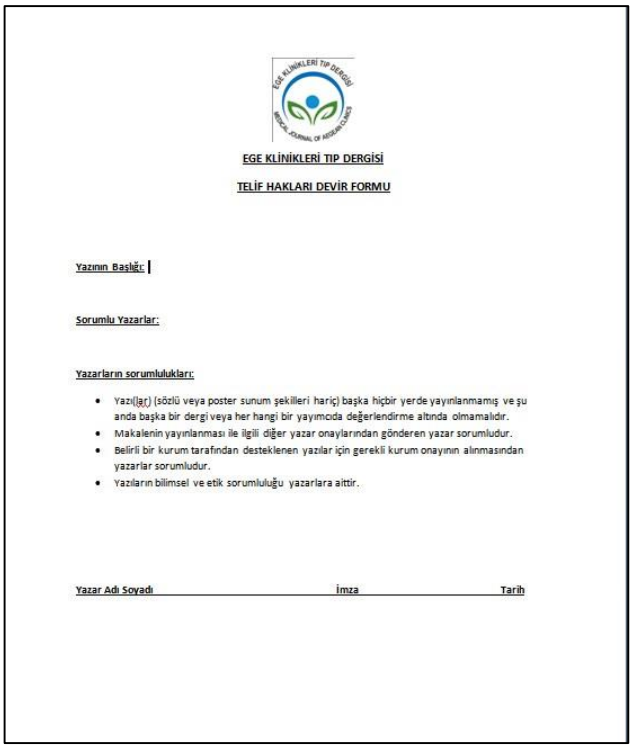

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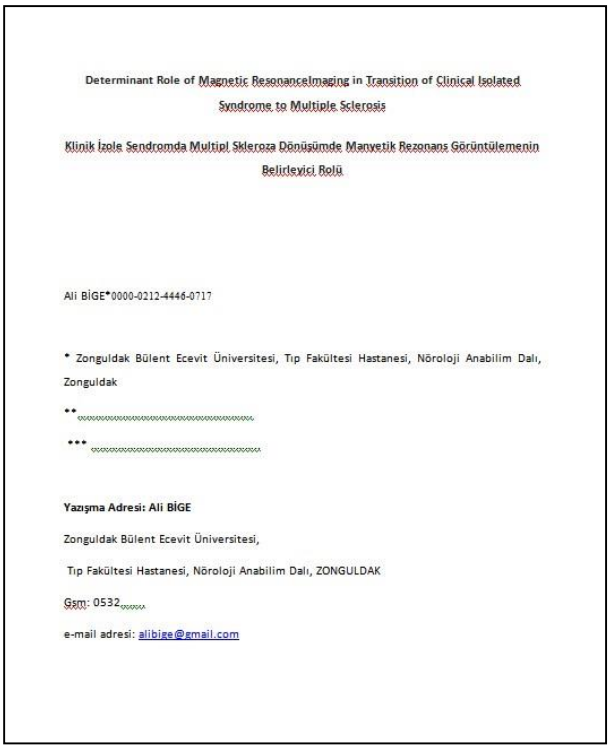

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Analyzing Quality of YouTube Videos about Coronary Angiography

Koroner Anjiyografi ile İlgili YouTube Videolarının Kalitesinin Analizi

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Geliş Tarihi: 31.05.2023
Kabul Tarihi:15.12.2023

Abstract

Introduction: To explore the quality and reliability of YouTube videos about coronary angiography (CA) in the Turkish language.

Methods: The present study was conducted between March 7 and March 15, 2023. The terms 'coronary angiography', 'CAD and angiography', 'cardiac angiography', and 'angiography' were searched on YouTube and ranked by relevance. Characteristics of videos, and Patient Education Materials Assessment Tool (PEMAT), Global Quality Score (GQS), and Modified DISCERN Score of each video were recorded. The videos were divided into two groups according to the upload source: professional and nonprofessional.

Results: In total 92 (68.1%) were uploaded by professional sources and 43 (31.9%) were uploaded by nonprofessional sources. The mean number of views was higher in the professional videos group (p= 0.005). The mean number of likes and dislikes were significantly higher for the professional videos group (p= 0.002, and p= 0.009). In total, 85 (92.4%) videos in the professional video group and 27 (62.8%) videos in the nonprofessional group had PEMAT score above 70% (p= 0.001). Mean GQS was 3.6 in the professional video group and 2.4 in the nonprofessional group (p= 0.001). The modified DISCERN score was statistically significantly higher for the professional video group than the nonprofessional group (p= 0.001). There were significant correlations between modified DISCERN score and number of views, number of likes, and number of comments (p= 0.001, p= 0.006, and p= 0.001). A statistically significant correlation was found between GQS and the number of video views and number of comments (p= 0.001, and p= 0.001).

Conclusion: Professional YouTube videos about CA had significant quality and reliability in terms of modified DISCERN score, GQS, and PEMAT score. Moreover, professional YouTube videos about CA had significantly higher 'view number', 'like number', 'dislike number', and 'comment number' in comparison with nonprofessional videos.

Keywords: coronary angiography, DISCERN score, GQS, PEMAT, YouTube

Öz

Amaç: Koroner anjiyografi (KA) ile ilgili Türkçe YouTube videolarının kalitesini ve güvenilirliğini değerlendirmek.

Yöntem: Bu çalışma 7 Mart - 15 Mart 2023 tarihleri arasında gerçekleştirildi. "Koroner anjiyografi", "KAH ve anjiyografi", "kardiyak anjiyografi" ve "anjiyografi" terimleri YouTube'da arandı ve alaka düzeyine göre sıralandı. Videoların özellikleri ve her bir videonun Hasta Eğitim Materyalleri Değerlendirme Aracı (PEMAT), Küresel Kalite Puanı (GQS) ve DISCERN Puanı kaydedildi. Videolar, yükleme kaynağına göre profesyonel ve profesyonel olmayan olarak iki gruba ayrıldı.

Bulgular: Toplam 92 (%68,1) video profesyonel kaynak tarafından, 43 (%31,9) video profesyonel olmayan kaynaktan yüklendi. Ortalama izlenme sayısı profesyonel videolar grubunda daha yüksekti (p= 0,005). Ortalama beğeni ve beğenmeme sayısı profesyonel videolar grubunda anlamlı olarak daha yüksekti (p= 0,002 ve p= 0,009). Toplamda profesyonel video grubunda 85 (%92,4) video ve profesyonel olmayan grupta 27 (%62,8) videonun PEMAT puanı %70'in üzerindeydi (p= 0,001). Ortalama GQS, profesyonel video grubunda 3,6 ve profesyonel olmayan grupta 2,4 idi (p= 0,001). Profesyonel video grubu için değiştirilmiş DISCERN puanı, profesyonel olmayan gruba göre istatistiksel olarak anlamlı derecede yüksekti (p= 0,001). Değiştirilmiş DISCERN puanı ile izlenme sayısı, beğeni sayısı ve yorum sayısı arasında anlamlı korelasyonlar vardı (p= 0,001, p= 0,006 ve p= 0,001). GQS ile video izlenme sayısı ve yorum sayısı arasında istatistiksel olarak anlamlı bir ilişki bulundu (p= 0,001 ve p= 0,001).

Sonuç: KA ile ilgili profesyonel YouTube videoları, DISCERN puanı, GQS ve PEMAT puanı açısından önemli kalite ve güvenilirliğe sahipti. Ayrıca, KA ile ilgili profesyonel YouTube videoları, profesyonel olmayan videolarla karşılaştırıldığında önemli ölçüde daha yüksek "izlenme sayısı", "beğenme sayısı", "beğenmeme sayısı" ve "yorum sayısı"na sahipti.

Anahtar Kelimeler: koroner anjiyografi, DISCERN skoru, GQS, PEMAT, YouTube

Introduction

Coronary artery disease (CAD) ranks first among all causes of death, and almost one fifth of people who die do so due to CAD and CAD-related complications all around the world (1). Coronary angiography (CA) is the main method to diagnose possible CAD, and CA also gives the cardiologist the chance to manage coronary artery pathologies during the procedure (2). CA is very common in cardiology practice, and previous reports stated that almost 1,000,000 CA cases were performed in North America per year, and 250,000 procedures were done in United Kingdom per year. Additionally, almost 20% of CA cases were performed on patients who were not diagnosed with any CAD previously (3). Due to easy access to information resources, many patients and patient relatives use written and visual resources apart from consulting with the professional health care system, including magazines, television, and social media applications.

YouTube, which was founded in 2005, is the biggest social media platform, and application has almost 3 billion users in over 120 countries. Nowadays, YouTube hosts billions of videos about all subjects, and thousands of items are uploaded to the application every day (4). A study examining the attractiveness of the information source according to its content revealed that visual content was more attractive than audio and written texts (5). In addition, many authors showed the importance of YouTube videos for patients obtaining information about diseases and making decisions on treatment modality.

Ergul evaluated the reliability of YouTube videos about uterine leiomyomas, and the authors demonstrated the low quality of YouTube videos about uterine leiomyomas, despite the high ratings of the videos (6). In another study, Kumar and colleagues found that many YouTube videos about hypertension included misleading information (7).

Although numerous studies investigated YouTube video quality about many medical conditions and surgical interventions, to our knowledge no study has analyzed video quality about CA. In this study, we attempted to explore the quality and reliability of YouTube videos about CA in the Turkish language.

Methods

The present study was conducted between March 7 and March 15, 2023. The terms 'coronary angiography', 'CAD and angiography', 'cardiac angiography', and 'angiography' were searched on YouTube and ranked by relevance. Two experienced cardiologists reviewed the videos and only videos from the last 5 years were analyzed. Re-uploaded videos, videos in different languages, silent videos, self-promotional videos, and videos with off-topic content were excluded. Videos shorter than one minute or longer than 15 minutes were excluded. Ethics committee approval was not obtained because patient data were not used.

The videos were divided into two groups according to the upload source: professional (doctor, nurse, hospital, etc.) and nonprofessional (patient, patient relatives, news, etc.). The number of views, likes and dislikes, number of comments, and video lengths were recorded. The target groups for the videos were grouped as patients or healthcare professionals. Questionnaire scales for video quality assessment were evaluated by two physicians and mean values were noted in case of different results.

Patient Education Materials Assessment Tool (PEMAT), Global Quality Score (GQS), and Modified DISCERN Score

Three different scoring systems were used to assess the quality of the videos. PEMAT consists of a total of 17 items, including 13 items for comprehensibility and 4 items for applicability. Each question is answered as yes (1) and no (0). The final ratings are computed as a percentage of agreed responses for all items. Scores above 70% are indicative of easy comprehensibility and easy applicability (8).

The GQS scale is scored from 1 to 5 points related to video quality and usability. A score of 1 indicates low quality, 3 indicates medium quality and 5 indicates high quality (9).

The modified DISCERN scale was developed to assess the reliability of videos. DISCERN is a valid and reliable short questionnaire to assess the quality of written and visual information about treatment options for a health problem. The highest quality is scored 5 points and the lowest quality is scored 1 point (10).

Statistically analysis

The Statistical Package for the Social Sciences version 26 (SPSS IBM Corp., Armonk, NY, USA) program was used. The Kolmogorov Smirnov test was used to check normal distribution of the variables. The independent student t test was used for comparison of the continuous variables. Categorical variables were compared using the $\chi 2$ test. The correlation of DISCERN score and GQS score with video features was examined with Pearson correlation coefficient. The data were analyzed at 95% confidence level, and p value <0.05 was accepted as statistically significant.

Results

The Flowchart of the videos that met the inclusion criteria is shown in Figure 1.

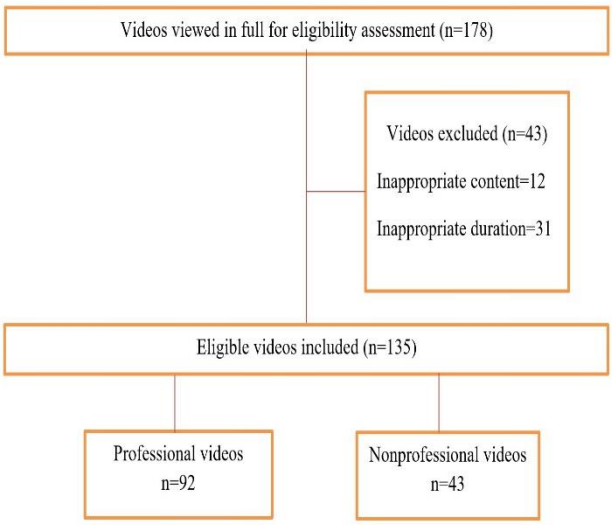

Figure 1: Flowchart of the videos

Comparison of video features between groups according to video sources is presented in Table 1. In total 92 (68.1%) were uploaded by professional sources and 43 (31.9%) were uploaded by nonprofessional sources. The mean number of views was higher in the professional videos group (p= 0.005). The mean video length and duration on YouTube did not differ between the groups (p= 0.882, and p= 0.103). The mean number of likes and dislikes were significantly higher for the professional videos group than the nonprofessional videos group (p= 0.002, and p= 0.009). The mean number of comments made was 66.3 for professional videos and 33.6 for non-professional videos (p= 0.001). In total, 70.7% of professional videos and 83.7% of nonprofessional videos were patient-oriented videos (p= 0.103).

Table 1: Comparison of video properties by upload status

	Professional	**Nonprofessional**	***P value***
Number of videos	92 (68.1%)	43 (31.9%)	
Number of views	5180.6±4005.6	3049.9±2969.5	***0.005***
Video length (min)	5.7±3.5	5.8±3.3	0.882
Duration on YouTube (days)	246.2±216.1	310.2±200.2	0.103
Likes	106.2±115.7	46.7±48.9	***0.002***
Dislikes	11.9±8.4	7.8±7.9	***0.009***
Comments	66.3±81.7	33.6±25.7	***0.001***
Target group, n (%) Patients Healthcare providers	 65 (70.7%) 27 (29.3%)	 36 (83.7%) 7 (16.3%)	0.103

*: mean ± standard deviation

The comparison of the scores for the scales assessing video quality between the groups is presented in Table 2. In total, 85 (92.4%) videos in the professional video group and 27 (62.8%) videos in the nonprofessional group had PEMAT score above 70% (p= 0.001). Mean GQS was 3.6 in the professional video group and 2.4 in the nonprofessional group (p= 0.001). The modified DISCERN score was statistically significantly higher for the professional video group than the nonprofessional group (p= 0.001).

Table 2: Comparison of video quality scores between groups

	Professional	**Nonprofessional**	***P value***
PEMAT score			***0.001***
(≤70%)	7 (7.6%)	16 (37.2%)	
(>70%)	85 (92.4%)	27 (62.8%)	
Global quality score*	3.6±1.0	2.4±0.9	***0.001***
Modified DISCERN score*	3.7±1.1	2.3±1.0	***0.001***

*: mean ± standard deviation, PEMAT: Patient Education Materials Assessment Tool

The correlation between modified DISCERN score and GQS, and video features is described in Table 3. There were significant correlations between modified DISCERN score and number of views, number of likes, and number of comments (p= 0.001, p= 0.006, and p= 0.001, respectively). A statistically significant correlation was found between GQS and the number of video views and number of comments (p= 0.001, and p= 0.001).

Table 3: Correlation of video features with DISCERN and GQS scores.

	Number of views	Like number	Dislike number	Comment number
Modified DISCERN Score				
Correlation coefficient	0.518	0.234	0.133	0.594
p value	0.001	0.006	0.125	0.001
Global Quality Score				
Correlation coefficient	0.356	0.138	0.071	0.407
p value	***0.001***	0.110	0.416	***0.001***

Discussion

Widespread use of social media platforms significantly changed habits of patients and patient relatives when getting information about their symptoms, illness, and treatment methods. Current data revealed that more than 90% of internet users prefer to watch the YouTube platform (11). Thus, we conducted a study to investigate the quality of YouTube videos about CA. Our findings revealed view numbers, numbers of likes and dislikes, and comment numbers were significantly higher for YouTube videos about CA which were uploaded by professional sources. In addition, videos uploaded by professional sources had significantly better quality and reliability in comparison with nonprofessional videos.

To assess YouTube video quality, modified DISCERN and GQS were developed. In a study by Yuksel and Cakmak, which evaluated the quality of YouTube videos about pregnancy and the COVID-19 pandemic, they stated that YouTube videos about COVID-19 and pregnancy had poor quality. In addition, Yuksel and Cakmak showed that videos shared by professional sources had better reliability with regards to DISCERN score (12). Similarly, Ferhatoglu and colleagues found significantly higher DISCERN score for YouTube videos about obesity surgery which were uploaded by professional sources (13). In another study, Kılınc and Sayar used GQS to evaluate the reliability of YouTube videos about dental health, and GQS was significantly higher for YouTube videos shared by professional heath care providers (14). In this study, YouTube videos produced by professional sources had significantly better modified DISCERN score and GQS. Thus, we recommend heath care professionals should provide more social media content for the public to reach more accurate information.

PEMAT is determined to assess the intelligibility of an education source which was developed to inform patients. PEMAT was used to evaluate the understandability of YouTube videos about overactive bladder, and the authors stated that professional videos had better PEMAT score than nonprofessional videos (15). However, Wong and colleagues analyzed the intelligibility of YouTube videos about larynx cancer, and found that YouTube videos had insufficient PEMAT score, even if uploaded by professional health care providers. Additionally, Wong et al. claimed that most YouTube videos about larynx cancer included so much information that it made the videos incomprehensible (16). In the present study, professional videos about CA shared by professional sources were found to be significantly more understandable according to PEMAT score.

Parameters about YouTube videos including 'view number', 'like count', and 'comment count' are crucial to receive more interaction. Sevgili and Baytaoglu analyzed characteristics of YouTube videos about cardiac disease in their study and did not find a significant difference between professional and nonprofessional videos with regards to 'like number' and 'dislike number' (17). Similarly, the study by Yuksel and Cakmak, which evaluated YouTube videos about COVID-19 and pregnancy, stated that 'comment numbers' were similar between professional videos and nonprofessional videos (12). In contrast, Ergul found significantly higher 'comment numbers' for professional YouTube videos about uterine leiomyomas (6). In the present study, we found significantly higher numbers for 'view', 'like', 'dislike', and 'comment', indicating significantly higher interactions for professional YouTube videos about CA.

The present novel study is the first to evaluate YouTube videos about CA, nevertheless, there are a few limitations of our study. First of all, the study included only YouTube videos in the Turkish language. We believe that analyzing more than one language will be confusing during data analysis and when presenting outcomes. Additionally, this study included a certain study period; however, new videos are constantly being uploaded to the YouTube platform. Finally, we searched for four terms; however, inclusion of more words about CAD and CA would ensure a greater number of videos for analysis.

The present study demonstrated that YouTube videos about CA are popular and easy accessible information sources for the public. In addition, professional YouTube videos about CA had significant quality and reliability in terms of modified DISCERN score, GQS, and PEMAT score. Moreover, professional YouTube videos about CA had significantly higher 'view number', 'like number', 'dislike number', and 'comment number' in comparison with nonprofessional videos.

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Ege Klin Tıp Derg 2024;62 (1):6-12

Diagnostic Efficacy of Endobronchial Ultrasound Assisted Transbronchial Needle Aspiration and Conventional Bronchoscopic Transbronchial Needle Aspiration in Isolated Mediastinal and Hilar Lymphadenopathy

İzole Mediastinal ve Hiler Lenfadenopatide Endobronşial Ultrason Yardımlı Transbronşial İğne Aspirasyonu ve Konvansiyonel Bronkoskopik Transbronşial İğne Aspirasyonunun Tanısal Etkinliği

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Geliş Tarihi: 18.10.2023
Kabul Tarihi: 25.01.2024

Abstract

Objectives: Isolated mediastinal and/or hilar lymphadenopathy (IMHL) can be seen in many diseases and sometimes it may be not easy to diagnose. We aimed to determine the effectiveness of conventional transbronchial needle aspiration (c-TBNA) and endobronchial ultrasound (EBUS) guided-TBNA in patients with IMHL.

Materials and Methods: In this retrospective study, c-TBNA and/or EBUS performed patients for IMHL between 2014 and 2019 were screened. The diagnostic efficiency of c-TBNA and EBUS was calculated and compared with each other. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results: 130 patients were included in the study, c-TBNA was performed in 46 (35.4%) patients, EBUS in 77 (59.2%) patients, and c-TBNA + EBUS in 7 (5.4%) patients. The diagnosis was achieved in 22 patients (41,5%) with c-TBNA and 60 patients (71,4%) with EBUS. Diagnostic accuracy of EBUS was higher than 80% in sarcoidosis, anthracosis, and malignancies. EBUS was statistically more diagnostic in granulomatous diseases. However, the diagnostic success of c-TBNA was higher in granulomatous diseases compared to non-granulomatous diseases if it is the only method. EBUS was statistically more diagnostic in all sizes of lymphadenopathies ($p<0.05$). c-TBNA diagnostic accuracy was increasing in lymph nodes >2 cm. Overall sensitivity, specificity, PPV, and NPV of c-TBNA were 44.9%, 100%, 100%, and 12.9%, and of EBUS were 81.08%, 100%, 100%, and 41.67% respectively.

Conclusion: EBUS is a safe and successful diagnostic procedure in the diagnosis of IMHL. In centers without EBUS, c-TBNA can be tried first in patients with lymph nodes larger than 2 cm and suspected granulomatous disease.

Keywords: Bronchoscopy, endobronchial ultrasonography, lymphadenopathy, transbronchial needle aspiration

Öz

Amaç: İzole mediastinal ve/veya hiler lenfadenopati (IMHL) birçok hastalıkta görülebilir ve bazen tanı koymak zor olabilir. Bu çalışmada IMHL'li hastalarda konvansiyonel transbronşiyal iğne aspirasyonu (c-TBİA) ve endobronşiyal ultrason (EBUS) kılavuzluğunda yapılan TBİA'nın etkinliğini belirlemeyi amaçladık.

Gereç ve Yöntemler: Bu retrospektif çalışmada, 2014-2019 yılları arasında IMHL nedeniyle c-TBNA ve/veya EBUS yapılan hastalar taranmıştır. c-TBNA ve EBUS'un tanısal etkinliği hesaplanmış ve birbirleriyle karşılaştırılmıştır. Duyarlılık, özgüllük, pozitif prediktif değer (PPV), negatif prediktif değer (NPV) hesaplanmıştır.

Bulgular: Çalışmaya 130 hasta dahil edilmiş, 46 (%35,4) hastaya c-TBİA, 77 (%59,2) hastaya EBUS, 7 (%5,4) hastaya c-TBİA + EBUS uygulanmıştır. Tanı c-TBİA ile 22 hastada (%41,5), EBUS ile 60 hastada (%71,4) elde edildi. EBUS'un tanısal doğruluğu sarkoidoz, antrakoz ve malignitelerde %80'in üzerindeydi. EBUS granülomatöz hastalıklarda istatistiksel olarak daha tanısaldı. Ancak c-TBİA'nın tanısal başarısı granülomatöz hastalıklarda tek yöntem olması durumunda granülomatöz olmayan hastalıklara kıyasla daha yüksekti. EBUS tüm boyutlardaki lenfadenopatilerde istatistiksel olarak daha tanısaldı ($p<0.05$). c-TBİA tanısal doğruluğu >2 cm lenf nodlarında artmaktaydı. Genel duyarlılık, özgüllük, PPV ve NPV c-TBNA için sırasıyla %44.9, %100, %100 ve %12.9 iken EBUS için %81.08, %100, %100 ve %41.67 idi.

Sonuç: EBUS, IMHL tanısında güvenli ve başarılı bir tanı yöntemidir. EBUS olmayan merkezlerde, 2 cm'den büyük lenf nodları ve granülomatöz hastalık şüphesi olan hastalarda ilk olarak c-TBNA denenebilir.

Anahtar Kelimeler: Bronkoskopi, endobronşial ultrasonografi, lenfadenopati, transbronşiyal iğne aspirasyonu

Introduction

Isolated mediastinal and/or hilar lymphadenopathy (IMHL) is a pathological situation that pulmonologists are frequently encountered and may be difficult to diagnose. Many diseases may be involved in etiology. Tuberculosis, sarcoidosis, lymphoma, and malignant carcinomas are the most common causes. Benign lymph nodes (LN) called 'reactive lymphadenopathy' can be seen in diseases such as chronic heart disease, chronic obstructive pulmonary disease (COPD), bronchiectasis, and pulmonary hypertension. Reactive lymph nodes are seen in 50% of the patients with COPD (1,2). Among the rare causes of IMHL; Castleman disease, histoplasmosis, and primary hypogammaglobulinemia can be sorted (3). Since IMHL can be seen in many diseases, a pathological diagnosis is necessary.

Conventional transbronchial needle aspiration (c-TBNA) is a method that provides blinding LN sampling that can be applied during conventional bronchoscopic procedures. Diagnostic efficiency in lung cancer, mediastinal, and hilar LN sampling is approximately 80% (4). It has the advantage of performing mediastinal sampling in the same session in addition to biopsy in patients with lung cancer. However, its diagnostic efficiency in benign mediastinal and hilar pathologies ranges from 21.4% to 76% (5). The diagnostic success of c-TBNA depends on many factors; location and size of the sampled lymph node, the experience of the pulmonologist performing the procedure, number of samples, presence of rapid onsite evaluation (ROSE), and benign disease status (4).

Endobronchial ultrasonography (EBUS), which allows sampling by providing visualization, has started to be used more frequently by pulmonologists. It is widely used for mediastinal staging and diagnostic purposes in patients without endobronchial lesions in malignant patients. Diagnostic success in mediastinal staging varies between 81-95%. It has a high diagnostic success rate of up to 98.5% in lung cancer. Samples taken from malignant patients have been found sufficient for molecular studies (6). Diagnostic success in benign diseases varies between 73.3% -91% (2,3,5). In a prospective study, the diagnostic efficiency of EBUS was 92%, sensitivity was 92% and negative predictive value was 40% in the diagnosis of isolated mediastinal lymphadenopathy, and it was shown that it prevented going to mediastinoscopy in 87% of the patients (7).

In this study, it was intended to determine the effectiveness of c-TBNA and EBUS in IMHL.

Materials and Methods

It was a retrospective study performed between January 1st, 2014, and October 31st, 2019, in our clinic at an education and research hospital in Turkey. Ethical approval was acquired from the local Ethics Committee (decision no: 2020/4-5, date: 08/05/2020). The study was conducted by the Declaration of Helsinki.

EBUS and conventional bronchoscopy procedures by our clinic during the study period were scanned from the hospital information processing system. Patients who have isolated mediastinal and/or hilar lymphadenopathy without parenchymal lesions were included in to study. The inclusion criteria were: 1) age over 18 years 2) no active malignant disease in the last year 3) having isolated mediastinal and/or hilar lymphadenopathy without parenchymal lesion at thorax computed tomography (CT). The exclusion criteria were: 1) age under 18 years 2) having active malign disease and suspicion of metastasis 3) having parenchymal lesions at thorax CT.

From the hospital database; demographic characteristics, comorbidities, thorax CT and positron emission tomography (PET)-CT imaging findings, conventional bronchoscopy, and EBUS report, complications, and cytopathologic and microbiological reports were collected. The International Association for the Study of Lung Cancer Lymph Node Staging Map was used for the classification of LN stations (8).

Procedure

The EBUS and conventional bronchoscopy procedures were performed using conscious sedation with midazolam and topical lidocaine. Heart rate, blood pressure, and oxygen saturation were monitored in real-time. Conventional bronchoscopic procedures were performed with flexible fiberoptic bronchoscopy (FOB) (BF-1TQ180 Olympus, Tokyo, Japan) and a 22 gauge endoscope biopsy sampling needle (DT-EN-W122) was used to sample lymphadenopathy. The CP-EBUS scope (Fujifilm EB- 530US with VP-3500HD processor) was used to evaluate the mediastinal and hilar regions. The LN to be sampled was determined using EBUS. 22-gauge needle (Echotip*Ultra- ECHO-HD-22-EBUS-O) was advanced to the target LN and the jabbing technique was used. Suction and 12-17 agitations were performed in the lesion per pass. Specimens were sent to cytopathology.

During the bronchoscopic procedures, on-site cytology (ROSE) was not used in our hospital. After the procedure, patients were monitored for adverse event detection and registration before being discharged.

The samples were sent to be smeared for Ziehl-Neelsen staining when a diagnosis of tuberculosis was suspected. Specimens were considered "inadequate" if there were no lymphocytes or abnormal cells. Patients were followed for at least 12 months to confirm the diagnosis of benign diseases. For the diagnosis of reactive lymphadenopathy clinical-radiological stability was sought for at least 12 months.

Statistical Methods

The Statistical Package for Social Sciences (SPSS) Version IBM Statistic 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses of the study data. Categorical variables were presented as a number and a percentage, continuous variables were presented as mean and standard deviation. Chi-square testing and t-tests were used for categorical and continuous factors, respectively. Statistical significance was considered when $p < 0.05$.

Results:

In this study period, 3215 conventional bronchoscopy and 385 EBUS procedures were performed. 130 patients were involved in the study according to inclusion criteria (Figure 1).

Fifty-one (39%) patients were male and 79 (61%) patients were female. Demographics of the patients according to final diagnosis can be seen in Table 1. The mean age was 47.03±12.7 (min-max: 21-81). Fifty (38.5%) patients had comorbidities; 20 (15.4%) had hypertension, nine (7%) had asthma, four (3%) had heart failure and valvular heart disease, three (2.3%) had coronary artery diseases, two (1.5%) had COPD, two (1.5%) had gastroesophageal reflux, nine (%7) had diabetes mellitus (DM), three (2.3%) had thyroid disease, one (0.8%) had polyneuropathy, one (0.8%) had vitiligo, one (0.8%) had ulcerative colitis and eight (6.2%) had malignancy.

64% (n:83) of the patients were symptomatic. Mostly seen symptoms were; cough (28.7%), dyspnea (26.9%), chest pain (15.5%), fatigue (11.6%), and sputum (8.5%), respectively. Thorax CT findings according to the final diagnosis can be seen in Table 1. At Thorax CT, 121 (93%) LNs were seen at 4R, 118 (90.7%) seen at 7, 110 (84.6%) seen at 10 R, 103 (79.2%) seen at 10 L, 59 (45.3%) seen at 4L and 25 (19.4%) seen at 2R. Fewer lymph nodes were observed at other stations.

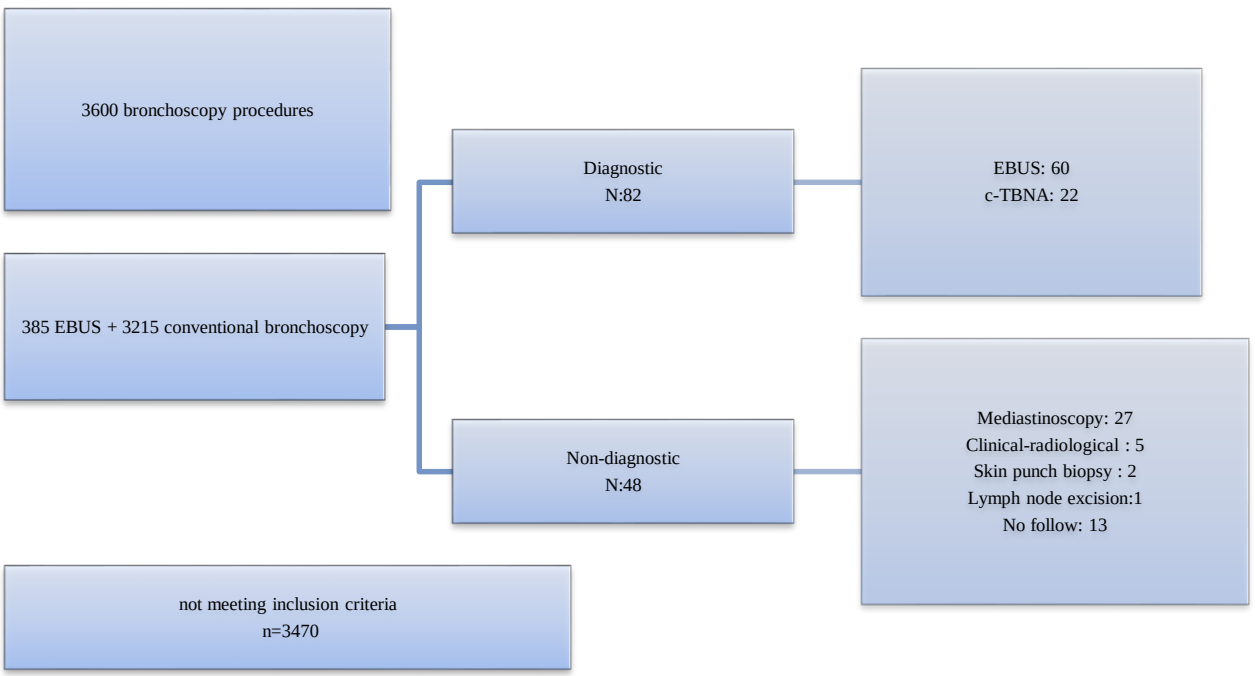

Figure 1: Clinical characteristics of the patients included in the study

Table 1: Demographics and the computed tomography findings of the patients according to the final diagnosis

	Final Diagnosis						
	Sarcoidosis (n:80)	**Tuberculosis (n:8)**	**Reactive LAP* (n:12)**	**Antracosis (n:11)**	**Malignancy (n:6)**	**No diagnosis and follow (n:13)**	**Total (n:130)**
Age (Mean years ±SD)	43.63±11.68	41.38±11.15	50.25±10.99	57.36±12.72	55.67±11.94	55.77±12.04	47±12.7
Sex n(%)							
Female	50 (62.5)	6 (75)	5 (41.7)	4 (36.4)	3 (50)	11 (84.6)	79 (61)
Male	30 (37.5)	2 (25)	7 (58.3)	7 (63.6)	3 (50)	2 (15.4)	51 (39)
Comorbidities n(%)							
Yes							
No	24 (30)	4 (50)	6 (50)	5 (45.5)	4 (67.3)	7 (53.8)	50 (38.5)
	56 (70)	4 (50)	6 (50)	6 (54.5)	2 (33.3)	6 (46.2)	80 (61.5)
Smoking n(%)							
Nonsmoker	67(83.8)	7 (87.5)	5 (41.7)	7 (63.6)	3 (50)	11 (84.6)	100 (76.9)
Smoker	8 (10)	1 (12.5)	4 (33.3)	3 (27.3)	1 (16.6)	2 (15.4)	19 (14.6)
Ex-smoker	5 (6.2)	0	3 (25)	1 (9.1)	2 (33.4)	0	11 (8.5)
LAP at CT n(%)							
Mediastinal(M)	8 (10)	6 (75)	1 (8.3)	3 (27.3)	1 (16.6)	0	19 (14.5)
Hilar(H)	0	0	1 (8.3)	0	1 (16.6)	0	2 (1.5)
M+H	72 (90)	2 (25)	10 (83.3)	8 (72.7)	4 (66.7)	13 (100)	109 (84)
Bilateral	6 (86.2)	6 (75)	7 (58.3)	8 (72.7)	4 (66.7)	13 (100)	107 (82.3)
Unilateral	11 (13.8)	2 (25)	5 (41.7)	3 (27.3)	2 (33.3)	0	23 (17.7)
Size of LAP n(%)							
<2 cm	20 (25)	3 (37.5)	4 (33.3)	8 (72.7)	2 (33.3)	7 (53.8)	44 (33.8)
≥2 cm	60 (75)	5 (62.5)	8 (66.7)	3 (27.3)	4 (66.7)	6 (46.2)	86 (66.2)
Max LAP size (mm median±SD)	24.5±9.1	20±4.7	21.5±7.8	16±5.1	20±5.9	18±8.7	23.3±8.7

*n:number of patients, LAP: Lymphadenopathy, CT: Computed tomography

Seventeen patients (13%) had PET-CT. Ninety-six LNs had FDG uptake. The mean highest Suv-max value was 12.56 ± 4.50 SD (min-max: 4-22). According to LN localization, seven lymph nodes in 2R, four in 2L, one in 3, 15 in 4R, 10 in 4L, five in 5, five in 6, 16 in 7, four in 8, 12 in 10R, and 12 lymph nodes in 10L were detected at PET-CT.

c-TBNA was performed in 46 (35.4%) patients, EBUS in 77 (59.2%) patients, and c-TBNA + EBUS in 7 (5.4%) patients. With c-TBNA, 106 lymph nodes were sampled and 149 lymph nodes were sampled with EBUS. With c-TBNA, in 10 patients (18.9%) one station was sampled, two stations were sampled in 33 patients (62.3%) and three stations were sampled in 10 patients (18.9%). Most sampled stations were; 7 (36 patients), 4R (33 patients), and 10 R (28 patients). With EBUS, one station was sampled in 31 patients (37%), two stations were sampled in 42 patients (50%), three stations were sampled in 10 patients (12%), and in one patient (1%) four stations were sampled.

Mostly sampled stations were; 7 (n=73), 4R (n=35), 10L (n=23) and 10R (n=14). The mean number of samples per station was 1.95 ±0.61 SD in all patients. In c-TBNA, the mean number of samples per station was 2.2±0.5 SD and in EBUS it was 1.8±0.6 SD. There were no major complications. Hypertension was seen in five patients, hemorrhage was seen in five patients and controlled with medical treatment. Ziehl-Neelsen staining was sent in 125 patients and all of them were negative.

c-TBNA was diagnostic in 22 patients (41,5%) and EBUS was diagnostic in 60 patients (71.4%). When patients with no final diagnosis and follow-up are excluded, the diagnostic accuracy of the two procedures according to the final diagnosis can be seen in Table 2.

Table 2: Diagnostic accuracy of c-TBNA and EBUS according to the final diagnosis

	c-TBNA		EBUS	
	Diagnostic	Non-diagnostic	Diagnostic	Non-diagnostic
Sarcoidosis n (%)	17 (48.6)	18 (51.4)	44 (86.3)	7 (13.7)
Tuberculosis n (%)	0	4 (100)	2 (50)	2 (50)
Reactive LAP n (%)	2 (40)	3 (60)	3 (42.9)	4 (57.1)
Antracosis n (%)	2 (100)	0	8 (88.9)	1 (11.1)
Malignancy n (%)	1 (33.3)	2 (66.7)	3 (100)	0
Total n (%)	22 (41.5)	27 (58.5)	60 (71.4)	14 (28.6)

*n:number of patients, c-TBNA: Conventional- transbronchial needle aspiration, EBUS: Endobronchial ultrasound, LAP: Lymphadenopathy

Diagnostic accuracy of EBUS was higher than 80% in sarcoidosis, anthracosis, and malignancies. In benign diseases, c-TBNA was diagnostic in 21 patients (45.6%) and EBUS was diagnostic in 57 patients (80%). Although the number of patients was small in the malignancy group, EBUS was diagnostic in all patients (n=3, 100%) but c-TBNA was diagnostic in 33,3% of malign patients (n=1). In 7 patients who underwent c-TBNA+EBUS, sarcoidosis was diagnosed with EBUS in 5 patients (71.4%) and advanced surgical procedures were prevented. The factors that may affect the diagnostic efficacy of c-TBNA and EBUS are summarized in Table 3. There was no statistical relation between the factors and the diagnostic efficiency of procedures. There was no statistically significant difference in the mean number of samples per LN in both groups. EBUS was performed in 17 patients who had PET-CT. While the mean SUV-max was 13.2 ± 5.2 SD in the diagnostic group with EBUS, the mean SUV-max was 9.5 ± 3.4 SD in the non-diagnostic group and the difference was not statistically significant.

Table 3: The factors that may affect the diagnostic accuracy of c-TBNA and EBUS

	c-TBNA diagnostic	c-TBNA non-diagnostic	P-value	EBUS diagnostic	EBUS non-diagnostic	P-value
Age, year ±SD	43.8 ±12.8	45.9 ±12.6	.559	47.55 ±12.42	48.04 ±13.57	0.874
Sex n (%) Male Female	9 (40.9) 13 (59.1)	13 (41.9) 18 (58.1)	0.942	24 (40) 36 (60)	7 (29) 17 (71)	0.359
Comorbidities n(%) Yes No	4 (18) 18 (82)	11 (36) 20 (64)	0.175	28 (47) 32 (53)	9 (38) 15 (62)	0.449
Symptom n (%) Yes No	16 (72.7) 6 (27.3)	19 (61.3) 12 (38.7)	0.390	37 (61.7) 23 (38.3)	15 (62.5) 9 (37.5)	0.945
LN localization at thorax CT n (%) Bilateral Unilateral	17 (77.3) 5 (22.7)	25 (80.6) 6 (19.4)	0.774	51 (85) 9 (15)	21 (87.5) 3 (12.5)	0.765
LN size at thorax CT n (%) <2cm >2cm	5 (22.7) 17 (77.3)	8 (25.8) 23 (74.2)	0.801	24 (40) 36 (60)	8 (33) 16 (67)	0.572

*n:number of patients, c-TBNA: Conventional- transbronchial needle aspiration, EBUS: Endobronchial ultrasound, LAP: Lymphadenopathy, CT: Computed tomography

When compared the diagnostic efficiency of c-TBNA and EBUS, EBUS was statistically effective at diagnosis. For granulomatous diseases, EBUS was statistically more diagnostic. Although there was no statistical significance in the diagnostic efficiency of EBUS in non-granulomatous diseases, there was a higher percentage of diagnostic success compared to C-TBNA. According to LAP size, in all sizes, EBUS was statistically more diagnostic ($p<0.05$). The diagnostic efficiency of both procedures was increased in lymph nodes larger than 2 cm (Table 4). However, when logistic regression analysis was applied, no significant relationship was found between the factors affecting the diagnostic efficiency of both procedures.

Table 4: Comparison of the diagnostic accuracy of c-TBNA and EBUS

	c-TBNA	EBUS-TBNA	P-value
Overall diagnostic rate n (%)	22/53 (41.5)	60/84 (71.4)	**0.001**
Diagnosis n (%)			
Granulomatous (Tbc+Sarcoidosis)	17/39 (43.5)	46/51 (90.1)	<**0.0001**
Nongranulomatous (Reactive,antrakozis,malign)	5/14 (35.7)	14/29 (48.2)	0.653
Size n (%)			
<20 mm	5/13 (38.5)	24/32 (54.5)	**0.037**
≥20 mm	17/40 (42.5)	36/52 (69.2)	**0.018**

*n:number of patients, c-TBNA: Conventional- transbronchial needle aspiration, EBUS: Endobronchial ultrasound

Overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of c-TBNA were 44.9% (95% CI 50.67-59.77), 100% (95% CI 39.76-100.00), 100%, and 12.9% (95% CI 10.32-16.02) respectively. Overall sensitivity, specificity, PPV, and NPV of EBUS were 81.08% (95% CI 70.30-89.25), 100% (95% CI 69.15-100.00), 100% and 41.67% (95% CI 30.83-53.38) respectively.

Discussion

The diagnostic efficiency, sensitivity, and NPV of EBUS were higher than c-TBNA in the diagnosis of IMHL in this study. While EBUS had higher diagnostic rates in all lymph node sizes, the diagnostic efficiency of c-TBNA was higher in lymph nodes ≥2 cm. In Sarcoidosis patients, who constitute an important part of our study, the diagnosis rate was 48.6% with c-TBNA, while this rate was 86.3% with EBUS. No major complications were observed with either procedure. EBUS has been used routinely for years for lung cancer diagnosis and staging. It has been used before mediastinoscopy in staging and entered the guidelines. Its sensitivity in mediastinal staging in malignant diseases is between 90-95% (9,10). The diagnostic efficiency of C-TBNA in mediastinal LNs varies between 30-70% (5). In the literature, there was no clear data on the success of c-TBNA diagnosis in malignant patients within the IMHL group. In the study of Burkett et al., the diagnostic success rate of c-TBNA was found to be 54.3% in the group of which approximately 80% were diagnosed with malignant disease (4). In this study, the diagnostic efficiency of c-TBNA was 33.3% in malignant patients and all malignant patients who underwent EBUS were diagnosed. The low diagnostic success rate with c-TBNA may be due to the low number of malignant patients. The diagnostic efficiency of EBUS in IMHL is as high as 82.7%–92% (11). In the study of Shen et al.(5), the diagnostic efficiency of EBUS in benign LNs was found to be 76.84%. When dividing the diseases into granulomatous and non-granulomatous, the diagnostic efficiency of EBUS was 65.18% in granulomatous diseases and 96.92% in non-granulomatous diseases.

The diagnostic efficiency of EBUS in granulomatous diseases was found to be 83.3% in the study by Caglayan et al.(12). In our study, similar to the literature, the diagnostic efficiency of EBUS was 80% in the benign disease group and 90% in the granulomatous disease group. The diagnostic efficiency of c-TBNA in the diagnosis of benign mediastinal LNs was found to be 61.1% in the study of Shen et al (5). In the study of Öztürk et al., the diagnostic success rate with c-TBNA was found to be 71% in all diseases, and in the study by Bonifazi et al., the diagnostic success rate with cTBNA was shown to be 75.3%. However, in both studies, diagnostic success rates for benign diseases were not given and it is not known whether the patients had isolated mediastinal LN (13,14). In our study, the diagnostic efficiency of c-TBNA in the benign disease group was 45.6% and the rate was found to be low compared to the study of Shen et al. Since diagnostic adequacy is compared with many different reasons and no significant factor affecting the diagnosis other than lymph node size has been found, it is possible that the proficiency of the person performing c-TBNA may be effective in these results. In this study, EBUS was found to be a procedure with a higher diagnostic value than c-TBNA in the diagnosis of malignant and benign IMHL. The NPV of EBUS was found to be lower in our study compared to other studies. Although there are studies stating the NPV of EBUS as 33-42.8%, in the study of Santos et al. (2), this rate was found to be 77-97%. In our study, we had 25 patients who could not be diagnosed with EBUS. Since 10 of these patients were not followed up, we did not have information about their outcomes. Our NPV value may be low since these patients were also included in the calculation of NPV.

Although c-TBNA diagnostic efficiency is lower than EBUS, some factors may increase the diagnostic accuracy of c-TBNA. Some studies in the literature are showing that the diagnostic accuracy increases by increasing the number of LNs sampled, increasing the experience of the pulmonologist performing the procedure, and the sampling of LNs with high SUV-max values in PET-CT (13,15). LN sampling from the subcarinal area also increases the success of c-TBNA (16). However, these studies were performed for mediastinal LNs for all diseases. It has been shown in a study that the diagnostic accuracy of c-TBNA is higher in patients with IMHL above 2 cm (5). In our study, the accuracy of c-TBNA was found to be higher in LNs larger than 2 cm and in granulomatous diseases. Since EBUS cannot be performed in every center, we think that c-TBNA can be applied in patients with IMHL who have LNs larger than 2 cm and suspected granulomatous disease.

Study Limitations

The limitations of our study can be summarized as; since it is a retrospective study, the inability to select patient populations has led to an imbalance in the number of patients with different diagnoses. In our study, the number of patients other than sarcoidosis and tuberculosis in the malignant group and the benign group was very small. The procedures have been done by different pulmonologists, although we know they are experienced.

Conclusion

EBUS is a reliable and successful diagnostic method in the diagnosis of IMHL. In centers where there is no access to EBUS, c-TBNA can be tried first in patients with IMHL who have LNs larger than 2 cm and suspected granulomatous disease.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 13-19

Sağlıklı Bireylerde Ön Uyaran Aracılı İnhibisyonun Elektromiyografi ve Elektroensefalografi ile İncelenmesi

Examination Of Prepulse Inhibition in Healthy Individuals Using Electromyography And Electroencephalography

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Geliş Tarihi:15.11.2023
Kabul Tarihi:10.01.2024

Öz

Giriş ve Amaç: Ön uyaran aracılı inhibisyon (ÖUAİ) duyusal-motor kapılama mekanizmasını değerlendirmek için kullanılmaktadır. Bu mekanizma, insanlarda *orbicularis oculi* (*OOc*) kas aktivitesinin elektromiyografi (EMG) ile kaydedilmesiyle değerlendirilir. Beyin bilişsel süreçleri üzerinde ÖUAİ'ni elektroensefalografi (EEG) ile araştıran az sayıda araştırma bulunmaktadır. Bu çalışmada, işitsel uyaranlarla göz kırpma refleksinde ve beyin işitsel uyarılma potansiyellerinde ön uyaran aracılı inhibisyonu araştırmak amaçlanmıştır.

Yöntem ve Gereçler: Çalışmada herhangi bir nöropsikiyatrik hastalığı olmayan, sağlıklı 22 bireyin EEG ve EMG verisi değerlendirildi. S1 (ön uyaransız) ve S2 (ön uyaranlı) işitsel uyaranlar kullanılarak *OOc* kası EMG yanıtları ve 32 kanal EEG aktiviteleri eş zamanlı kaydedildi. Ön uyaranın, EMG latansını nasıl etkilendiği Cumulative Sum (CUSUM) tekniği ile de incelendi. Ayrıca, ön uyaran uygulanmasının P50, N100, P200 ve P300 beyin potansiyellerinin latans ve genlikleri üzerindeki etkisi araştırıldı.

Bulgular: EMG latansının ön uyaran uygulanmasından etkilenmediği fakat EMG genliğinin zayıfladığını gösterdik. P50, N100, P200 ve P300 beyin potansiyellerinin genlik ve latanslarında S1 ve S2 uyaranlarına karşı farklılık izlenmedi.

Sonuç: Bu çalışmada, şiddetli bir ses uyaranından 120 ms önce daha düşük şiddette ses uyaranı uyguladığımızda *OOc* kasından kaydettiğimiz göz kırpma refleksinin literatürle uyumlu olarak inhibisyona uğradığını gösterdik. Bununla birlikte, ön uyaran uygulanmasının beyin elektrik aktivitesinin genlik ve latanslarında bir etkisinin olmadığını gözlemledik. Ön uyaran uygulanmasının oluşturduğu sensori-motor kapılama ile, beyin bilgi işlemleme süreçlerindeki duyusal kapılama süreçlerinin aynı mekanizma ve aynı beyin yapıları ile yürütülmediği söylenebilir.

Anahtar Kelimeler: Ön uyaran aracılı inhibisyon, Elektromiyografi, Elektroensefalografi

Abstract

Introduction and Purpose: Prepulse inhibition of the startle reflex (PPI) is used to assess sensory-motor gating. This mechanism is evaluated in human subjects by recording the electromyography (EMG) of the orbicularıs oculi muscle activity. There are a few studies investigating the effect of PPI on cognitive processes using electroencephalography (EEG). It is aimed to investigate the auditory prepulse inhibition in the eyeblink reflex and brain auditory potentials.

Methods and Materials: EEG and EMG data of 22 healthy individuals without any neuropsychiatric disease were evaluated in the study. EMG responses of *OOc* muscle and 32-channel EEG activities were recorded simultaneously using auditory stimuli S1 (without prepulse) and S2(with prepulse).

How the latency of the EMG response was affected by prepulse was also examined with the Cumulative Sum (CUSUM) technique. Furthermore, the effect of prepulse on the latencies and amplitudes of P50, N100, P200, and P300 brain potentials was also investigated.

Results: We demonstrated that prepulse application did not affect EMG latency, but EMG amplitude was weakened. No differences were observed in the amplitudes and latencies of P50, N100, P200, and P300 brain potentials against S1 and S2 stimuli.

Conclusion: In this work, we demonstrated that consistent with previous research, the blink reflex we recorded from the OOc muscle was reduced when a lower-intensity auditory stimulus was administered 120 ms before a loud auditory stimulus. Nevertheless, we found that the amplitude and latency of brain electrical activity were unaffected by the prepulse treatment. It might be claimed that different brain structures and mechanisms are involved in the sensorimotor gating induced by prepulse application and the sensory gating processes in brain information processing.

Keywords: Prepulse Inhibition, Electromyography, Electroencephalography

Giriş

İrkilme yaratan yüksek şiddetli bir uyarandan hemen önce daha düşük şiddetli bir uyaran uygulandığında, irkilme refleksi zayıflamaktadır (1-3). Bu olgu, ön uyaran aracılı inhibisyon (ÖUAİ) olarak adlandırılmaktadır ve duyusal-motor kapılama adı verilen bir mekanizmayı değerlendirmek için kullanılmaktadır (4, 5). Duyusal-motor kapılama, kişinin ilgisiz bilgilerden ilgili olanları filtrelediği süreçtir (6) ve birçok nöropsikiyatrik hastalıkta bozulduğu bilinmektedir (3, 4). Bu süreç insanlarda, yaygın olarak yüksek şiddetli işitsel uyaranlarla ortaya çıkan göz kırpma refleksinin elektromiyografi (EMG) kullanılarak *orbicularis oculi* (OOc) kas aktivitesinin kaydı ile değerlendirilmektedir. ÖUAİ yanıtları yaklaşık olarak uyarandan sonra 20-180 ms aralığında ortaya çıkan maksimum EMG genliği ve bu genliğin ortaya çıktığı latans değerleri ölçülerek değerlendirilmektedir (6). Bu araştırmada refleksin başlangıç ve bitiş süreleri hakkında güvenilir bilgi veren kümülatif toplam (Cumulative Sum - CUSUM) yöntemi kullanılmıştır (7).

Motor yanıtlarda olduğu gibi ön uyaran uygulanması, beyin bilgi işlemleme süreçlerinde de bir inhibisyon oluşturabilir ve bu süreçler elektroensefalografi (EEG) ile kaydedilerek izlenebilir. İrkilmeyi ortaya çıkarmak ve EMG aracılığıyla ÖUAİ'yi ölçmek için gerekli olan şiddetli uyarının, EEG sinyalini bozan kas artefaktları (OOc ve diğer yüz kaslarının aktivitesi) oluşturması, ÖUAİ'nin ortaya çıkardığı beyin elektrik yanıtlarının değerlendirmesini zorlaştırmaktadır. Bu araştırmada, işitsel ÖUAİ (İÖUAİ) uyaranları sağlıklı bireylere uygulandığında eş zamanlı olarak EMG ve EEG kayıtları alınarak motor ve beyin bilgi işlemleme süreçlerindeki yanıtlar incelenmiştir. EEG ile kaydedilen P50, N100 ve P200 gibi işitsel uyarılma potansiyellerinin (İUP) latans ve genliklerinde de ÖUAİ ölçüleceği öngörülmüştür. Ayrıca, İÖUAİ uyaran deseni ile kaydedilen ortalama EMG yanıtlarındaki refleks latansını ve süresini CUSUM tekniği ile hesaplayarak geleneksel yönteme göre daha farklı ve daha objektif bilgiler elde edileceği öngörülmüştür.

Materyal Metod

Bu araştırma için İzmir Kâtip Çelebi Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan 02.09.2021 tarihli ve 74 numaralı onay alınmıştır.

Katılımcılar

Çalışmaya, nörolojik ve psikiyatrik bozukluğu olmayan, yaşları 20-35 (yaş ort. ±std.=30±4,5) arasında, nikotin kullanmayan (sigara, tütün, nikotin bandı kullanmayan vb.), işitme ile ilgili herhangi bir rahatsızlığı olmayan sağlıklı erişkin bireyler dahil edildi. Katılımcılar, araştırma hakkında bilgilendirilmişler ve gönüllü onam formunu imzalamışlardır. Çalışmamızda toplam 30 bireyden (17 kadın) kayıt alındı. Kayıt esnasında çok fazla spontan göz kırpması, kas artefaktları vb. gürültüler nedeniyle EEG sinyalleri bozulan 8 bireyin verisi analizlere dahil edilmedi. Yaş ortalaması 30±4,6 olan 22 kişinin (12 kadın) verisi analiz edilmiştir.

Uyaranlar

ÖUAİ uyaran deseninde S1 ve S2 olmak üzere iki tip uyaran bulunuyordu. Beyaz gürültüden oluşturulmuş uyaranlardan S1; irkilme yaratan yüksek şiddetli uyarandır. S2 ise; S1 uyaranı ve ondan 120 ms önce uygulanan daha düşük şiddetteki ön uyaranı da içeren bir uyaran çiftidir. Ön uyaran; 25 ms süreli ve 87 dB şiddetinde, irkilme uyaranı ise; 30 ms süreli ve 107 dB şiddetinde işitsel uyaranlardır. Toplamda 60 uyaran (30'u S1) rastgele sırayla ve uyaranlar arasındaki süre 7-22 s arasında rastgele değişecek şekilde uygulandı.

Ayrıca, farklı bir kayıt oturumunda 2000 Hz frekanslı 80 dB şiddetinde saf tondan oluşan 30 uyaran 3-7 s rastgele aralıklarla uygulandı ve basit bir ses tonuna karşı ortaya çıkan işitsel uyarılmış potansiyelleri (İUP) kaydedildi.

EMG ve EEG Kayıt ve Analizleri

EEG/EMG kayıt oturumları Faraday kafesli (elektromanyetik gürültüden arındırılmış), sessiz ve loş ışıkla aydınlatılmış bir kayıt odasında gerçekleştirildi. Kayıtlar toplamda bir saat sürdü. EEG/EMG kayıtları ve analizlerinde Brainvision EEG/ERP Sistemi (Brain product GmbH, Germany) kullanıldı. EEG kaydı 10/20 Jasper kayıt sistemine göre yerleştirilmiş 32 elektrotlu bone ile, EMG kaydı sol gözün *orbicularis oculi* (OOc) kasından göz altına yerleştirilmiş yüzeyel elektrotlarla kaydedildi. EEG analizleri Fz, Cz, Pz, Oz, T7, T8 elektrotlarında gerçekleştirildi. Uyaran öncesi ve sonrasında 1000 ms, toplamda iki saniyeden oluşan epoklar oluşturuldu. ÖUAİ uyaran deseninde S1 uyaranı temel alınarak epoklar oluşturulmuştur. Uyaran öncesi 600 ms, uyaran sonrası 0-20 ms ve 400-600 ms zaman dilimlerinde göz kırpmaları bulunan epoklar dışlandı. Uyaran öncesi zaman dilimi temel alınarak bazal hat düzeltmesi yapıldı. EEG analizlerinde her birey için uyaran etrafı ortalama alındı. EMG verisinde ise doğrultma (rektifiye) işlemi sonrasında uyaran etrafı ortalama alındı. EMG verisindeki maksimum genlik değeri, uyaran sonrası 20-180 ms aralığında görülen en yüksek genlik değeri olarak belirlendi (6, 8, 9). Latans değeri ise uyaran sonrası yanıt aktivitesinin başladığı ilk sapma olarak belirlendi.

EMG verisinde CUSUM kullanılması: Uyaran etrafı EMG ortalaması verisinden EMG-CUSUM grafikleri elde edildi ve göz kırpma refleksinin latans ve süreleri belirlendi (10). Uyarandan sonra eksitasyona kadar geçen süre refleksin latansıdır. Eksitasyon bitiş anından refleksin başlangıç anının çıkarılmasıyla refleks süresi elde edildi.

EMG verisinde % ÖUAİ aşağıda verilen formül ile hesaplandı (11).

$$\text{ÖUAİ}\ [\%] = (\text{Genlik}_{\text{uyaran}} - \text{Genlik}_{\text{ön uyaran + uyaran}}) \times 100 \,/\, \text{Genlik}_{\text{uyaran}}$$

İstatistiksel Analizler

İstatistiksel analizlerde SPSS 25.0 programı kullanıldı. Tüm analizlerde yanılma olasılığı 0,05 olarak seçildi, p<0,05 ve güven aralığı %95 olan veri anlamlı kabul edildi.

EMG İstatistik Analizleri

Hem geleneksel yöntemle hesaplanan hem de CUSUM (Kümülatif toplam) ile hesaplanan EMG verisine ait tanımlayıcı istatistikler olarak aritmetik ortalama ve standart sapma belirlendi. Verilerin normal dağılıma uygunluğu Shapiro Wilk testi ile gerçekleştirildi. Grup varyansların homojenliği Levene testi ile değerlendirildi. Sürekli ölçümlerin iki kategorik grup ile karşılaştırılmasında normallik dağılım varsayımı göz önüne alınarak bağımsız örneklem t-test ya da Mann Whitney U testi, ikiden fazla bağımsız grup karşılaştırılmasında ise tek yönlü varyans analizi (ANOVA) ya da Kruskal Wallis H testi kullanıldı. Bağımlı ölçümlerin karşılaştırılmasında Wilcoxon işaret testi kullanıldı.

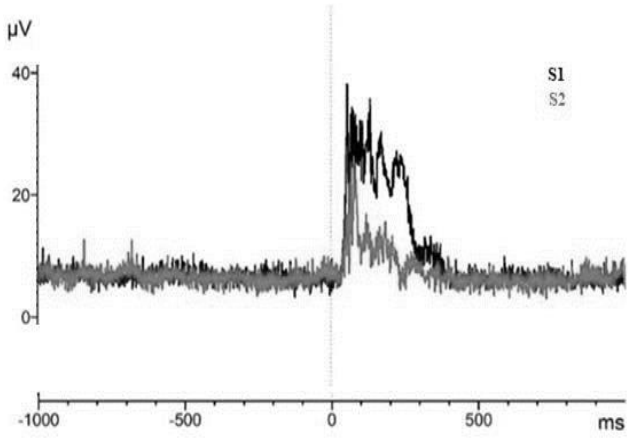
EEG İstatistik Analizleri

Uyaran tipleri İUP, S1, S2'den oluşmaktadır. Birinci faktör *uyaran tipleri* olarak tanımlandı. İkinci faktör ise Fz, Cz, Pz, Oz, T7 ve T8 olmak üzere 6 farklı elektrot yeri olarak sınıflanan e*lektrotlar* ismi ile tanımlandı. P50, N100, P200 ve P300 *uyarılma potansiyelleri* olmak üzere üçüncü faktör olarak tanımlandı. Bu üç faktörün genlik ve latanslar üzerindeki etkisini incelemek için üç yönlü varyans analizi uygulandı. Faktör düzeyleri arasındaki istatistiksel önemliliği belirlemek için Bonferroni testi kullanıldı.

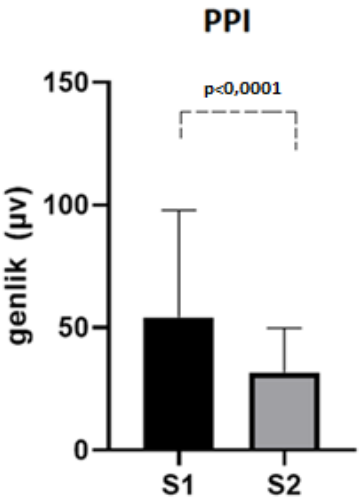
Bulgular

EMG Yanıtları

Şekil 1'de bir gönüllünün S1 ve S2 EMG yanıtları doğrultulmuş ve uyaran etrafında ortalamaları alınarak gösterilmiştir. Uyarandan sonra EMG aktivitesinin ilk görüldüğü an itibari ile belirlenen S1 latansının (medyanı 0,049 s (IQR=0,01)), S2 latansından (medyanı 0,046 s (0,02)) büyüktü (Z=3,32, p=0,001). S1 genliği (medyanı 43,02 µV (IQR=42,93)), S2 genliğinden (29,44 µV (IQR=22,87)) büyüktü (Z=4,11, p=0,001). % ÖUAİ değeri=31,88 elde edilmiştir. Yani S2 yanıtının genliği, S1 yanıtının genliğinden %31,88 daha küçüktü.

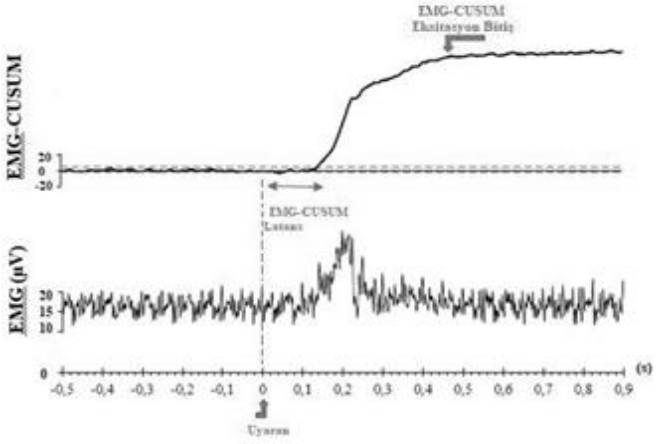


Şekil 1. Bir katılımcının S1 ve S2 uyaranlarına verdiği ortalama EMG yanıtı. S1 uyaranına verilen yanıt siyah renk ve S2 yanıtı gri renk ile gösterilmiştir



Şekil 2. S1 ve S2 uyaranına karşı ortaya çıkan EMG yanıtlarının genlikleri.

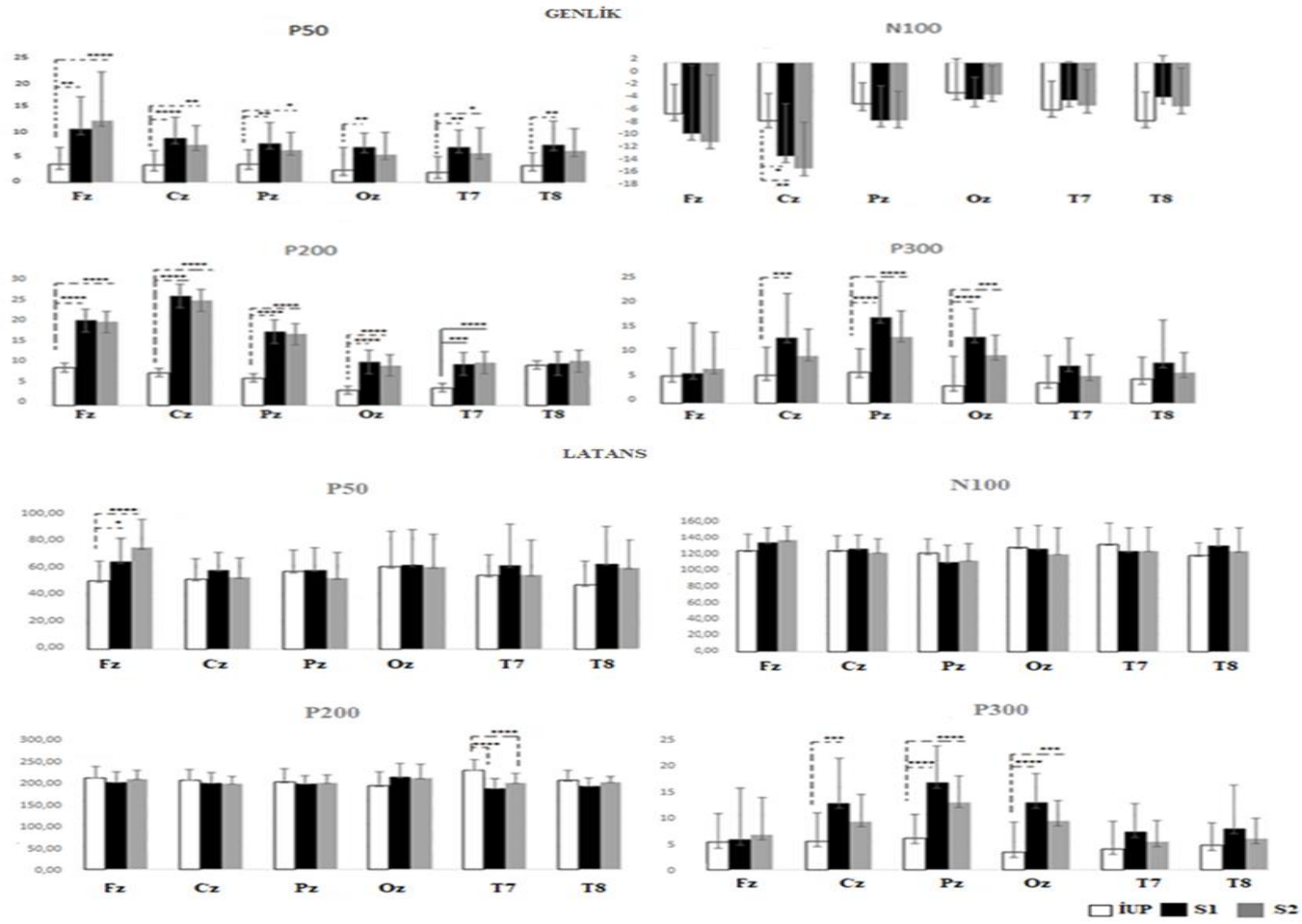
Şekil 3'de bir gönüllüye ait uyaran etrafı ortalama ve bunun CUSUM grafiği izlenmektedir. CUSUM ile elde edilen S1 ve S2 latans değerleri üstteki paragrafta ifade edilen latans değerlerine göre daha uzun ve sırasıyla medyan 0,12 s (0,02), 0,11 s (0,04) olarak bulunmuştur. S1 ve S2 latans değerleri arasında istatistiksel anlamlı fark bulunmamıştır (Z=1,11, p=0,27). S1 uyaranına ait refleks süresinin ortalaması 0,47 s ±0,09, S2 uyaranı için ise 0,49 s ±0,06 hesaplanmıştır. CUSUM ile elde edilen refleks süreleri arasında fark bulunmamıştır (p=0,61).



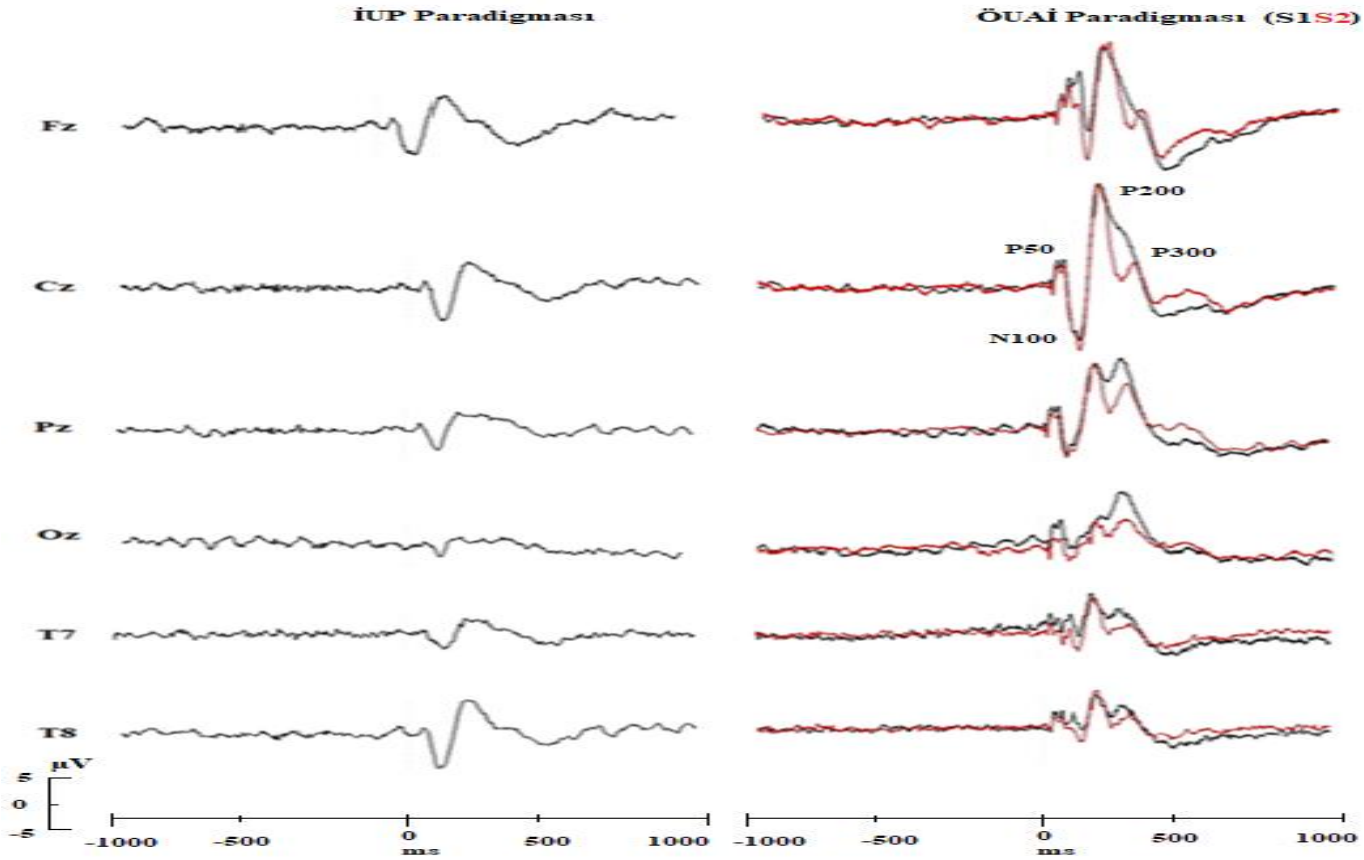
Şekil 3. Üstte EMG yanıtı, altta ise bu yanıtın EMG-CUSUM eksitasyon grafiği sunulmuştur. CUSUM grafiğindeki yatay kesikli çizgiler 'hata kutusunu' göstermektedir.

EEG Yanıtları

Çalışmada Fz, Cz, Pz, Oz, T7 ve T8 elektrotlarından elde edilen sinyaller değerlendirilmiştir. Genel lineer model kullanarak yaptığımız üçlü karşılaştırmalara göre; uyaran tiplerinin ($F(2,1468) = 91,55$, $p=0,001$, $\eta^2=0,11$), elektrotların ($F(5,1468) =10,26$, $p = 0,001$, $\eta^2=0,03$) ve uyarılma potansiyellerinin ($F(3,1468) = 963,03$, $p=0,001$, $\eta^2=0,66$) genlikleri üzerinde istatistiksel anlamlı etkisi bulunmuştur (Uyarlanmış R kare=%71,5). Uyaran tipleri olarak belirlediğimiz İUP, S1 ve S2 arasında yapılan Bonferroni post hoc (ikili) karşılaştırmalarına göre İUP ($\bar{x}$=1,67 μV±0,24) ile S1 ($\bar{x}$=6,04 μV±0,24), İUP ile S2 ($\bar{x}$=5,05 μV±0,23) genlikleri arasında fark bulundu (p=0,0001). S1 ve S2 genlikleri de anlamlı farklılık gösterdi (p=0,008). S1 genliği, S2 ve İUP genliğinden büyüktü. Elektrotlar arasındaki ikili karşılaştırmalarda; Fz genliği ($\bar{x}$=4,84 μV±0,33), T7 ($\bar{x}$=2,77 μV±0,34) (p=0,001) genliğinden ve T8 ($\bar{x}$=3,46 μV±0,33) (p=0,05) genliğinden büyüktü. Cz ($\bar{x}$=5,15 μV±0,32) genliği, T7 ($\bar{x}$=2,77 μV±0,34) (p=0,001) ve T8 ($\bar{x}$=3,46 μV±0,33) (p=0,004) genliklerine göre büyüktü. Pz ($\bar{x}$=5,50 μV±0,33) genliği, Oz ($\bar{x}$=3,79 μV±0,34) (p=0,005), T7 ($\bar{x}$=2,77 μV±0,34) (p=0,001) ve T8 ($\bar{x}$=3,46 μV±0,33) (p=0,001) genliklerine göre büyüktü. Ancak tüm faktörlerin ortak etkisi dikkate alındığında S1-S2 uyaran tipleri arasında hem genlik hem de latans bakımından bir farklılık bulunmadı (Şekil 4).



Şekil 4. İUP ve ÖUAİ paradigması ile ortaya çıkan uyarılma potansiyellerinin (P50, N100, P200 ve P300) genlikleri (üstte) ve latansları (altta).



Şekil 5. İUP ve ÖUAİ (S1ve S2) ile elde edilen EEG potansiyelleri.

Tartışma

Akustik irkilme yanıtı oluşturan yüksek şiddetli S1 uyaranı ve ön uyaran + irkilme uyaranından oluşan S2 uyaranına karşı elde edilen EMG yanıtlarının genlik ve latansları arasında anlamlı farklılık bulundu. S1 uyaranına karşı elde edilen genlik ve latans değerleri, S2 uyaranına karşı elde edilenlerden daha büyüktü. Literatürle uyumlu olarak, ön uyaranın irkilme yanıtının genliğini zayıflattığını gösterdik (12). Diğer polisinaptik refleksler gibi işitsel irkilme yanıtı da tekrarlayan uyaranlara karşı zayıflamaktadır. Aynı uyaran ikinci kez verildiğinde bile habitüasyon gelişebilir (13, 14). Habitüasyonun engellenmesi için ya uyarının uzun zaman aralıkları ile uygulanması ya da farklı ton ve frekanslarda uygulanması gerekir (15, 16). Bizim çalışmamızda uyaranlar arasında (7-22 s) uzun zaman aralıkları uygulandığından, EMG genliğinin zayıflaması habitüasyon nedeniyle değil ön uyaranın oluşturduğu inhibisyon sonucudur. Ön uyaranın varlığı sadece irkilme refleksinin genliğini değiştirmemekte, aynı zamanda latansını da etkilemektedir (17, 18). Latans sürelerinin kısalmasının işlevsel önemi çok iyi anlaşılamamıştır. Genel olarak, irkilme latansının kısalmasının ve irkilme genliğinin inhibisyonunun farklı nöral mekanizmalar tarafından kontrol edilebileceği düşünülmektedir (12).

Yüksek ses uyaranı ile *OOc* kasında ortaya çıkan irkilme polisinaptik olarak meydana gelen beyin sapı yanıtıdır. EMG yanıtı için araştırmamızda hem uyaran etrafı ortalaması hem de EMG verisinden elde edilen CUSUM grafikleri kullanılmıştır (Şekil 3). Ortalama EMG yanıtının başlangıç ve bitişleri net şekilde belirlenip, ölçülememektedir. CUSUM grafiğinde hata kutusu aralığını aşan olay refleks olarak değerlendirilir ve uyarana yanıtın başlangıç anı net belirlenebilir. Böylece uyarana cevap olarak gerçekleşen elektrofizyolojik olayların latansları ve süreleri daha doğru ölçülebilmektedir (10, 19).

S1, S2 ve basit ses uyaranına karşı aynı (P50, N100, P200 ve P300) potansiyellerin ortaya çıktığı bununla birlikte, S1 ve S2 yanıtlarının daha büyük genlikte oldukları göze çarpmaktadır (Şekil 5). Bunun iki nedeni olabilir; birincisi, İÖUAİ paradigmasındaki S1 ve S2 uyaranlarının, İUP paradigmasındaki ses uyaranlarından daha yüksek şiddette olmasıdır. İkincisi ise, S1 ve S2 uyaranları göz irkilme yanıtları oluşturduğu için bu kas aktivitesinin EEG yanıtlarına eklenmiş olmasıdır. İUP ile kaydedilen EEG verisinin analizlerinde göz kırpma artefaktları ayıklanmıştır.

Araştırmamızda birincil amacımız, ÖUAİ paradigması ile beyin potansiyellerinde gerçekleşebilecek olası inhibisyonu araştırmaktır.

Uyaranın fiziksel özelliklerine (şiddet, frekans, süre vb.) duyarlı olan N100 ve P200 potansiyellerinin, ön uyaran uygulanması ile genliklerinin zayıflayacağı öngörülmüştü. Şekil 4'de, S2 uyaran genliklerinin S1 uyaranına kıyasla hafifçe zayıfladığı görülmekle birlikte bu zayıflama istatistiksel olarak anlamlı bulunmamıştır. Fraga ve ark. (6) ve San Martin ve ark. (9) ön uyaran ve irkilme uyaranı arasında 30, 60, 120 ms zaman aralıkları uygulamışlar, ön uyaran uygulandığında N100, P200 potansiyellerinin genliklerinde zayıflama bulmuşlardır. Araştırmamızda S1 ve S2 uyaranları ile ortaya çıkan beyin potansiyellerinin genliklerinde anlamlı farklılık yoktu. Bizim çalışmamızda irkilme uyaranının şiddet seviyesi 107 dB iken Fraga (6) ve San Martin ve arkadaşları (9) 115 dB irkilme uyaranı uygulamışlardır. Bu iki ses şiddeti seviyesi arasında yaklaşık 6,3 kat fiziksel ses şiddeti farkı bulunmaktadır. Yüksek ses şiddeti nedeniyle oluşan yüksek genlikli beyin potansiyelleri ön uyaran nedeniyle daha büyük inhibisyon göstermiş olabilir. Fakat, bu araştırmacılar N100 ve P200 potansiyel genliklerinde görülen ön uyaran aracılı inhibisyonun göz kırpma refleksindeki inhibisyon ile korele olmadığını bildirmişlerdir. Kedzior ve arkadaşları da (20, 21) motor yanıtlardaki inhibisyon ile beyin yanıtlarında gördükleri inhibisyon arasında korelasyon olmadığını ve bu nedenle beyin potansiyellerinin, sensori-motor yanıtlarla kısmen örtüşen fakat farklı nöral yapılarında katıldığı bağlantılarla kontrol edildiğini öne sürmüşlerdir. Araştırmamızda, ön uyaran uygulaması ile motor yanıtlarda anlamlı bir zayıflama olduğunu fakat uyarılmış beyin potansiyellerinin genlik ve latanslarını etkilemediğini saptadık. Sonuç olarak, duyusal kapılama süreçleri ile sensori-motor kapılama süreçlerinin farklı beyin yapıları ve mekanizmaları ile kontrol edildiği söylenebilir.

Literatürde, ön uyaran ile uyaran arasındaki süre 120 ms olduğunda ÖUAİ`nin en yüksek gerçekleştiği bildirilmiştir. Bu nedenle, araştırmamızda uyaran ve ön uyaran arasındaki süre 120 ms olarak belirlenmiştir. Kısa zaman aralıkları habitüasyon ve beklenti gelişmesine neden olmaktadır (17, 18). ÖUAİ uyaran deseninde kullanılan büyük zaman aralıkları bu etkiyi zayıflatmaktadır, fakat bu durumda kayıt süresi uzamaktadır. Bu etkileri göz önüne alarak, uygun sayıda uyaran ve kayıt süresini belirlemeye çalıştığımız araştırmamızda tek bir oturumda, 30'ar adet S1 ve S2 uyaranı rastgele sırayla ve 7 ile 22 s arasında değişen zaman aralıklarıyla uygulanmıştır. Fraga ve arkadaşları (6), her bir oturumda 85 uyaran bulunan iki oturumla, Pascalis ve arkadaşları (22), toplamda 86 uyaran uygulayarak ÖUAİ'ni incelemişlerdir. Kedzior ve arkadaşları (21), tek oturumda 130 uyaran uygulamışlardır. Bu çalışmalarda daha kısa zaman aralıklarında uyaranlar uygulandığı için N100, P200 yanıtlarında habitüasyon gelişmiş ve daha düşük S2 genlikleri elde edilmiş olabilir. Bu çalışmalarla bizim EEG bulgularımız arasındaki farklılıkların nedenlerinden birisi toplam veri sayısındaki farklılık olabilir.

Sonuç Ve Öneriler

Bu çalışmada, şiddetli bir ses uyaranından 120 ms önce daha düşük şiddette ses uyaranı uyguladığımızda *OOc* kasından kaydettiğimiz göz kırpma refleksinin literatürle uyumlu olarak inhibisyona uğradığını gösterdik. EMG-CUSUM ile elde ettiğimiz S1 ve S2 uyaranlarının latansı daha uzun bulunmuştur. İşitsel uyaranlarla meydana gelen motor yanıtlarda bilinenden daha fazla sayıda sinaptik bağlantı olabilir. Diğer beyin sapı refleksleri yüzeyel EMG yanı sıra intramüsküler EMG ile de çalışılarak latans ve süre değerleri EMG-CUSUM yöntemiyle karşılaştırıldığında daha doğru bir sonuca ulaşılabilir. Ses uyaranları ile EEG ve irkilme kas yanıtları birlikte incelenecekse, *OOc* kası yerine beyne daha uzak olan kaslardan (*m. sternocleidomastoideus ve m. trapezius* gibi) kayıt alındığında EEG değerlendirilmesini daha sağlıklı yapılabilir.

Sensori-motor zayıflamaya neden olan ön uyaran uygulanmasının beyin bilgi işleme süreçlerinde de bir baskılamaya neden olabileceğini düşündürmektedir. Bu konuda az sayıda bulunan araştırmalardan farklı olarak ön uyaran uygulanmasının beyin elektrik aktivitesinin genlik ve latanslarında anlamlı bir etkisinin olmadığını gözlemledik. Literatürde mevcut olan çalışmalar temel olarak benzer görünse de uyaranların ses şiddetleri, uyaranlar arasındaki süreler ve uyaran sayısı gibi birçok farklılıklar içermektedir. Bu fiziksel özelliklerin etkilerini daha açık ortaya koyabilmek için her defasında sadece tek bir parametrenin değiştirildiği bir dizi araştırma planlanmalıdır. Ancak, mevcut bulgularımız ışığında, ön uyaran uygulanmasının şiddetli işitsel uyarana karşı oluşturduğu sensori-motor yanıtlarla, beyindeki bilgi işleme süreçlerinin aynı mekanizma ve aynı beyin yapıları ile yürütülmediği söylenebilir. Bu araştırmanın kısıtları olarak; EMG ve EEG'yi aynı anda incelemek için bazı verileri gözden çıkartmak durumunda kalınması ve kas-beyin aktivitesinin birlikte incelenmesinde crosstalk artefaktları zorlukları söylenebilir.

TEŞEKKÜR

Bu araştırma İzmir Kâtip Çelebi Üniversitesi Bilimsel Araştırma Projeleri Koordinatörlüğü tarafından 2022-GAP-TIPF-0034 numaralı proje ile desteklenmiştir.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 20-25

Determination of Endoplasmic Reticulum Stress Protein Expression Levels in Nasal Polyp Tissue

Nazal Polip Dokusunda Endoplazmik Retikulum Stres Proteinlerinin İfadelenme Düzeylerinin Belirlenmesi

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Geliş Tarihi: 21.12.2023
Kabul Tarihi: 02.02.2024

Abstract

Objective: This study aims to explore the role of the endoplasmic reticulum (ER) stress pathway in developing nasal polyps.

Materials and Methods: Nasal polyp (NP) samples were collected from 30 individuals diagnosed with nasal polyposis. Participants were categorized into three groups: those with NP only, asthma and NP, and Samter's syndrome. Control tissues were obtained from the nasal mucosa of 10 healthy individuals. Western blot analysis was used to measure the expression levels of ER stress proteins (Bip/Grp78, eIF2a, and CHOP) in both study and control groups.

Results: The expression of Bip/GRP78 increased by 1.94-fold, 2.68-fold, and 1.92-fold in the first, second, and third groups, respectively, compared to the control group (p=0.275). CHOP expression increased by 2.20-fold, 2.60-fold, and 3.45-fold in the first, second, and third groups, respectively, compared to the control group (p=0.050). P-eIF2α expression increased by 1.66-fold, 2.60-fold, and 4.15-fold in the first, second, and third groups, respectively, compared to the control group (p=0.127).

Conclusion: This study provides initial insights into the potential involvement of the ER stress pathway in nasal polyp development. While our results suggest a correlation, further investigations with larger sample sizes and consideration of additional elements of the ER stress pathway are necessary for definitive conclusions.

Keywords: Er stress, nasal polyp, unfolded protein response

Öz

Amaç: Araştırmanın amacı, nazal polip gelişiminde endoplazmik retikulum (ER) stresinin etkilerini incelemektir.

Gereç ve yöntemler: Nazal polip (NP) örnekleri, nazal polipozisli 30 hastadan rastgele alınmıştır. Çalışma grubu sırasıyla üçe ayrılmıştır; birinci grup sadece NP olanlar, ikinci grup astım ile NP birlikteliği olanlar ve üçüncü grup ise Samter hastalığı olanlar. Kontrol dokuları ise 10 sağlıklı bireyin burun mukozasından alınmıştır. Çalışma grubu ve kontrol grubunda ER stres proteinlerinin (Bip/Grp78, eIF2a, and CHOP) ifadelenme düzeyleri western blot yöntemi ile ölçülmüştür.

Bulgular: Bip/GRP78 düzeyi kontrol gruba göre sırasıyla; 1. grupta 1.94 kat, 2. grupta 2.68 kat ve 3. grupta ise 1.92 kat artmıştır (p=0.275). CHOP düzeyi kontrol gruba göre sırasıyla; 1. grupta 2.20 kat, 2. grupta 2.60 kat ve 3. grupta ise 3.45 kat artmıştır (p=0.050). P-eIF2α düzeyi kontrol gruba göre sırasıyla; 1. grupta 1.66 kat, 2. grupta 2.60 kat ve 3. grupta ise 4.15 kat artmıştır (p=0.127).

Sonuç: Çalışmamız ER stres yolağının nazal polip gelişimindeki rolünü irdeleyen öncü araştırmalardandır.

Sonuçlarımız ER stres yolağının nazal polip gelişiminde etkisi olabileceğini desteklemekle beraber, kesin yargıya varabilmek için, daha fazla deneğin kullanıldığı ve ER stres yolağının diğer elemanlarını da içeren çalışmaların planlanması gerektiğini göstermektedir.

Anahtar Kelimeler: Er stres, nazal polip, unfolded protein response

Introduction

Nasal polyposis (NP) is a chronic inflammatory disease affecting the mucosa of the nasal cavity and paranasal sinuses. Its pathogenesis is controversial, and high recurrence rates challenge physicians. A consensus points to a chronic inflammatory process as the cause of polyp development (1). Understanding the inflammatory mechanisms leading to polyp formation is crucial for improved disease management.

The endoplasmic reticulum (ER), an intracytoplasmic organelle, serves various functions within the cell. When the ER's capacity is exceeded, unfolded and misfolded proteins accumulate in the cytosol, activating multiple inflammatory and stress signaling pathways known as "ER stress" (2). The stress initiates "Unfolded Protein Response" (UPR) to preserve vital cell functions, regulating metabolic signals, oxidative stress, and inflammatory pathways (3).

Recent studies point out that endoplasmic reticulum (ER) stress plays a crucial role in the development of inflammation (4). Given that NP is an inflammatory-based disease, it suggests that ER stress could be a fundamental factor in the development of NP and needs further clarification. This study specifically investigates the role of the unfolded protein response (UPR) triggered by ER stress. Using western blotting, we evaluated the expression levels of three essential proteins associated with UPR (Bip/Grp78, eIF2a, and CHOP). The proteins in polyp tissues from NP patients were compared with control tissues from healthy individuals. In summary, the study aims to contribute new insights into the inflammatory origins of NP disease.

Materials and Methods

The local institutional ethical committee approved this study, and informed consent was obtained from all participants before samples were collected.

Sample collection and preparation

We collected nasal polyp tissue samples from 30 subjects (21 males and nine females) undergoing endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps (NP). We separately studied cases with asthma and acetylsalicylic acid (ASA) intolerance (Samter's triad) due to their impact on NP, excluding those with other systemic diseases from the study.

Control subjects were healthy individuals without any systemic disease. We obtained control tissues from the healthy inferior turbinate mucosa of 10 subjects (six males, four females) without rhinosinusitis or nasal polyps.

For western blot analysis, all tissue samples underwent saline wash in the operating room and were then stored in frozen liquid nitrogen at -80 °C.

Tissue Homogenization

Nasal polyp and control tissues washed once with PBS (Saline phosphate buffer, HyClone™, US) were stored at -80°C until use.

Tissues weighed with a precision scale (Shimadzu, Japan) were taken into RIPA buffer (tissue disintegrating buffer, Cell Signaling Technology, Inc. US) and fragmented with the help of a tissue homogenizer (1000µL RIPA buffer was used for 100mg tissue).

Tissue homogenates were placed in microcentrifuge tubes and centrifuged at 13000 x g at +4°C for 15 minutes.

The BCA (biquinchoninic acid) method was used to determine the amount of protein in the samples whose supernatants were taken after centrifugation.

The samples whose protein contents were determined were mixed with 5X sample loading buffer (Laemmli buffer) in the appropriate ratio, boiled at 95°C for 5 minutes, and denaturation was carried out.

Samples were stored at -20 °C until used for western blotting.

Preparation of SDS (Sodium dodecyl sulfate)-Polyacrylamide Gel

A 5 mL SDS-polyacrylamide gel mixture was prepared at two different densities, 4% and 12%. A comb containing ten wells was placed after filling the gel solution between the glass surfaces. The gel was then left at room temperature for 30 minutes to freeze.

Loading and Electrophoresis of SDS-Polyacrylamide Gel

After polymerization of the SDS-polyacrylamide gel, it was placed in the electrophoresis tank. Each of the gels had ten wells. 10 µL (20 µg of each sample) from 3 polyps and one control tissue were loaded into the wells. 5 µL of molecular weight marker was loaded into the last well. After the samples were loaded, the electrodes of the electrophoresis system were placed. Electrophoresis was performed at 100 volts for 2 hours in a cold room.

Transfer of Proteins on SDS-Polyacrylamide Gel to Nitrocellulose Membrane

After electrophoresis, the proteins in the gel were transferred to the membrane. The membrane-gel cassette of the small polyacrylamide gel system was used during this process. Transfer of proteins from the gel to the nitrocellulose membrane was performed in a cold room at 200 mAmp currents for 2 hours. After the transfer process, the cassette was opened, and the membrane was taken for immunological detection.

Immunological Detection of Proteins on Nitrocellulose Membrane

In immunological detection, firstly, after protein transfer, the nitrocellulose membrane was kept in a closure solution containing TBST (Tris-salt-tween 20, Cell Signaling Technology, Inc. US) and skimmed milk powder (Cell Signaling Tech, Inc. US) for one hour. This capping process aimed to prevent the antibodies from misbinding by covering the non-protein-bound membrane regions with powdered milk.

Then, the membrane was washed in TBST solution. After washing, the membrane was treated overnight with primary antibody diluted in TBST+5% skim milk powder solution.

The primary antibody (Cell Signaling Tech, Inc. US) specific to the investigated protein was used in this study. The membrane was treated with the primary antibody overnight and then washed three times for five minutes with TBST (Tris-salt-tween 20) solution. After washing, the membrane was incubated in an HRP-conjugated secondary antibody (Cell Signaling Tech, Inc. US) solution diluted in TBST+5% skimmed milk powder solution for one hour on an orbital shaker (BioSan, Latvia). Next, the holding process was done on a horizontal shaker. Following this step, the membrane was washed three times for five minutes with TBST solution. Then, the ECL (SuperSignal™ West-Femto chemiluminescent substrate, US) solution, which is the substrate of HRP, was dripped onto the membrane for imaging purposes to cover the surface, and the chemiluminescent radiation was photographed in the Gel-Logic 2200 Pro imaging and documentation (CareStream, US) system.

Presentation of the digital data and statistical analysis

The obtained digital images were recorded for pixel analysis by proportioning the band structures formed by the target proteins in the polyp and control tissues to the band structures of a housekeeping protein (GAPDH- Cell Signaling Tech, Inc. US). The results were interpreted in comparison with controls. Densitometric analysis of pixel data (px) was presented numerically and graphically with a trend curve. Statistical analysis was performed on numerical variables using the IBM SPSS v21 program. The Shapiro-Wilk and Kolmogorov-Smirnov tests were employed to assess normality in continuous variables. As our results deviated from normal distribution, the Mann-Whitney U test was used to evaluate mean differences between independent and control groups, aiming to identify any difference. A significance level of $p < 0.05$ indicated statistical significance.

Results

Demographic and clinical characteristics

A total of 40 subjects were included in the study. The NP group consisted of 30 subjects (21 males and nine females; median age: 45,2 ±13,28). This group was divided into three subgroups. The first group (group 1) was classified as only NP patients (20 subjects), the second group (group 2) with asthma and NP coexistence (4 subjects), and the third group (group 3) as the NP group with Samter's disease (6 subjects) (table 1).

Table 1. Distribution of patients in the NP group

	Group 1	Group 2	Group 3	**Total**
Female	6	1	2	9
Male	14	3	4	21
Total	20 (%67)	4 (%13)	6 (%20)	30 (%100)

The control group consisted of 10 subjects (6 males and four females; the median age was 28,1 ±10,39).

Western blot analysis

Band structures obtained from western blot analysis of Bip/GRP78, CHOP, and P-eIF2α proteins in study and control tissues are shown in Figure 1.

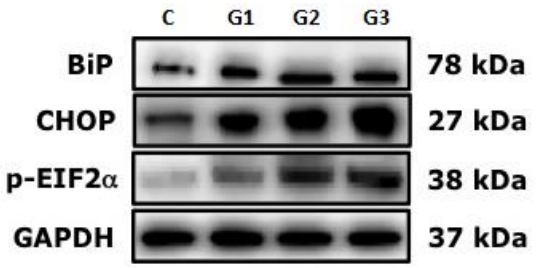

Figure 1. Western blot results of Bip/GRP78, CHOP and P-eIF2α proteins (kDa: Kilodalton, C: control, G1: Only NP group, G2: Asthma+NP group, G3: NP+Samter group.)

The expression of Bip/GRP78 increased by 1.94-fold, 2.68-fold, and 1.92-fold in the first, second, and third groups, respectively, compared to the control group ($p=0.275$) ($R^2=0.3397$) (Figure 2).

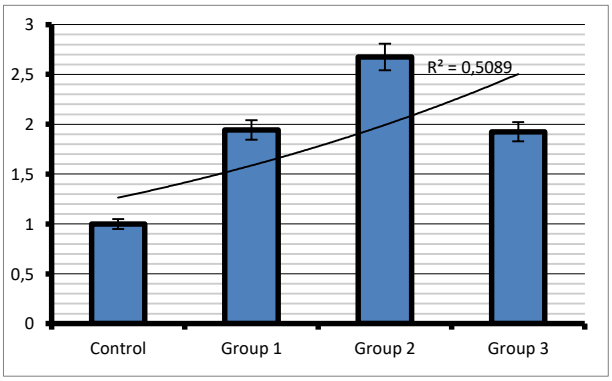

Figure 2. Graph and exponential trend curve of the Bip/GRP78 protein expression level in the study and control groups.

CHOP expression showed increases of 2.20-fold, 2.60-fold, and 3.45-fold in the first, second, and third groups, respectively, compared to the control group ($p=0.050$) ($R^2=0.9112$) (Figure 3).

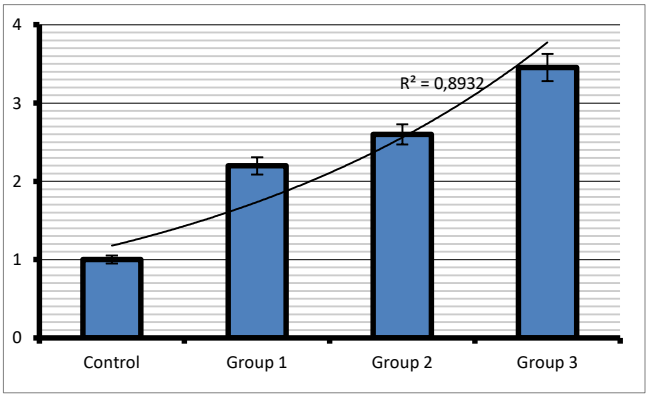

Figure 3. Graph and exponential trend curve of the expression level of CHOP protein in the study and control groups.

P-eIF2α expression increased by 1.66-fold, 2.60-fold, and 4.15-fold in the first, second, and third groups, respectively, compared to the control group (p=0.127) (R^2=0.9997) (Figure 4).

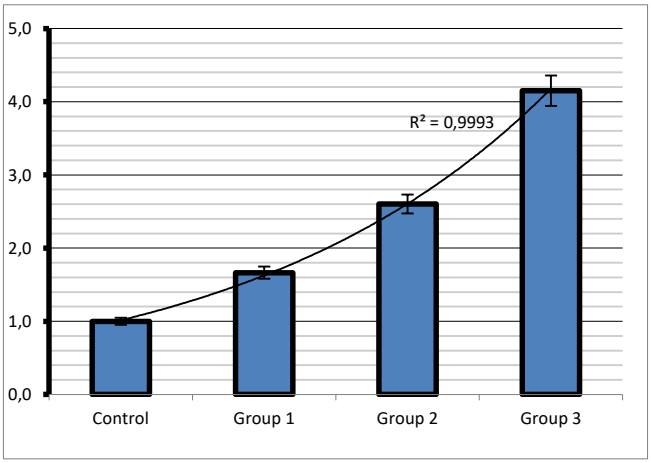

Figure 4. Graph and exponential trend curve of the expression level of P-eIF2α protein in the study and control groups.

Discussion

The nasal cavity and paranasal sinuses are the initial contact points for respiratory antigens, making them prone to specific and nonspecific inflammatory responses. While certain inflammatory reactions can lead to nasal polyps, the precise triggers are not fully understood. It is widely acknowledged that bacteria, viruses, airborne allergens, and fungal elements contribute to inflammation. However, the mystery persists as to why not all individuals exposed to these stimuli develop nasal polyposis.

Although extensive research has explored the roles of various inflammation mediators, immunoglobins, superantigens, and oxidative stress parameters, the exact cause remains elusive (5).

The ER stress phenomenon, with its crucial role in inflammatory and apoptotic pathways, may play a critical role in the pathogenesis of nasal polyposis. Previous investigations by Kim et al. demonstrated an increased ER-stress response in nasal polyp tissues exposed to Staphylococcus aureus superantigens (6). Similarly, Jeanson et al. observed increased UPR response in nasal mucosa cells exposed to external oxidative stress (7). However, these studies focused on ER stress mediators induced by external interventions. In contrast, our study directly examined the role of ER stress in polyp development without external interventions on the tissue. Additionally, considering the frequent co-occurrence of asthma and ASA sensitivity (Samter triad) in nasal polyposis, the investigation evaluated three distinct groups: patients with sole nasal polyposis (group 1), patients presenting with both asthma and nasal polyposis (group 2), and patients exhibiting Samter's triad (group 3).

Proteins fold and complete maturation within the endoplasmic reticulum (ER), which provides an oxidative microenvironment crucial for accurate folding. However, inflammatory stress disrupts this microenvironment, accumulating misfolded and unfolded proteins (8). These proteins accumulate in the cytosol, causing cell damage and inducing ER stress (9).

After ER stress is triggered, unfolded protein response (UPR) signaling pathways are activated to maintain vital cell functions (10). UPR counters the stress stimulus, stimulating protein folding by increasing chaperone proteins and protein foldases (11). Although overall protein production decreases during this stage, stress proteins continue to be produced. If folding capacity is exceeded, unfolded proteins are removed by ER-associated protein degradation (ERAD) (12).

The UPR regulates intracellular metabolic stress, oxidative damage, and inflammation pathways. Recent research indicates that UPR might initiate inflammation and play a crucial role in the development of inflammatory diseases (13).

In our study, the expression levels of three main proteins crucial in the UPR pathway were evaluated: intracellular chaperone Bip/GRP78, translation initiating factor eIF2α, and transcription factor CHOP. Furthermore, expression profiles were assessed in three subgroups considering the effect of asthma and ASA sensitivity.

Bip/GRP78, a master regulator of UPR, plays a crucial role in maintaining cell survival in stress conditions (14). It suppresses the caspase system, slowing down apoptosis (15,16). Downregulation of this mechanism may contribute to polyp growth. Although the expression level of Bip/GRP78 increased in all three NP groups, the lack of statistical significance is attributed to the limited number of subjects. Nevertheless, the results guide future studies with a larger population.

CHOP, generally not expressed without stress stimuli, is strongly expressed in response to ER stress (17). Our study revealed a significant increase in CHOP expression within polyp tissue compared to the control group, suggesting a role in nasal polyps by triggering pro-apoptotic effects, activating oxidative damage mechanisms, and enhancing inflammatory functions (18). Notably, the elevated CHOP expression in the Samter group amplifies stress signals, potentially contributing to treatment resistance and increased likelihood of relapses.

Stress stimulus impairs protein synthesis of the cell. When the folding of newly synthesized proteins is disrupted, mRNA translation is reduced to suppress further production of unfolded proteins (19). The eukaryotic initiating factor-2α (eIF2α) mediates the binding of the translation initiator met-tRNA to the ribosome (20). However, phosphorylation of the alpha subunit of eIF2α interrupts this step and stops protein production. Then, protein translation is decreased, and mRNAs required for the UPR are stimulated (21).

Our study revealed a substantial increase in eIF2α expression, especially in polyps from Samter's syndrome patients. Although not reaching statistical significance, the results suggest potential activation of the PERK branch in the UPR pathway due to ER stress in polyp tissue. The underlying implication is that inflammatory processes in polyp tissue contribute to an elevated stress stimulus in individuals with Samter's syndrome.

Nasal polyposis is a complex and costly disease with a significant impact on social life and workforce. The coexistence of asthma and Samter's disease adversely affects prognosis (22).

Due to the inflammatory nature, physicians often resort to steroids as the most effective treatment for NP (23). However, recurrences persist even after current drug and surgical treatments (24). By elucidating its etiopathogenesis, more effective and less costly treatment approaches can be developed.

While ER stress has recently been implicated in inflammation, its role in nasal polyps requires further investigation. If the relationship between NP and ER stress is proven, treatment options related to ER stress inhibition may be considered in the future. However, our study includes limited subjects, necessitating further research for definitive conclusions.

In conclusion, the ER stress-induced UPR pathway, with proven effects in the etiology of many inflammatory diseases, appears to have a role in the pathogenesis of NP. This study serves as a pilot investigation on this subject, emphasizing the need for further studies involving other elements of the UPR pathway in a larger population.

Acknowledgment

We express our appreciation to Prof. Dr. Necat Alataş for his invaluable contributions during the statistical evaluation phase of the study

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 26-33

Knowledge, Attitude and Behavior of Health Workers About Travel Health

Sağlık Çalışanlarının Seyahat Sağlığına İlişkin Bilgi, Tutum ve Davranışları

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Geliş Tarihi: 08.01.2024
Kabul Tarihi: 18.03.2024

Abstract

Objective: The purpose of this study was to investigate the knowledge, practices, and attitudes of medical professionals about travel medicine who were sent by the Ministry of Health to the endemic zone on a voluntary basis.

Method: This cross-sectional study was conducted in the Mogadishu Somalia Türkiye Recep Tayyip Erdoğan Training and Research Hospital between March 23 and July 20, 2023. The study involved 95 healthcare workers who reported for work at certain times over the course of four months. The poll was filled out by 91 participants, as 4 individuals declined to participate. Participants were given the option to tick more than one option. The sample size could not be established since every medical practitioner who attended the hospital during the course of the four months was included.

Results: The participants' average age was 42.09, and 75 (82.4%) were men. 66 people, or 72.5%, were married. Of the participants, 32 (35.2%) were physicians, 28 (30.8%) were midwives and nurses, 30 (33%) were staff members in the administrative domain, and 1 (1%), was a pharmacist. Three individuals (3.3%) held a high school diploma, 54 individuals (59.3%) held a university degree, and 34 individuals (37.3%) held a master's or doctorate degree. Of the participants, 18 (19.8%) were there for educational/research goals, 78 (85.7%) for financial reasons, 21 (23.1%) for exploratory reasons, and 40 (43.9%) traveled to Somalia for volunteer work

Conclusion: People visiting endemic areas might make better use of travel clinics to protect themselves against any possible risks prior to, during, and following their trip.

Keywords: Health workers; public health; endemic diseases; travel.

Öz

Amaç: Bu çalışmanın amacı, Sağlık Bakanlığı tarafından endemik bölgeye gönüllü olarak gönderilen tıp çalışanlarının seyahat hekimliği konusundaki bilgi, uygulama ve tutumlarının araştırılmasıdır.

Yöntem: Kesitsel tipte olan bu çalışma, Mogadişu Somali Türkiye Recep Tayyip Erdoğan Eğitim ve Araştırma Hastanesi'nde 23 Mart - 20 Temmuz 2023 tarihleri arasında gerçekleştirildi. Araştırmaya dört ay boyunca belirli zamanlarda işe başvuran 95 sağlık çalışanı dahil edildi. Ankete 91 kişi katıldı, 4 kişi katılmayı reddetti. Katılımcılara birden fazla seçeneği işaretleme seçeneği sunuldu. Dört ay boyunca hastaneye başvuran tüm tıp doktorlarının dahil edilmesi nedeniyle örneklem büyüklüğü belirlenemedi.

Bulgular: Katılımcıların yaş ortalaması 42,09 olup 75'i (%82,4) erkektir. 66 kişi yani %72,5'i evliydi. Katılımcıların 32'si (%35,2) hekim, 28'i (%30,8) ebe ve hemşire, 30'u (%33) idari personel, 1'i (%1) ise eczacıydı. Üç kişi (%3,3) lise diplomasına, 54 kişi (%59,3) üniversite diplomasına ve 34 kişi (%37,3) yüksek lisans veya doktora derecesine sahipti.

Katılımcıların 18'i (%19,8) eğitim/araştırma amacıyla, 78'i (%85,7) maddi nedenlerle, 21'i (%23,1) keşif amacıyla ve 40'ı (%43,9) gönüllü çalışma amacıyla Somali'ye gitmişti.

Sonuç: Endemik bölgeleri ziyaret eden kişiler, seyahat öncesinde, seyahat sırasında ve sonrasında olası risklere karşı kendilerini korumak için seyahat kliniklerinden daha iyi yararlanabilirler.

Anahtar Kelimeler: Sağlık çalışanları; Halk Sağlığı; endemik hastalıklar; seyahat.

Introduction

The United Nations World Tourism Organization (UNWTO) reports that 1 billion 186 million individuals visited other countries in 2015. With 674 million travelers in 2010, it is clear that the number of travelers is growing annually. This number doubles in 2022 compared to the previous year following the epidemic, with more than 900 million individuals traveled worldwide. In 2023, the rate is predicted to be between 80 and 90 percent of the rates prior to the pandemic[1].

Of all the trips aboard, 52% of the travels is done for vacation, 16% is for business, and the remaining 24% is for pilgrimage, visiting family, and receiving medical care[2,3]. Travel to developing nations accounts for about half of all travel worldwide. Latin America, Africa, and the Middle East Asia are regarded as the most risky regions in terms of infection risk[4].

Many travelers are unaware that particular destinations can increase the chances of exacerbating various health problems, thus they may fail to take the necessary precautions before their trip. Experts in health have a crucial role in counseling on travel diseases both before and after the trip[5,6].

Medical practitioners should also be able to identify patients who may need follow-up after returning from travel and administer therapeutic drugs while on the go[7].

The idea of travel diseases is highlighted by the annual rise in travel to underdeveloped nations[8]. As a result, vaccinations and travel medicine are now more important than ever. Furthermore, it is now much more crucial to research the destination's risks before visiting and to take protective measures[9].

A new interdisciplinary area called travel medicine seeks to preserve the health and well-being of travelers[10]. Travel medicine is a branch of medicine that deals with all medical conditions related to travel, including trauma, cardiac disorders, embolism, jet lag, sunburn, and similar conditions that may arise during travel. It also includes infectious diseases like malaria, traveler's diarrhea, and yellow fever[11].

The most important strategies for preventing illness are immunizing travelers based on the destination area, educating them about the dangers of disease there, and administering prophylaxis if needed[12,13].

Travel medicine clinics are considered essential for Turkey, given factors including its geopolitical location, tourism potential, Istanbul's significant airline traffic role, and the ongoing global refugee crisis.

Currently offering pre- and post-travel advice, and treatment applications are conducted in55 centers, with the "Turkish General Directorate of Borders and Coasts" being the organization in our nation that offers the most thorough and extensive service on this subject.

The purpose of this study was to investigate the knowledge, practices, and attitudes of medical professionals about travel medicine who were sent by the Ministry of Health to the endemic zone on a voluntary basis.

Material and Methods

Setting and Sample

This cross-sectional study was conducted in the Mogadishu SOMALIA-TURKIYE Recep Tayyip Erdogan Training and Research Hospital between March 23 and July 20, 2023. The study involved 95 healthcare workers who reported for work at certain times over the course of four months. The poll was filled out by 91 participants, as 4 individuals declined to participate. The sample size could not be established since every medical practitioner who attended the hospital during the course of the four months was included.

Procedure

Turkish medical staff members who worked in the hospital were personally surveyed by an infectious diseases specialist. Information was gathered from those who replied. Participants received information on the survey's objective, data protection, and confidentiality. Participants in the survey were informed that the entire process was completely voluntary, that they were required to answer every question, and that they could discontinue at any moment. Participants were given the option to tick more than one option. They were asked to specify whether or not they wanted to participate. Prior to initiating the survey, each participant provided verbal consent. Participation in the survey was free of charge.

Survey Tool

The survey's questions were established through a search of the literature and utilizing information from the Turkish General Health Directorate of Borders and Coasts website. The poll consisted of 42 questions in total. Six questions were about sociodemographic information, and sixteen included multiple choice options with the options yes, no, or I'm not sure. The final twenty questions addressed mindset and behaviour. The questions were designed in accordance with the most common diseases and disorders in the region visited. Subjects like demographic information, pre-travel screening and examination, vaccinations, diseases of the respiratory system like Covid-19 and tuberculosis, parasitic diseases spread by mosquitos such as malaria, tetanus, STDs, and sun exposure risks were all considered when creating the questions. Age, gender, occupation, marital status, reason for visiting the endemic area, and prior visits to the destination were among the demographic information gathered.

Questions about individuals behaviour and outlook were designed featuring a yes/no response option. The questions evaluating participants knowledge were designed in such a way that some of the responses were yes, no, and not sure, while others were multiple choice. The study was approved by the ethics committee on May 30, 2023, with decision number 781 and MSTH/14297 from Mogadishu Somali-Turkey Recep Tayyip Erdoğan Training and Research Hospital.

Statistical Analysis

The SPSS 25.0 package application was used to perform statistical analysis on the data. Descriptive statistics are shown as number(s), percentage (%) and mean±standard deviation (SD) values.

Results

The participants' average age was 42.09, and 75 (82.4%) were men. 66 people, or 72.5%, were married. Of the participants, 32 (35.2%) were physicians, 28 (30.8%) were midwives and nurses, 30 (33%) were staff members in the administrative domain, and 1 (1%), was a pharmacist. Three individuals (3.3%) held a high school diploma, 54 individuals (59.3%) held a university degree, and 34 individuals (37.3%) held a master's or doctorate degree. Of the participants, 18 (19.8%) were there for educational/research goals, 78 (85.7%) for financial reasons, 21 (23.1%) for exploratory reasons, and 40 (43.9%) traveled to Somalia for volunteer work (Table 1). Some participants checked more than a single answer option.

Table 1: Demographic data of participants

	Number	%	Mean±SD
Age (Years)			**42.09**±8.23
Gender			
Male	75	82.4	
Female	16	17.6	
Marital Status			
Married	66	72.5	
Single	25	27.5	
Occupation			
Doctor	32	35.2	
Midwife-nurse	28	30.8	
Administrative staff	30	33	
Pharmacist	1	1	
Educational Status			
High school	3	3.3	
University	54	59.3	
Master's-Ph.D.	34	37.4	
Reason for coming to Somalia			
Education-research	18	19.8	
Economic	78	85.7	
Adventure	21	23.1	
Volunteer help	40	43.9	

Pre-travel vaccination status of the participants revealed that 39 (57.1%) had tetanus, 24 (26.4%) had hepatitis B, 14 (15.4%) had polio, 6 (6.6%) had chickenpox, 4 (4.4%) had whooping cough, 9 (9.9%) had influenza, 30 (33.3%) had covid-19, 10 (11%) had hepatitis A, 1 (1.1%) had rabies, and 44 (48.4%) had yellow fever vaccinations prior to travel (Table 2).

Table 2: Vaccination behaviors of participants.

	Number	%
Tetanus vaccine		
Yes	39	57.1
No	52	42.9
Hepatitis B vaccine		
Yes	24	26.4
No	67	73.6
Measles-Rubella-Mumps Vaccine		
Yes	14	15.4
No	77	84.6
Polio vaccine		
Yes	14	15.4
No	77	84.6
Varicella vaccine		
Yes	6	6.6
No	85	93.4
Pertussis Vaccine		
Yes	4	4.4
No	87	95.6
Influenza Vaccine		
Yes	9	9.9
No	82	90.1
Covid-19 vaccine		
Yes	30	33.0
No	61	67.0
Hepatitis A vaccine		
Yes	10	11.0
No	81	89.0
Typhus vaccine		
Yes	52	57.1
No	39	42.9
Rabies vaccine		
Yes	1	1.1
No	90	98.9
Yellow fever vaccine		
Yes	44	48.4
No	47	51.6

Of the participants in our study, 44 (48.4%) had routine health screening tests, and 66 (72.5%) had applied to a health institution prior to their trip. Twenty-one (23.1%) of the participants had previously traveled to an African nation. Thirteen individuals (18.7%) had taken antibiotics or loperamide to avoid diarrhea, while twenty-six (28.6%) had taken malaria prophylaxis before to departure. A total of 51 (56%) participants carried either sunglasses or sunscreen. Prior to their trip, 58 (63.7%) participants received information regarding sexually transmitted diseases (Table 3).

Table 3. Behavior-attitude data of the participants

	Number	%
Did you go to a travel health center before your trip?		
Yes	66	72.5
No	25	27.5
Have you had routine health screening tests before travel?		
Yes	44	48.4
No	47	51.6
Have you traveled to any African country before?		
Yes	21	23.1
No	70	76.9
Did you take malaria prophylaxis before travelling?		
Yes	26	28.6
No	65	71.4
Did you bring medications such as loperamide or antibiotics to prevent diarrhea?	17	18.7
Yes	74	81.3
No		
How often do you use a mask for diseases such as Covid-19 and tuberculosis?	46	50.5
Always	23	25.3
Sometimes	17	18.7
Rarely	5	5.5
Never		
Did you buy sun protection glasses or cream before traveling?	51	56.0
Yes	40	44.0
No		
Did you get information about sexually transmitted diseases before traveling?	58	63.7
Yes	33	36.3
No		

In our survey, 17 (18.7%) individuals answered yes to the question of whether long-sleeved clothing and mosquito nets can protect against malaria. A total of 62 individuals (68.1%) agreed that malaria was a life threatening disease. Table 4 shows the answers given to what the risk factors for malaria are, how its definite diagnosis is made, what its symptoms are, whether there are alternative transmission pathways other than mosquitos, and what medications are used for prophylaxis.

Table 4. Participants' malaria knowledge level data.

	Number	%
Sinkov, do long sleeves and mosquito nets definitely protect against malaria?	17	18.7
Yes	74	81.3
No		
Is malaria a fatal disease? Yes	62	68.1
No	29	29.7
No idea	2	2.2
What are the risk factors of malaria?		
Region visited	11	12.1
Region and length of stay	2	2.2
Region and season	1	1.1
All	72	79.1
No idea	5	5.5
How is malaria diagnosed definitively?		
Rapid test	6	7.0
Rapid test, peripheral smear, routine blood	1	1.0
Rapid test, peripheral smear	1	1.0
Peripheral smear	69	75.0
Routine blood	5	6.0
No idea	9	10.0
What are the symptoms of malaria?		
Fever	1	1.1
Fever, sweating	1	1.1
Fever, tremor	3	3.3
Sweating, tremor	1	1.1
Tremor	1	1.1
All	84	92.3
Are there any other ways malaria is transmitted other than flies?	30	33.0
Yes	58	63.7
No	3	3.3
No idea		
Which drugs are used in malaria prophylaxis?		
Mefloquine	11	12.1
Mefloquine, doxycycline	4	4.4
Doxycycline	9	9.9
Atovaquone proguanil	16	17.6
All	21	23.1
No idea	30	33.0

Of all the participants, 73 (80.2%) said that tuberculosis is a life-threatening disease, 78 (85.7%) stated Covid-19 is a life-threatening condition, and 82 (89%) stated that tetanus is a life-threatening condition. When asked if getting a tetanus vaccination is a straightforward process in Somalia, 39 (42.9%) answered it is, while 47 (51.6%) said they had no idea. When asked about mosquito-borne diseases, 32 (35.2%) respondents claimed malaria and 44 (48.4%) answered all options. Fifty-five (60.4%) respondents answered they were unsure whether there was a chance of contracting leptospirosis or schistosomiasis in Somalia.

Fifty-two (57.1%) persons believe typhoid is not a mortal disease. 54 respondents, or 59.3%, stated that any number of conditions could result in traveler diarrhea.

Consuming sanitized food and water is the most effective way to avoid diarrhea, according to 72(%79,1) of the patients. Table 5 displays the participants' level of knowledge about endemic illnesses.

Table 5. Participants' knowledge level of endemic diseases

	Number	%
Is tuberculosis a fatal disease?		
Yes	73	80.2
No	18	19.8
Is Covid-19 a fatal disease?		
Yes	78	85.7
No	13	14.3
Is tetanus a fatal disease?		
Yes	81	89.0
No	8	8.8
No idea	2	2.2
Is it easy to get a tetanus vaccine in Somalia?		
Yes	39	42.9
No	5	5.5
No idea	47	51.6
Which diseases are transmitted by mosquitoes?		
Malaria	32	35.2
Filariasis	0	0.0
Malaria, yellow fever	9	9.9
All	44	48.4
No idea	6	6.6
Is there a risk of schistosomiasis, filariasis, leishmaniasis in Somalia?		
Yes	3	3.3
No	33	36.3
No idea	55	60.4
Is typhoid a fatal disease?		
Yes	38	41.8
No	52	57.1
No idea	1	1.1
Which ones cause traveler's diarrhea?		
Bacteria	14	15.4
Viruses	6	6.6
Parasites	5	5.5
Bacteria, parasites	1	1.1
Bacteria, viruses	1	1.1
All	54	59.3
No idea	10	11.0
What is the main way to protect yourself from diarrhea?		
Antibiotics, fluid support, general food and drink cleaning	4	4.4
Fluid support	9	9.9
Fluid support, general food and drink cleaning	4	4.4
General food and drink cleaning	72	79.1
No idea	2	2.2

Discussion

Travel Medicine is a new but developing field in the medical community that directly affects more than 1 billion people worldwide and is a discipline that concerns the entire world due to greater travel options and easier international travel. With the Covid-19 pandemic, we have lately grown more accustomed to importance of this branch of medical practice.

The average age of our study participants was 42.09, and the majority were male, married, and university graduate health workers. Physicians, midwives, and nurses made up more than half of the participants. Most of the attendees were in Somalia for economic purposes. The average age of the participants in a South African study was comparable to our study's[14].

The majority of our participants received pre-trip counseling from travel clinics that provide pre-travel and post-travel advisory services as determined by Turkey's General Directorate of Border Coasts and Health, and around half of them underwent normal health screening tests.

Recommended vaccinations in these travel clinics are based on the traveler's intended destination. Despite the fact that the majority of participants visited a travel clinic before their departure, their attitudes toward immunization were shown to be unfavorable. Similar to our study, studies done in Oman and Dubai have revealed unfavorable opinions regarding vaccination[16,17]. Despite having received vaccinations against tetanus, typhoid, and yellow fever, almost half of the individuals in our study did not have sufficient adherence with other recommended vaccinations. Similar findings were seen in a Nigerian study which also found a failure to comply with the recommended yellow fever vaccine[18].

Contrary to our findings, a Chinese study revealed that nearly all tourists had received the yellow fever vaccination[19]. The low percentage of yellow fever vaccination in our study could be attributed to the fact that, rather than being required, the immunization is one of the recommended vaccinations at travel clinics. The fact that the participants are medical professionals and have yearly screening tests where they are made aware of possessing protective antibodies against diseases could be the cause of their reservations toward other vaccines.

Malaria is a parasitic disease that has claimed the lives of millions of people in endemic places. Malaria-related deaths increased from 15% in 2019[20] to 30% in the 2000s. Travelers visiting endemic locations and residents alike must be mindful of the features of malaria, since the disease can be highly mortal if left untreated[21]. In our study, 68.1 percent of people believed malaria is a life-threatening disease. According to a different African study, 90.7% of participants thought that malaria could be lethal if it wasn't treated properly[22]. In a survey of college students from a malaria-endemic area in Turkey, 15.1% of respondents stated that malaria is not a lethal disease[22].

The fact that Africans have greater understanding about this subject can be attributed to their frequent experiences with malaria. Most of the participants in our study (81.3%) were aware that mosquito nets, long sleeves, and sunscreen do not always provide protection from malaria.

In our study, one third of participants answered "yes," while the majority responded "no," when asked whether they knew about any additional vectors for malaria transmission outside mosquitoes. In an Ethiopian community research, 242 (85.2%) out of 426 respondents associated mosquito bites to malaria. The remaining individuals, however, believed that eating maize stalks (33.8%), starvation (33.1%), poor personal hygiene (23.2%), and exposure to cold weather (13.7%) were the causes of malaria. Malaria can be transferred betweeen individuals, according to 48% of participants[23]. Participants in other previously published survey research have likewise indicated that they consider mosquito bites as the most common mode of transmission[24-26].

While female Anopheles mosquito bites are the most frequent form of transmission, other uncommon methods include blood transfusions, transplantation, nosocomial and vertical transmission, and the use of contaminated needles[27]. Understanding the modes of transmission is crucial for implementing fundamental principles of safety for both the general public and medical practitioners. The majority of participants in our study were aware of the symptoms, eventual diagnosis, and risk factors for malaria. In our survey, one-third of individuals said they were unaware of any medications used in malaria prevention, while roughly 25% of respondents thought that all medications may be used as preventative measures.

An important concern for travel medicine is parasitic infections[16]. Out of the 5965 patients who sought care from travel health clinics after visiting Europe in 2011, 482 (8.1%) had malaria, 221 (3.7%) had giardasis, 131 (2.2%) had schistosomiasis, 154 (2.6%) had cutaneous larva migrans, and 46 cases (0.8%) had cutaneous leishmaniasis[28]. Our research also revealed that the participants' responses to the question on the likelihood of contracting parasitic infections in Somalia revealed a lack of knowledge on their part.

In our study, more than half of the participants packed sunscreen or sunglasses to protect themselves from the sun's damaging rays before their arrival. Similarly, more than half of them had received information regarding sexually transmitted diseases.

The percentage of participants in our study who took medicine before traveling in order to avoid diarrhea was quite low. The question "What are the main ways to protect against diarrhea and what are the factors of tourist diarrhea?" was accurately answered by the majority of participants. According to a review, before visiting risky areas, people should take medication to avoid diseases that lead to diarrhea[29].

In our study, vaccination rates against tetanus are not as high, despite the fact that most individuals believe the disease to be life-threatening. Tetanus immunization is also advised before visiting high-risk regions[30].

In our study, mask use was relatively low despite a high incidence of individuals believing tuberculosis to be a life-threatening infection. One of the most dangerous infectious diseases still existing today is tuberculosis (TB), which still poses a serious threat to global health[31]. Based on population-based estimations, the African continent has the highest case and death rates due to tuberculosis[32].

Living in a crowded household increases the likelihood of contacting acute respiratory infections, meningococcus, influenza, and tuberculosis, according to various studies[33]. It is known that the Covid-19 disease spread in a rapid fashion in African countries, causing thousands of deaths and impacting significant populations[34]. Despite the fact that most individuals believe that Covid-19 is a deadly illness, our survey revealed that fewer persons utilize masks and received the Covid-19 immunization reminder dose prior to travel.

Limitations

Our study's limitations include the small sample size of healthcare professionals that made up the participants and the hospital's policy prohibiting staff from leaving the campus.

Conclusion

The number of travelers is rising daily as a result of greater opportunities for travel around the globe. Travel to developing nations accounts for a large percentage of travel, and visiting to African nations is becoming more and more popular every day. As a result, travel medicine, which includes prevention and management of both infectious and non-infectious disorders, promises to be a field that requires further attention. Based on the findings of our research, people visiting endemic areas might make better use of travel clinics to protect themselves against any possible risks prior to, during, and following their trip.

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Ege Klin Tıp Derg 2024;62 (1): 34-40

Evaluation of Factors Affecting Prognosis in Community-Acquired Infection Cases of Older Ages and Being Hospitalized in a Training and Research Hospital

Bir Eğitim ve Araştırma Hastanesinde Yatırılarak İzlenen İleri Yaş Toplum Kökenli Enfeksiyon Olgularında Prognozu Etkileyen Faktörlerin Değerlendirilmesi

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Geliş Tarihi: 18.01.2024
Kabul Tarihi: 27.03.2024

Abstract

Background and aim: Despite developments in healthcare, geriatric infections are an important of morbidity and mortality. In this study, factors affecting prognosis in elderly patients hospitalized due to infectious disease were investigated.

Material and methods : The study was conducted prospectively, and patients aged 65 and over who were hospitalized with a diagnosis of acute bacterial infection were included as the study group, and patients hospitalized for any reason other than infection were included as the control group. The EuroQoL-5D-5L (EQ-5D-5L) quality of life scale was applied to both groups. Blood samples were taken to measure neutrophil CD15 (nCD15) and CD64 (nCD64) and monocyte CD64 (mCD64) levels. In the study group, the Sequential Organ Failure Assessment (SOFA) score was calculated. Data obtained during the twenty-eight-day follow-up period were recorded. Data analysis was done with SPSS 26 program. Pearson's Chi Square test was used to compare categorical variables. P <0.05 was considered significant.

Results : 168 patients were included in the study group and 70 patients were included in the control group. EQ-5D-5L quality of life index, EQ-5D-5L VAS score, total leukocyte count, nCD64 value, nCD15 value, mCD64 value was significantly higher in the study group. Twenty-one (12.5%) patients died. According to logistic regression analysis, SOFA score value on day 7 was found to be the most important parameter associated with survival.

Conclusion: In the follow-up of elderly patients who develop infection, monitoring of SOFA score has been found to be more useful than specific and non-specific laboratory tests.

Keywords: Geriatric infections, EQ-5D-5L, flow cytometry, SOFA score

Öz

Giriş ve amaç: Sağlık hizmetlerindeki gelişmelere rağmen geriatrik enfeksiyonlar önemli bir morbidite ve mortalite nedenidir. Bu çalışmada enfeksiyon hastalığı nedeniyle hastaneye yatırılan yaşlı hastalarda prognozu etkileyen faktörler araştırılmıştır.

Gereç ve Yöntemler: Çalışma prospektif olarak yapılmış olup, çalışma grubuna akut bakteriyel enfeksiyon tanısıyla yatan 65 yaş ve üzeri hastalar, enfeksiyon dışında herhangi bir nedenle hastaneye yatırılan hastalar ise kontrol grubu olarak dahil edilmiştir. Her iki gruba da EuroQoL-5D-5L (EQ-5D-5L) yaşam kalitesi ölçeği uygulanmıştır. Nötrofil CD15 (nCD15) ve CD64 (nCD64) ile monosit CD64 (mCD64) seviyelerini ölçmek için kan örnekleri alınmıştır. Çalışma grubunda Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) puanı hesaplanmıştır. Yirmi sekiz günlük takip süresi boyunca elde edilen veriler kaydedilmiştir. Veri analizi SPSS 26 programıyla yapılmıştır. Kategorik değişkenlerin karşılaştırılmasında Pearson'un Ki Kare testi kullanılmıştır. p<0.05 anlamlı kabul edilmiştir.

Bulgular : Çalışma grubuna 168 hasta, kontrol grubuna ise 70 hasta dahil edildi. EQ-5D-5L yaşam kalitesi indeksi, EQ-5D-5L VAS skoru, toplam lökosit sayısı, nCD64 değeri, nCD15 değeri, mCD64 değeri çalışma grubunda anlamlı olarak yüksekti. Yirmi bir (%12,5) hasta kaybedildi. Lojistik regresyon analizine göre 7. gündeki SOFA skor değerinin hayatta kalma ile ilişkili en önemli parametre olduğu belirlendi.

Sonuç: Enfeksiyon gelişen yaşlı hastaların takibinde SOFA skorunun izlenmesinin spesifik ve spesifik olmayan laboratuvar testlerine göre daha faydalı olduğu bulunmuştur.

Anahtar Kelimeler: Geriatrik enfeksiyonlar, EQ-5D-5L, akım sitometri, SOFA skoru

Introduction

In todays world, the elderly population in society is increasing with access to safe water and food, better living conditions, and the development of new diagnosis and treatment methods for various diseases. In older people, the immune system begins to respond more slowly and weakly to the antigens it encounters, and the body's resistance to infectious diseases decreases. This situation is due to the fact that the elderly have malnutrition and chronic diseases; It is associated with deterioration of functional status and decreased quality of life (QoL). These factors lead to higher healthcare utilization and thus colonization with hospital-acquired bacteria with multidrug resistance. Therefore, older people are prone to developing infections (1,2).

Infectious diseases may present with different clinical and laboratory findings in older people compared to younger people. Delays in diagnosis and treatment may cause a worse clinical course in older individuals. It prolongs hospital stay, increases mortality rate and treatment costs. Therefore, there is a need for indicators that will enable rapid and specific diagnosis and can also be used to determine prognosis (3,4). Today, the Sequential Organ Failure Assessment Score (SOFA) is used as a common indicator to predict prognosis in patients who develop sepsis. However, the effectiveness of the SOFA score has generally been evaluated in patients under the age of 65 and in patients monitored in intensive care units. Acute phase reactants such as CRP and procalcitonin have also been reported to be useful in diagnosis and monitoring (5). Recently, studies investigating the value of flow cytometry and leukocyte indicators in determining the diagnosis and prognosis of sepsis are presented(6-9). Flow cytometry is routinely used in the field of hematology and immunology, but is not used in the field of infectious diseases.

Developed by the EuroQoL Group, the EuroQoL-5D (EQ-5D) questionnaire is one of the most widely used quality of life scales (2). It has been reported in the literature that it is useful in predicting hospitalization and mortality in older people. However, its value in determining the prognosis of infections developing in these patients has not been investigated. In this study, the value of SOFA score, neutrophil CD15 (nCD15) and CD64 (nCD64), monocyte CD64 (mCD64) indicators, and EQ-5D-5L quality of life scale in determining diagnosis and prognosis in elderly patients hospitalized with a diagnosis of acute bacterial infection were investigated.

Material and methods

This study was conducted prospectively with the approval of the local ethics committee numbered 2022/94 and dated 25.5.2022. Between June 1, 2022 and June 1, 2023, 168 patients aged 65 and over who were hospitalized with a diagnosis of acute bacterial infection in the Infectious Diseases clinic and 35 control patients hospitalized in the Internal Medicine clinic for a reason other than infection were included in the study.Infection diagnosis; Symptoms such as high fever, purulent sputum production, increased skin temperature, redness and pus, watery and frequent defecation, dysuria, pollakiuria; It is diagnosed by isolating the agent with bacteriological culture in addition to findings such as meningeal irritation, hearing cracks and rhonchi on lung auscultation.

Criteria for inclusion in the study were:

1.Being sixty-five years of age or older and agreeing to participate in the study

2.For the study group, being hospitalized with infectious disease,

3.For the control group, being hospitalized for a reason other than infectious disease

Criteria for exclusion from the study were:

1.Patients with natural and acquired immunodeficiency

2.Patients receiving chemotherapy, immune modulator therapy, radiotherapy

3.Patients diagnosed with viral infection

4.Patients who can not evaluate and answer the Q-5D quality of life scale questions

During their first hospitalization, age and gender demographic data, underlying diseases (hypertension, chronic obstructive pulmonary disease, diabetes mellitus, congestive heart failure, chronic renal failure, cerebrovascular diseases) of the patient and control groups were recorded and the Charlson comorbidity index (CCI) was calculated. The Turkish version of the 5 level EQ-5D scale developed by EuroQol Group was applied to both the study and control groups in a face-to-face interview (permission was obtained from EuroQol Group, registration no:56864). The EQ-5D-5L basically consists of 2 pages: the EQ-5D descriptive system and the EQ visual analog scale (EQ VAS). The descriptive system consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, mild problems, moderate problems, severe problems and extreme problems. The patient is asked to indicate his or her health status by checking the box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number representing the level selected for that dimension. The digits of the five dimensions can be combined into a 5-digit number that describes the patient's health status.

The EQ VAS records the patient's self-rated health on a vertical visual analogue scale where the endpoints are labeled 'The best health you can imagine' and 'The worst health you can imagine'. VAS can be used as a quantitative measure of health outcome that reflects the patient's own judgment (7-9).

Once again, on the first day of hospitalization, blood samples were taken to measure neutrophil CD15 and CD64 and monocyte CD64 levels using hemogram, routine biochemistry and flow cytometry methods. In the patient group, Charlson Comorbidity Index (CCI) and SOFA score were calculated on the first day of admission and on the 3rd and 7th days. Blood samples were taken for leukocyte (/mm³) and CRP values (0-5 mg/L) on the first day of hospitalization, on the 3rd and 7th days of hospitalization, and on the 3rd and 7th days of hospitalization. A case follow-up form containing the data obtained during the twenty-eight-day follow-up period, the focus of infection and survival status was filled out.

Flow cytometric method

A flow cytometry device (BeckmanCoulter, Dxflex, United States) with 3 lasers, 8 colors and 10 parameters was used to examine nCD15 and nCD64 and mCD64 indicator values in peripheral blood. For analysis, a 2 ml EDTA peripheral blood sample was taken and all samples were analyzed within 6 hours after collection. AntiCD45–APC, antiCD15-PC5, antiCD4-FITC fluorescent dyes were used. For each patient, the indicator values of nCD15, nCD64 and mCD64 are expressed as the median of fluorescence intensities (MFI).

Statistical Analysis

Statistical analyzes were performed with IBM® SPSS® 26 (SPSS Inc., Chicago, IL, USA). The conformity of the variables to the normal distribution was examined using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive analyzes were given as mean ± standard deviation, median, IQR, and min-max for continuous data. Descriptive statistics were made by giving frequency and percentage values of categorical variables obtained from sociodemographic and clinical information. In continuous data (age, index score etc.), t-test was used for independent groups when it showed normal distribution, and Mann-Whitney U test was used when there was non-parametric distribution to compare binary groups (ex vs. alive). Pearson's or Fisher's exact chi-square tests were used to compare categorical variables. The model was developed with logistic regression (using enter and backwards methods) analysis to determine mortality predict parameters. A p-value below 0.05 were considered statistically significant.

Results

168 patients who met the inclusion criteria were included in the study group. Six patients were excluded due to Covid-19 infection, two patients were receiving chemotherapy, and two patients were excluded due to acquired immunodeficiency. Seven patients were not included in the study because they could not evaluate and answer the EQ-5D survey questions. In the study group, 96 (57.1%) were men and 72 (42.9%) were women, and the average age was 73.8±7.

In the study group, the types of infections were soft tissue infection (59 patients, 35.1%), urinary tract infection (56 patients, 33.3%), pneumonia (34 patients, 20.2%), internal abdominal infection (9 patients, 5.4%), gastroenteritis (7 patients, 4.2%) and acute purulent meningitis (3 patients, 1.8%) and 70 patients are included in the control group. None of these patients had signs or symptoms of infectious disease.

Thirty-two (45.7%) are men and 38 (54.3%) are women. Comparison of the study group and control group in terms of demographic characteristics, disease scores and laboratory parameters is shown in Table 1.

Table 1. Demographic characteristics, disease scores and laboratory parameters of the study group and control group

Variables	Groups	N	Mean	Std. Deviation	Std. Error Mean	p value
Age	Control	35	73,5	6,4	1,1	0,801
	Patients	168	73,8	7,0	0,5	
CCI	Control	35	5,2	1,0	0,2	**0,041***
	Patients	168	4,8	1,9	0,1	
EQ-5D-5L Index	Control	35	0,678	0,2	0,0	***0,008****
	Patients	168	0,459	0,3	0,0	
EQ-5D-5L VAS Score	Control	35	76,6	13,2	2,2	***0,001****
	Patients	168	60,0	27,4	2,1	
Total leucocyte count D0	Control	35	7533,5	1859,1	314,2	***<0,0001****
	Patients	168	13427,8	8524,0	657,6	
nCD64 (MFI)	Control	35	3016,4	3649,0	616,8	***<0,0001****
	Patients	168	6304,1	5034,9	388,5	
nCD15 (MFI)	Control	35	10192,4	2951,3	498,9	**0,009***
	Patients	168	9917,1	9848,1	759,8	
mCD64 median (MFI)	Control	35	19245,3	9247,9	1563,2	***<0,0001***
	Patients	168	30242,3	11976,8	924,0	

*t test and *Mann-Whitney U test were applied in independent groups p<0.05 is statistically significant.*

Among these variables, EQ-5D-5L index (p: 0.008), EQ-5D-5L VAS score (p=0.001), leukocyte count (p<0001), nCD64 value (p<0.0001), nCD15 value (p=0.009), mCD64 value (p<0.0001) was significantly higher in the study group.

Twenty one (12.5%) patients died during clinical follow-up. EQ-5D-5L index (p<0.0001), EQ-5D-5L VAS score (p<0.0001), SOFA score on day 0 (p<0.0001), SOFA score on day 3 (p<0.0001), SOFA score on day 7 (p<0.0001), leukocyte day 7 (p:0.027), CRP day 7 (p= 0.002), lactate (p=0.007), nCD64 (p: 0.002) values were found to be significant in predicting survival. Table 2 shows the comparison of the study group in terms of age, disease scores and laboratory parameters and its relationship with survival.

Table 2. Age, laboratory findings and disease scores of patients who survived versus did not survive (mean ± standard deviation)

variables	Groups	N	Mean	Std. Deviation	Std. Error Mean	p Value
Age	Non-survivors	21	76,48	7,763	1,694	0,058
	Survivors	147	73,39	6,812	0,562	
CCI	Non-survivors	21	5,33	2,373	0,518	0,311
	Survivors	147	4,78	1,790	0,148	
EQ-5D-5L Index	Non-survivors	21	-0,10110	0,253735	0,055369	***<0,0001***
	Survivors	147	0,41843	0,311130	0,025662	
EQ-5D-5L VAS Score	Non-survivors	21	26,62	24,638	5,377	***<0,0001***
	Survivors	147	64,76	24,317	2,006	
SOFA Score D0	Non-survivors	21	3,29	1,488	0,325	***<0,0001***
	Survivors	147	1,57	1,395	0,115	
SOFA Score D3	Non-survivors	21	5,67	1,770	0,386	***<0,0001***
	Survivors	147	1,40	1,715	0,141	
SOFA Score D7	Non-survivors	16	7,38	2,029	0,507	***<0,0001***
	Survivors	147	0,74	1,117	0,092	
Total leucocyte count D0	Non-survivors	21	13016,19	6418,247	1400,576	0,814
	Survivors	147	13486,61	8799,919	725,805	
Total leucocyte count D3	Non-survivors	21	10507,62	3149,476	687,272	0,433
	Survivors	147	9574,69	5299,067	437,060	
Total leucocyte count D7	Non-survivors	16	11765,00	5943,061	1485,765	***0,027***
	Survivors	147	8087,54	2815,534	232,221	
CRP D0	Non-survivors	21	121,48	89,042	19,431	0,060
	Survivors	147	168,99	109,791	9,055	
CRP D3	Non-survivors	21	121,38	72,441	15,808	0,388
	Survivors	147	104,95	82,513	6,806	
CRP D7	Non-survivors	18	124,50	83,996	19,798	***0,002***
	Survivors	147	53,80	50,416	4,158	
Lactate	Non-survivors	21	2,467	1,5907	0,3471	***0,007***
	Survivors	147	1,414	0,7965	0,0657	
nCD64 median	Non-survivors	21	3883,524	3355,9658	732,3318	***0,002***
	Survivors	147	6649,888	5146,8913	424,5084	
nCD15 median	Non-survivors	21	11784,19	4908,867	1071,203	0,355
	Survivors	147	9650,41	10347,075	853,412	
mCD64 median	Non-survivors	21	28558,62	5594,790	1220,883	0,493
	Survivors	147	30482,84	12622,317	1041,071	

*t test and *Mann-Whitney U test were applied in independent groups. p<0.05 is statistically significant.*

According to logistic regression analysis, SOFA score on day 7 (p= 0.000, WALD: 18.991, Exp(B): 0.270, 0.150-0.486 with 95% confidence interval) was found to be the most important parameter associated with survival.

Discussion

There is a need for new indicators that will enable rapid and specific diagnosis of infectious diseases in older people and can also be used to determine prognosis (8). In this study, leucocyte count, neutrophil CD64, nCD15, mCD64 values were found to be higher in geriatric patients hospitalized with a diagnosis of acute bacterial infection than in non-patients. CD64 is an integral membrane glycoprotein, also known as an Fc receptor, that binds monomeric IgG-type antibodies with high affinity. It is found constitutively in macrophages and monocytes. High detection of CD64 in these cells represents activation and phagocytosis in the innate immune response. Therefore, CD64 levels on neutrophils and monocytes can be used as evidence of infection (8-12). The data obtained in the study support this. There are publications reporting that the neutrophil CD64 level is valuable in the diagnosis and prognosis of sepsis in newborns and intensive care patients (9-11). However, there are few studies investigating its value in diagnosing infection and determining prognosis in geriatric patients, a difficult patient group for clinicians. Otsuki et al. reported that the sensitivity of the neutrophil CD64 >2000 molecule level in the diagnosis of infectious disease was 88% and the specificity was 63% in older patients diagnosed with infectious disease (8). In this study, they reported that the quantitative level of neutrophil CD64 was useful in the early diagnosis of geriatric infections. In our study, in addition to these data, the quantitative level of CD64 on monocytes in older people was also found to be useful in the diagnosis of infectious diseases. Detecting CD64 levels on neutrophils and monocytes by flow cytometry, which is a rapid and accessible method, can protect geriatric patients from unnecessary antibiotic use and the development of bacterial resistance. Nong et al. found the neutrophil CD64 fluorescence intensity value to be significant in the diagnosis of pneumonia in elderly patients ($p<0.05$) (12). This study found that nCD64 fluorescence levels gradually decreased in surviving severe pneumonia cases, and in deceased individuals, the fluorescence level continued to increase and reached a peak at the time of death. There is also a need for studies to investigate the relationship between serial measurements of CD64 levels and prognosis in geriatric patients who develop infectious diseases.

Many laboratory parameters have been used in the diagnosis of infectious diseases in geriatric patients, and the most common ones are leukocytosis, neutrophilia, and left shift in the myeloid series, which are evaluated together and do not have high sensitivity. An increase in CRP level in serum is a simple and practical indicator in the diagnosis of bacterial infection (8,9,13). First, in 1986, Cox et al. found that basal CRP levels were higher in deceased individuals than in survivors (14).

In a subsequent study, it was reported that CRP levels were significant for short-term mortality in nursing home patients who developed pneumonia (15). In another study, CRP value was found to be significant in predicting mortality in patients who developed nosocomial sepsis at an older age (16). In our study, the CRP value on the 7th day was found to be significant in predicting survival in patients who developed infection at an older age. Otsuki et al. reported the sensitivity of CRP as 96% and its specificity as 10% in distinguishing infection in elderly individuals (8). Recently, the importance of procalcitonin in the diagnosis of infectious diseases has been mentioned. Zinciroğlu et al. reported that procalcitonin was more valuable than CRP in detecting infection and sepsis in elderly patients treated in the intensive care unit ($p < 0.001$) (17). Wang et al. found CRP and procalcitonin to be significant in determining severe pneumonia and survival in patients who were older and developed community-acquired pneumonia. However, procalcitonin is more significant in this study ($p<0.05$) (18). Since procalcitonin is a high-cost test, it is used more in units where critically ill patients are monitored, such as neonatal and intensive care units. The use of flow cytometry in the field of infectious diseases may play a different role from new molecular tests that are not routinely available, such as procalcitonin and sTREM-1, as a practical and rapid diagnostic method (18).

It has been reported that quality of life assessment with EQ-5D is useful in the field of infectious diseases such as HIV/AIDS and prolonged COVID-19 infection, as well as many chronic diseases (19,20). Cavrini et al. reported that the EQ-5D index was associated with the first hospitalization in older patients (2). Linn et al. reported that the EQ-5D-3L index in 102 patients admitted to the acute geriatric ward increased from 0.440 at admission to 0.648 at discharge ($p < 0.001$) (21). While the EQ-VAS score was 60 at admission, it increased to 70 at discharge ($p < 0.001$). The findings are associated with significant improvement of physical, cognitive function, frailty parameters and nutritional status at admission during hospitalization. In older patients, dynamic monitoring of the EQ-5D index during hospitalization during pre-admission and post-discharge checks may be useful to improve clinical practices.

According to logistic regression analysis in our study, the SOFA value on the 7th day is the most important indicator in determining survival. In the follow-up of older patients who develop infection, monitoring of respiratory, cardiovascular, hepatobiliary, coagulation, neurological and renal functions, which constitute the SOFA criteria, has been found to be more useful than specific and non-specific laboratory tests. Although studies evaluating geriatric sepsis patients separately are rare, it has been reported in many studies that the SOFA score at the time of diagnosis and the increase in the score predict mortality in patients who develop sepsis (22-24). Along with the SOFA score, there are also studies addressing specific laboratory parameters and other disease scores.

Chen et al. reported that evaluating nCD64 value and SOFA score together in adult patients is more useful in diagnosing sepsis and determining survival (9). The Charlson comorbidity index is a validated, simple, easy, old method to estimate the risk of death from comorbidity and is widely used as a predictor of long-term survival. It has been shown to be useful in determining survival in patients diagnosed with infection in both clinics and intensive care units (25). However, in patients who are older and develop infection, monitoring vital, clinical and laboratory parameters together has been found to be more useful than classification of comorbid conditions in predicting 28-day survival.

As a result, in the light of the data obtained in our study, EQ-5D-5L index, EQ-5D-5L VAS score, leukocyte count, nCD64, nCD15, mCD64 values were found to be useful in the differential diagnosis of acute bacterial infection in older patients. The most useful parameter in predicting 28-day survival was determined to be the SOFA score on day 7. The limited aspect of our study is; this is due to the relatively small number of patients because we included a specific patient group.

It is also a strength that there are few studies in the literature on the place of EQ-5D-5L quality of life scale and flow cytometry in the diagnosis and follow-up of infections developing in the geriatric age group. It draws attention to the use of quality of life scale and flow cytometry applications in the field of geriatric infectious diseases.

Financial support and sponsorship

This study was supported by the Erişkin Asi Dernegi (Izmir/Turkey).

Conflicts of interest

There are no conflicts of interest.

Acknowledgments: Authors thank to Eren Uzeken and Hatice Deniz for their help in the flow cytometry laboratory.

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Ege Klin Tıp Derg 2024;62 (1): 41-46

Our Central Venous Port Catheter Experiences

Santral Venöz Port Katater Deneyimlerimiz

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Öz

Amaç: Kliniğimizde onkolojik hastaların tedavi süreçlerinde kullanılmak üzere uygulanan venöz port katater takılması deneyimlerimizi sunmayı amaçladık.

Gereç ve Yöntemler: Kliniğimiz tarafından 01.01.2020 – 01.06.2023 tarihleri arasında onkolojik tedavide kullanılmak üzere santral venöz port katater takılan 18 yaş üzeri hastalar çalışmaya dahil edildi. Hastaların demografik verileri ile onkolojik hastalıkları, venöz port katater uygulanma şekli, kataterin yerleştirildiği vasküler yapı, işlem süresi, işleme bağlı peroperatif ve postoperatif komplikasyonlar, kataterin kullanım süresi, katater çıkarıldı ise çıkarılma sebepleri kayıt altına alındı. Elde edilen veriler istatistiksel olarak değerlendirildi.

Bulgular: Çalışmaya dahil edilen 540 hastanın 311'i (%57,6) erkek, 229'u (%42,4) kadındı. Yaş ortalaması 60,33±11,41 olup erkeklerde ortalama yaş 60,86±10,82; kadınlarda ise 59,62±12,16 olarak izlendi. Çalışmaya dahil edilen vakalar içinde en sık gastrointestinal sistem maligniteleri (n=347 %64.25), ikinci sıklıkta ise meme maligniteleri izlenmiştir (n=64 %11.85). En sık port takılan bölge sağ juguler ven iken, en az takılan bölge sol subklavien ven olarak izlenmiştir. 6 (%1,1) hastada ise işlem başarısız olmuş ve port takılamamıştır. Bu vakalardan birinde hastanın genel durum bozukluğu sebebiyle (dispne) işleme son verilirken, 5 vakada ultrasonografi (USG) eşliğinde işlem denenmesine rağmen başarısız olunmuştur. Hastaların yalnızca 19'unda işlem sırasında USG gereksinimi olmuştur. İşlem sırasında ve sonrasında 117 (%21,7) vakada komplikasyon gelişirken en sık izlenen komplikasyon venöz ponksiyon yapmada zorluk olarak izlendi. Sağ subklavien portlarda komplikasyon gelişme oranı, sağ juguler portlara göre yüksek saptanmıştır (p:0.001). Her iki port yerinde de en sık izlenen komplikasyon tipi venöz ponksiyon yapmada zorluk olarak izlenmişken komplikasyon türleri açısından iki port yeri arasında anlamlı farklılık saptanmamıştır (p:0,062).

Sonuç: Santral venöz port katater onkoloji hastalarının kemoterapi tedavisinde oldukça kolay kullanılabilir ve konforlu bir uygulama yöntemidir. Santral venöz port katater hastaya uygulanma şekli açısından da oldukça güvenli bir yöntemdir ve tecrübe arttıkça komplikasyon oranları da daha düşük olmaktadır.

Anahtar Kelimeler: Kemoterapi, kataterizasyon, port, venöz

Abstract

Purpose: We aim to present our experiences in venous port catheter insertion for use in the treatment processes of oncological patients in our clinic.

Material and Methods: Patients over the age of 18, who had a central venous port catheter inserted for use in oncological treatment by our clinic between 01.01.2020 and 01.06.2023, were included in the study.

The demographic data of the patients, their oncological diseases, the method of venous port catheter application, the vascular structure in which the catheter was placed, the duration of the procedure, peroperative and postoperative complications related to the procedure, the duration of use of the catheter, and the reasons for removal if the catheter was removed were recorded. The obtained data were evaluated statistically.

Results: Of the 540 patients included in the study, 311 (57.6%) were male and 229 (42.4%) were female. The average age is 60.33±11.41, and the average age for men is 60.86±10.82; In women, it was observed as 59.62±12.16. Among the cases included in the study, gastrointestinal system malignancies were the most common (n=347, 64.25%), and breast malignancies were the second most common (n=64, 11.85%). While the most common port insertion site was the right jugular vein, the least frequent port insertion site was the left subclavian vein. In 6 (1.1%) patients, the port procedure failed and the port could not be inserted. In one of these cases, the procedure was discontinued due to the patient's poor general condition (dyspnea), while in 5 cases, the procedure was unsuccessful even though the procedure was tried under USG guidance. While only 19 patients required USG during the procedure, USG-guided catheterization was successful in 14 (73.7%) cases. While complications developed in 117 (21.7%) cases during and after the procedure, the most common complication was difficulty in performing venous puncture. The complication rate in right subclavian ports was found to be significantly higher than in right jugular ports (p: 0.001). While the most common type of complication in both port locations was difficulty in performing venous puncture, no significant difference was detected between the two port locations in terms of complication types (p:0.062).

Conclusion: Central venous port catheter is a very easy to use and comfortable application method in the chemotherapy treatment of oncology patients. Central venous port catheter is a very safe method in terms of how it is applied to the patient, and as experience increases, complication rates decrease.

Keywords: Chemotherapy, catheterization, port, venous

Giriş

Tamamen implante edilebilen santral venöz port kataterler (TİSEP) özellikle onkolojik tedavi gören hastaların uzun süreli tedavilerinde kullanılmakla birlikte uzun süreli antibiyotik tedavisi gereken, enteral beslenme sorunu yaşayan ve parenteral beslenme uygulanan, tekrarlayan kan örneklemesi yapılan ancak periferik damarlara ulaşmakta zorluk çekilen hastalarda da kullanılmaktadır. TİSEP ilk olarak 1982 yılında Niederhuber ve arkadaşları tarafından kullanılmış ve o günden bu yana özellikle onkolojik tedavi gören hastaların tedavilerinde rutin olarak tercih edilmeye başlanmıştır (1,2).

Klinik uygulamada TİSEP sıklıkla internal juguler ven (IJV) ve subklavien vene (SCV) uygulanmaktadır. Çok daha nadir olarak diğer venlerin uygun olmadığı hastalarda femoral vene de TİSEP uygulaması yapılabilmektedir (2,3).

TİSEP kullanımı hastalarda konfor sağlamaktadır. Ancak, işleme bağlı çeşitli komplikasyonlarda gelişebilmektedir. Komplikasyonları erken ve geç komplikasyonlar olarak sınıfladığımızda erken komplikasyonlarda arter ponksiyonu yapılması, pnömotoraks, aritmi, hemotoraks ve hava embolisi gelişmesi sayılabilir. Geç komplikasyon olarak ise katater içi trombüs gelişimi, cilt rüptürü, enfeksiyon gelişimi, katater migrasyonu görülebilmektedir (2,4).

Bu çalışmamızda kliniğimizde uygulanan TİSEP deneyimlerimizi ve hastaların izlemleri sırasında karşılaşılan komplikasyonları sunmayı amaçladık.

Materyal- Metod

Kliniğimiz tarafından 01.01.2020 – 01.06.2023 tarihleri arasında onkolojik tedavide kullanılmak üzere TİSEP uygulanan 18 yaş üzeri 540 hasta çalışmaya dahil edildi. Hastaların demografik verileri ile onkolojik hastalıkları, venöz port katater uygulanma şekli, kataterin yerleştirildiği vasküler yapı, işleme bağlı peroperatif ve postoperatif komplikasyonlar, kataterin kullanım süresi, katater çıkarıldı ise çıkarılma sebepleri kayıt altına alındı. Kliniğimizde işlem uygulanan ancak verilerine ulaşılamayan, takip süreçleri bilinmeyen hastalar çalışma dışında bırakıldı.

Cerrahi Prosedür

Tüm hastalara işlem öncesi hemogram, protrombin zamanı (PT), aktive parsiyel tromboplastin zamanı (aPTT), international normalized ratio (INR) ve akciğer grafisi tetkikleri uygulandı. Tüm hastalara ameliyathanede rutin cerrahi asepsi sağlanarak supin pozisyonda işlem uygulandı. Tüm hastalarda uygulama için öncelikle sağ İJV tercih edildi. Hastanın başı işlemin yapılacağı yönün karşı tarafına çevrildi. Geçirilmiş boyun cerrahisi, boyun hareketlerinde kısıtlılık ya da çeşitli sebepler ile güvenli şekilde sağ İJV den ponksiyon yapılamayacağı düşünülen hastalarda sol İJV ya da SCV işlem için tercih edildi. Hastalara işlem sırasında periferik oksijen saturasyonu (SPO2), elektrokardiyografi (EKG) ve kan basıncı monitorizasyonu uygulandı. Port seti içerisinden çıkan katater, port tamburu, ponksiyon iğnesi, rehber tel ve dilatatör içerisinden heparin solusyonu (1 mL/100U) cerrahiden önce geçirilerek port katater hazırlandı.

Cerrah**,** hastanın baş kısmına yerleşerek ponksiyon yapılacak bölgeye lokal anesteziyi uyguladıktan sonra sternoklaidomastoid kaslarının oluşturduğu üçgenin üst kısmından ponksiyon iğnesi ile İJV'e ponksiyon uygulandı. Ponksiyon sonrası rehber tel damar içerisine gönderilerek kalp ritminde değişiklik olup olmadığı gözlendi. Daha sonra port tamburunun yerleştirileceği anterior pektoral bölgeye lokal anestezi uygulanarak 2 cm insizyon yapıldı. Port tamburu için cilt altı yağlı dokunun altına kas dokusunun üzerinde olacak şekilde bir cep oluşturuldu.

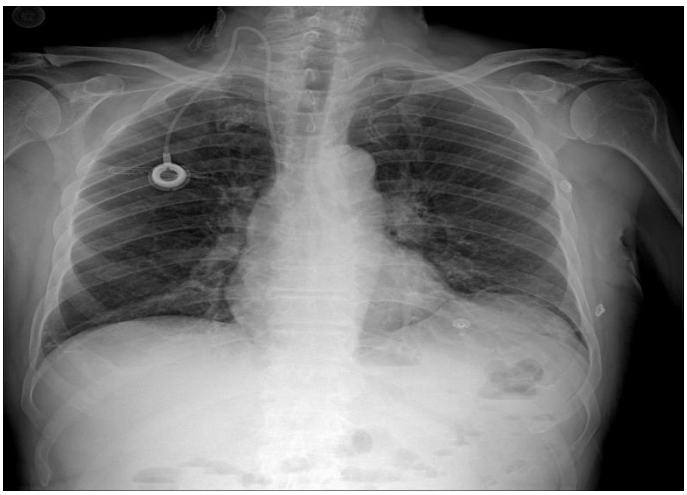
Boyunda ki rehber telin hemen yanından 0,5 cm insizyon yapılarak katater metal bir rehber ile cilt altından tamburdan boyun kısmına doğru yerleştirildi. Rehber tel üzerinden dilatatör gönderildikten sonra dilatatör içerisinden rehber tel çekilerek intravenöz kateter port İJV'e yerleştirildi. Port düzeneği Huber iğnesi ile kan alınarak denendi ve içerisinden heparinli solüsyon (1 mL/100U) uygulandı. İnsizyonlar absorbable suturler ile kapatıldı. İşlem sonrası çekilen direkt akciğer grafisinde patoloji saptanmayan hastalar aynı gün taburcu edildi (Resim 1). Ponksiyon yapılamayan ya da rehber tel ilerletilemeyen hastalarda öncelikle sağ SCV denendi. Bu işlemde klavikula alt uçtan ponksiyon iğnesi ucu juguluma bakacak şekilde ponksiyon yapılarak SCV e rehber tel yerleştirildi. Ponksiyon noktasının hemen alt kısmına da port tamburu yerleştirilerek cerrahi prosedür aynı şekilde uygulandı.

Ponksiyon denemeleri başarısız olan ya da rehber telin ilerletilemediği hastalarda ultrasonografi eşliğinde venöz yapılar görüntülenerek ultrasonografi rehberliğinde ponksiyon denendi. Venöz yapılar içerisinde trombüs görülmesi, ultrasonografi eşliğinde dahi ponksiyon yapılamaması durumlarında işlem sonlandırıldı.

İstatistiksel Analiz

Çalışmada elde edilen veriler istatistiksel olarak SPSS (Statistical Package for the Social Sciences Versiyon 22.0; SPSS Inc. Chicago, IL, USA) programı yardımıyla değerlendirildi. Sürekli değişkenler için basıklık ve çarpıklık düzeyleri ±2 arasında kalan değerler normal dağılım gösterdiği varsayıldı (5). Kategorik veriler sayı(n) ve yüzde(%) ile normal dağılım göstermeyen sürekli veriler medyan (25.-75. persantiller) ve normal dağılım gösteren sürekli veriler ise ortalama ±standart sapma ile sunuldu. Kategorik veriler arasındaki ilişki uygunluğuna göre Ki-Kare analizi, Fisher'in Kesin testi ile incelendi. Sürekli ve kategorik değişkenler arasındaki ilişki bağımsız gruplarda T testi ile incelendi. Yapılan analizlerde p değeri 0,05'in altında olan sonuçlar istatistiksel anlamlı kabul edildi.

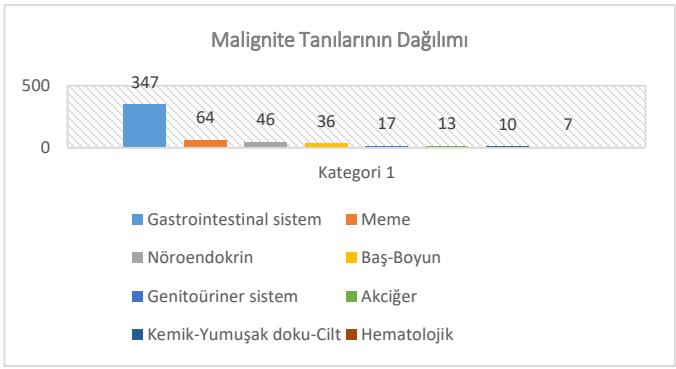
Çalışmamız, İzmir Katip Çelebi Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'nun 15.06.2023 tarih ve 0302 karar numaralı kararı sonrasında yapılmıştır.



Resim 1: Sağ juguler vene santral venöz port katater uygulanması sonrası çekilen akciğer grafisinde kataterin görünümü

Bulgular

Çalışmaya dahil edilen 540 hastanın 311'i (%57,6) erkek, 229'u (%42,4) kadındı. Çalışma popülasyonunun yaş ortalaması 60,33±11,41 olup erkeklerde ortalama yaş 60,86±10,82; kadınlarda ise 59,62±12,16 olarak izlendi. Hastaların tanılarına göre dağılımları Şekil 1'de sunulmuştur. Çalışmaya dahil edilen vakalar içinde en sık gastrointestinal sistem maligniteleri, ikinci sıklıkta ise meme maligniteleri izlenmiştir.



Şekil 1. Malignite tanılarının dağılımı

Çalışma popülasyonunda port yeri seçimi, işlem sırasında USG gereksinimi, komplikasyon gelişme durumu, portun aktif kullanılabilirliği, işlemin süresi ve hastanın hastanede yatış süreleri ile ilgili veriler Tablo 1'de sunuldu.

Buna göre en sık port takılan bölge sağ IJV iken en az takılan bölge sol SCV olarak izlendi. Hastaların 6'sında (%1,1) port işlemi başarısız oldu. Bu vakalardan birinde solunum sıkıntısı gelişmesi üzerine işleme son verilirken 5 vakada USG eşliğinde işlem denenmesine rağmen başarısız olundu. Yalnızca 19 hastada işlem sırasında USG gereksinimi olurken, 14 (%73,7) vakada USG eşliğinde katater başarılı bir şekilde yerleştirildi. İşlem sırası ve sonrasında 117 (%21,7) vakada komplikasyon gelişirken en sık izlenen komplikasyon venöz ponksiyon yapmada zorluk olarak izlendi ve bu hastalara multiple ponksiyon uygulamaları ile katater yerleştirme işlemi uygulandı. Diğer komplikasyonlar ise 34 hastada arter ponksiyonu, 13 hastada port yeri enfeksiyonu, 11 hastada pnömotoraks ve 3 hastada katater malpozisyonu ve 2 hastada ciddi aritmi olarak izlendi. Ciddi aritmisi olan hastalardan biri kardiyak arrest gelişmesi üzerine kısa süreli resüsitasyon uygulanması sonrası tekrar sinüs ritmine döndü.

Tablo 1. Çalışma popülasyonunda port ile ilişkili parametrelerin dağılımı

		n(%)
Port yeri	**Sağ Juguler**	460 (%85,2)
	Sağ Subklavien	70 (%13,0)
	Sol Juguler	3 (%0,6)
	Sol Subklavien	1 (%0,2)
	Port takılamadı	6 (%1,1)
İşlem sırasında USG ihtiyacı	**Hayır**	521 (%96,5)
	Evet	19 (%3,5)
Komplikasyon	**Yok**	421 (%78,8)
	Arter ponksiyonu	34 (%6,3)
	Ciddi aritmi	2 (%0,3)
	Port yeri enfeksiyonu	13 (%2,4)
	Venöz ponksiyon yapmada zorluk	56 (%10,4)
	Katater malpozisyonu	3 (%0,6)
	Pnömotoraks	11 (%2,0)
İşlem süresi (/dk)		20,0 (15,0-25,0)[a]
Yatış süresi	**1 günden kısa**	483 (%89,4)
	1 günden uzun	57 (%10,6)
Port aktif kullanım durumu	**Hayır**	38 (%7,0)
	Evet	502 (%93,0)

[a]: Medyan(25.-75. Persantil)

Başarılı şekilde port takılabilen 534 hastanın 32'sinde (%6,0) takip eden dönemde çeşitli nedenlerle TİSEP'in aktif kullanılamadığı izlendi.

Komplikasyon gelişimi ile çeşitli parametreler karşılaştırılmış olup Tablo 2'de sunulmuştur. Port yeri bakımından sol bölgeye TİSEP işlem sayısı yetersiz olduğu için karşılaştırmalı analizlere dahil edilmemiştir. Buna göre komplikasyon gelişimi bakımından yaş, cinsiyet ve malignite yeri açısından istatistiksel olarak anlamlı farklılık saptanmamıştır. En fazla komplikasyonun geliştiği izlenen GİS ve meme malignitelerindeki yükseklik, mevcut vaka sayılarının fazlalığına bağlanmıştır. Öte yandan her ne kadar istatistiksel anlamlılık izlenmese de malignite tanıları kendi içlerinde değerlendirildiğinde GÜS malignitesi ile TİSEP işlemi uygulanan 17 vakanın 7'sinde (%41,2) komplikasyon izlenmiş olup tanılar içinde en yüksek komplikasyon oranı bu hasta grubunda saptanmıştır. Sağ SCV portlarda komplikasyon gelişme oranı, sağ IJV portlara göre anlamlı olarak yüksek saptanmıştır.

Her iki port yerinde de en sık izlenen komplikasyon tipi venöz ponksiyon yapmada zorluk olarak izlenmişken komplikasyon türleri açısından iki port yeri arasında anlamlı farklılık saptanmamıştır (p:0,062).

Tablo 2. Komplikasyon gelişme durumuna göre parametrelerin dağılımı

			Komplikasyon gelişimi		p
			Yok	Var	
Yaş (/yıl)			60,14±11,36[a]	61,02±11,61[a]	0,463
Cinsiyet	**Erkek**		248 (%58,6)	63 (%53,8)	0,354
	Kadın		175 (%41,4)	54 (%46,2)	
Malignite yeri	**GİS**		270 (%63,8)	77 (%65,8)	0,591
	Meme		50 (%11,8)	14 (%12,0)	
	Nöroendokrin		37 (%8,7)	9 (%7,7)	
	Baş-Boyun		30 (%7,1)	6 (%5,1)	
	GÜS		10 (%2,4)	7 (%6,0)	
	Akciğer		12 (%2,8)	1 (%0,9)	
	Kemik-Yumuşak doku-Cilt		8 (%1,9)	2 (%1,7)	
	Hematolojik		6 (%1,4)	1 (%0,9)	
Port yeri	**Sağ juguler**		401 (%95,5)	59 (%53,6)	**0,001**
	Sağ subklavien		19 (%4,5)	51 (%46,4)	
Port aktif kullanım durumu		**Hayır**	22 (%5,2)	16 (%13,7)	**0,002**
		Evet	401 (%94,8)	101 (%86,3)	

GİS: Gastroİntestinal Sistem; **GÜS**: Genitoüriner Sistem; [a]: Ortalama±Standart Sapma.

Tartışma

Tamamen implante edilebilen santral venöz port kataterler (TİSEP) özellikle onkolojik tedavi gören hastalarda kolay ve güvenli bir şekilde intravenöz uygulanan kemoterapi tedavilerini almaları açısından önemli rol oynamaktadır. TİSEP hastalarda tedaviye sekonder periferik damar yolu bulma zorluğu açısından konfor sağlamakla birlikte periferik santral kataterlere göre venöz trombüs gelişme riskini azaltmaktadır (6). Taxbro ve arkadaşları (7) yaptıkları çalışmada periferik santral kataterlerde venöz tromboz riskini %8 olarak bulurken bu risk TİSEP uygulanan hastalarda %1 olarak saptamıştır.

TİSEP ilk olarak 1982 yılında John Niederhuber tarafından açık cerrahi yöntemi (cut down) ile sefalik vene uygulanmıştır (1,2,8). İlerleyen yıllarda onkolojik hastaların tedavilerinde yaygın kullanıma girmesi üzerine açık cerrahi yerine minimal invaziv bir girişim olan perkutan yolla uygulanmaya başlanmıştır (8). Biffi ve arkadaşları 1998 yılında yayınladıkları 333 vakalık serilerinde hastaların 297'sine perkutan yolla işlem uygularken, 36 hastaya cut down yöntemi ile katater uygulaması yapmışlardır. Çalışmamızdaki tüm hastalara perkutan olarak katater uygulaması gerçekleştirdik. Perkutan yolla uygulanan TİSEP de en çok tercih edilen vasküler yapılar İJV ve SCV dir.

Yanık ve arkadaşlarının (10) 3000 vakalık yayınladıkları serilerinde port katater yerleştirmek amaçlı hastalarının %70.33'ünde sağ İJV kullanılırken, %16.13'ünde sağ SCV'i kullanılmıştır. Buna karşın Moralar ve arkadaşları (11) hastalarının %96,8'inde sağ SCV'i tercih etmişler. Çalışmamıza dahil ettiğimiz hastaların %85.2'sinde port katateri yerleştirmek için sağ İJV'i kullanırken, %13'ünde sağ SCV'i kullandık.

Port katater uygulaması yapılırken hiçbir görüntülemeden yararlanmadan anatomik pozisyona göre vasküler yapının yerleşimine göre kör bir şekilde ponksiyon uygulanabileceği ve rehber tel yerleştirilerek aritmi oluşması ile yerimizin doğru olduğu anlaşılabileceği gibi USG eşliğinde vasküler yapı görülerek ponksiyon yapılabilir ve skopi eşliğinde rehber telin superior vena cava içerisine (SVC) yerleştiği de gösterilebilir. Yanık ve arkadaşları (10) çalışmalarında USG gereksinimini %1 olarak belirtirken, Saul ve arkadaşları (12) yayınlarında katater uygulaması sırasında USG kullanımın önemini, faydalarını ve önerdikleri kılavuzu paylaşmışlardır. USG ile işlem uygulanmasının işleme rehberlik yapması, pnömotoraks gelişimini değerlendirmesi ve kataterin ucunun konumunun belirlenmesi açısından önemli olduğunu vurgulamışlardır.

Çeşitli çalışmalarda farklılık göstermekle TİSEP genellikle meme ya da gastrointestinal tümörü olan ve bu sebeple uzun süreli onkolojik tedavi görmekte olan hastalarda kullanılmaktadır. İnce ve arkadaşlarının (2) yayınladıkları çalışmada TİSEP uyguladıkları hastaların %30,3'ü kolon kanseri, %16'sı mide kanseri, Salman ve arkadaşlarının (8) çalışmasında hastaların %27.9'u kolon kanseri, %14.1'i mide kanseri, Yanık ve arkadaşlarının (10) çalışmasında hastaların %25'i kolorektal kanser, %20'si meme kanseri, D'Souza ve arkadaşlarının (13) çalışmasında ise hastaların %39.7'si meme kanseri, %27.7'si kolon kanseri nedeniyle tedavi görmekteymiş. Çalışmamızda ise hastaların %64.25'i çoğunluğu mide ve kolorektal olmak üzere gastrointestinal sistem kanserleri ve %11.85'i meme kanseri nedeniyle tedavi görmekteydi.

TİSEP uygulanması kolay ve hasta konforu açısından önemli olmakla birlikte bazı komplikasyonlara da neden olabilmektedir. Bu komplikasyonları cerrahi sırasında meydana gelen erken dönem komplikasyonlar ve takip sürecinde ortaya çıkan geç komplikasyonlar olmak üzere sınıflandırabiliriz. Erken dönem komplikasyonlar içerisinde en sık karşılaşılan komplikasyonlar ponksiyonda yaşanan zorluk, arter ponksiyonu yapılması, aritmi, pnömotoraks, hemotoraks, cilt altı hematom, katater malpozisyonu olarak sayılabilir..

Geç komplikasyonlarda port yeri enfeksiyonu, port yerinde ciltte açılma, port kataterde tıkanma ve katater migrasyonu sayılabilir. İnce ve arkadaşları (2) yayınladıkları çalışmalarında en sık görülen erken komplikasyonları ponksiyonda zorlanma, arter ponksiyonu, pnömotoraks olarak, geç komplikasyonları da port tıkanması, superior vena cava sendromu, katater malpozisyonu olarak bildirmişlerdir. Yanık ve arkadaşları (10) ise erken dönem komplikasyonlardan en fazla arter ponksiyonu, geç dönem komplikasyonlardan port yerinde ciltte açılma gördüklerini bildirmişlerdir Port katater malpozisyonuda erken dönemde sebep genellikle işlemin bir görüntüleme yardımı olmaksızın yapılması ve kataterin vasküler yapı içerisine kör olarak gönderilmesidir. Geç dönemde ise malpozisyonun sebebi kataterin vasküler basınç değişikliklerine bağlı migrasyonu olarak söylenebilir. Gebauer ve arkadaşları (14) yayınladıkları 30 malpozisyonlu hastada; bir hastada katater malpozisyonunun kendiliğinden düzeldiğini, 27 hastada girişimsel radyoloji tarafından yapılan işlemler ile kataterin yerinin düzeltildiğini, 2 hastada ise malpozisyonun düzeltilemediğini bildirmişlerdir. Bazı çalışmalarda da tüm port katater komplikasyonları göz önünde bulundurulduğunda en çok gelişen komplikasyonların port yeri enfeksiyonu ve port tıkanması olduğu belirtilerek port katater çıkarılmasının en sık sebebi olarak da bu komplikasyonlar gösterilmiştir (11,13). Çalışmamızda da en çok görülen komplikasyon ponksiyon yapmada güçlük ya da arter ponksiyonu olarak öne çıkmaktadır. En önemli komplikasyonumuz ise bir hastamızda ciddi aritmiye sekonder kardiyak arrest gelişmesi ve resüsitasyon gereksinimi olmasıdır.

Sonuç

Sonuç olarak TİSEP uygulanması, özellikle onkolojik tedavi gören ve uzun süreli intravenöz tedavi ihtiyacı olan hastalarda tedavinin daha kolay, daha konforlu ve daha güvenli uygulanması açısından önemli bir işlemdir. Deneyimli ellerde herhangi görüntüleme işlemine ihtiyaç duymadan güvenli bir şekilde uygulanabilmektedir.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 47-52

Retrospective Evaluation of Cases with Fetal Abdominal Wall Defects Detected in the Intrauterine Period

İntrauterin Dönemde Fetal Batın Duvarı Defekti Saptanan Vakaların Retrospektif Olarak İncelenmesi

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Geliş Tarihi:14.02.2024
Kabul Tarihi: 25.03.2024

Abstract

Aim: It's aimed to evaluate the clinical features and prognosis of prenatally diagnosed fetal abdominal wall defects.

Material and Methods: Between the period of 2016-2021, the data of fetuses with abdominal wall defects were analyzed and compared in terms of maternal demographics, clinical characteristics, and pregnancy outcomes.

Results: 74 cases with fetal abdominal wall defects were diagnosed by ultrasonographic examination. 69% of the cases had omphalocele, 28% had gastroschisis, and 3% had body stalk anomaly. 36 (49%) of the cases chose the option of termination of pregnancy. 5 (7%) cases resulted in stillbirth and 3 (4%) cases resulted in missed abortion. 30 (41%) cases were followed up. Of the 13 (26%) omphalocele cases resulted in live birth, 2 (4%) were found to have neonatal exitus without being able to operated, 3 (6%) to have exitus during the intensive care unit period after the operation, 5 (10%) to be alive and healthy. Of the 17 (81%) gastroschisis cases that ended with live birth, 1 (5%) case was found to have neonatal exitus without any operation, 2 (10%) cases to have postoperative exitus, and 11 (52%) cases to be alive and healthy. The postnatal results of 3 (6%) cases with omphalocele and 3 (14%) cases with gastroschisis could not be able to obtained.

Conclusion: In this case series, although the postnatal survival rate was found to be higher in gastroschisis group than in omphalocele, the postnatal mortality rate was found to be higher in both groups when compared to the literature.

Keywords: Fetal abdominal wall defects, congenital anomaly, body stalk anomaly, gastroschisis, omphalocele

Öz

Amaç: Prenatal dönemde tanı konulan fetal batın duvarı defekti olgularının klinik özellikleri ve prognozunun değerlendirilmesi amaçlanmaktadır.

Gereç ve Yöntemler: 2016-2021 yılları arasında batın duvarı defekti olan fetüslerin verileri maternal demografik özellikleri, klinik bulguları ve gebelik sonuçları açısından analiz edilerek karşılaştırıldı.

Bulgular: Ultrasonografik değerlendirme ile fetal batın duvarı defekti olan 74 vaka teşhis edildi. Vakaların %69'unda omfalosel, % 28'inde gastroşizis, %3'ünde body stalk anomalisi mevcut idi. Vakalardan 36 (49%) tanesi gebelik terminasyonu seçeneğini kabul etti. 5 (7%) vaka ölü doğum, 3 (4%) vaka missed abortus ile sonuçlandı ve 30 (41%) vaka takip edildi. Canlı doğum ile sonuçlanan 13 (26%) omfalosel vakasından 2 (4%)'si doğum sonrası neonatal ölüm ve 3 (6%)'ü operasyon sonrası yoğun bakım sürecinde ölüm ile sonuçlandı. 5 (10%) olgu postnatal sağ ve sağlıklı idi. Canlı doğumla sonuçlanan 17 (81%) gastroşizis vakasından 1 (5%) olgu neonatal ölüm ve 2 (10%) olgu postoperatif ölüm ile sonuçlandı.

11 (52%) olgu sağ ve sağlıklı idi. Omfaloseli olan 3 (%6) ve gastroşizisli 3 (%14) olgunun postnatal sonuçlarına ulaşılamadı.

Sonuç: Bu olgu serisinde, gastroşizis grubunda doğum sonrası sağkalım oranı omfalosele göre daha yüksek bulunmasına rağmen, literatürle karşılaştırıldığında her iki grupta da postnatal mortalite oranının daha yüksek olduğu saptanmıştır.

Anahtar Kelimeler: Fetal batın duvar defekti, konjenital anomali, body stalk anomalisi, omfalosel, gastroşizis

Introduction

Gastroschisis and omphalocele are seen as the most common fetal abdominal wall defects. Less common ones are body-stalk anomaly, bladder and cloacal exstrophy (1). These anomalies can be easily detected by ultrasonographic examination in today's conditions (2). The incidence is estimated to be 1:4000 live births for omphalocele and 1:12,000 live births for gastroschisis (3).

Omphalocele is an anomaly resulting from herniation of abdominal internal organs into the base of the umbilical cord secondary to an unsuccessful fusion of the lateral folds during early embryonic development (4). Besides gastroschisis is a paraumbilical abdominal wall defect. Generally, intestines herniated from the right side of the umbilical cord are observed as free-floating in the amniotic fluid (5). It is important to distinguish between gastroschisis and omphalocele. Although they may have similar appearances on ultrasound, they have very different fetal and neonatal outcomes. Unlike gastroschisis, omphalocele may be associated with neurological, cardiac, pulmonary, and renal system anomalies as well as genetic syndromes (6,7).

Body stalk anomaly is the rarest, most severe, and always fatal abdominal wall defect. It is a serious defect in which the abdominal wall does not develop, so the peritoneal cavity is open to the extraembryonic coeloma and the fetus is attached to the placenta. It is generally not associated with chromosomal anomalies (8). It should be suspected when abnormalities of the axial skeleton such as kyphosis or scoliosis, and a short or missing umbilical cord are existing together with a large abdominal wall defect. Its incidence is 0.12 per 10,000 births (including live and stillbirths) (9).

In particular, antenatal diagnosis of these defects provides a potential opportunity to determine the mode, place, and time of the delivery and to ensure that birth occurs under optimal conditions in order to reduce postnatal complications. The aim of this study was to examine the natural history and detailed outcome of antenatally diagnosed abdominal wall defects.

Methods

Patients diagnosed with fetal abdominal wall defects who applied to the Department of Perinatology in Izmir Tepecik Training and Research Hospital between 2016 and 2021 were included in this retrospective cohort study. Data were collected by scanning the hospital database and phone calls with the parents to obtain information about the postnatal process and conditions of the babies.

Omphalocele was diagnosed when the fetal intra-abdominal organs herniated from the top of the umbilical cord and were surrounded by a membrane. It was observed that the diagnosis of gastroschisis was made when a normal umbilical cord and intestines floating in the amniotic fluid were seen, while the diagnosis of body stalk anomaly was made when a short or absent umbilical cord and kyphoscoliosis were present in addition to the abdominal wall defect. The cases were informed about their conditions, and upon parental request, fetal karyotyping was performed. Depending on the gestational age, chorionic villus biopsy, amniotic fluid, or cord blood samples were collected in order to perform fetal genetic tests. The families were informed about the possible poor fetal prognosis and the termination option was presented to the family in pregnancies below 22 weeks, and this was done according to the families' wishes. Close perinatological follow-up was performed on pregnant women who chose to continue their pregnancy. The cases were compared in terms of maternal demographics (age, gravida, parity), clinical characteristics (associating anomalies, karyotype result), and pregnancy outcomes (birth, termination of pregnancy, intrauterine death, postnatal prognosis).

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the University of Health Sciences Izmir Tepecik Training and Research Hospital (09.12.2022/ 2022/11-02.). Written informed consent was obtained from all of the patients.

Statistical Analysis

Statistical data were analyzed using the SPSS (Statistical Package for the Social Sciences) software program version 26.0. Categorical data were obtained by using frequency analysis and given as numbers and percentages. Numeric data were obtained by using descriptive analysis and presented as means, standard deviations, and minimum-maximum values.

Results

During the 5-year period, a total of 74 cases with abdominal wall defects were detected, of which 51 (69%) had omphalocele, 21 (28%) had gastroschisis, and 2 (3%) had body stalk anomaly (Table 1).

Table 1: Maternal demographics and fetal clinical characteristics of the cases

Case	n (%)	Mean±SD MA (min-max)	Mean±SD GA (min-max)	Parity (M/N)	Additional anomaly n(%)	Aneuploidy n(%)	TOP n(%)	Stillbirth n(%)	Delivery n(%)
Omphalocele	51 (%69)	30 ± 6,9 (17-43)	16,2 ± 3,7 (11-23)	33/18	30 (%59)	10 (%29)	31 (%60)	5 (%10)	13 (%26)
Gastroschisis	21 (%28)	24,8 ± 7,6 (16-39)	19,3 ± 4,8 (11-33)	9/12	5 (%24)	-	3 (%14)	-	17 (%81)
Body stalk anomaly	2 (%3)	29,5 ± 3,5 (27-32)	15,5 ± 2,12 (14-17)	1/1	2 (%100)	-	2 (%100)	-	-

GA,Gestational age; MA, Maternal age; M, Multiparous; max, maximum; min, minimum; N, Nulliparous; n, number of cases; SD, standard deviation; TOP, termination of pregnancy

Omphalocele

The mean maternal age in omphalocele cases was 30 ± 6,9 years (minimum 17 – maximum 43). The cases were diagnosed at the mean 16,25 ± 3,75 (minimum 11 - maximum 23) weeks of gestation. It was determined that 23 (45%) cases were diagnosed in the first trimester and 28 (55%) cases were diagnosed in the second trimester. 18 (35%) cases were primigravida and 33 (65%) cases were multiparous. 19 (37%) cases did not accept invasive fetal karyotyping. Of the 32 (63%) cases who accepted karyotyping, 2 (6%) cases had trisomy 21, 1 (3%) case had trisomy 13, 6 (19%) cases had trisomy 18, 1 (3%) case had Turner Syndrome (45 X0), and 22 (69%) cases were observed to have a normal karyotype. While omphalocele was found to be isolated in 21 (39%) cases, an associating anomaly was found in 30 (61%) cases.

The most common associating anomaly was the cardiovascular system anomaly (41%) (Table 2). 31 (60%) cases were terminated upon parental request. Of the terminated cases, 19 (37%) had additional serious anomalies, 10 (19%) had aneuploidy, and 2 (4%) had large abdominal wall defects involving both the liver and intestine. It was observed that 5 (25%) of 20 patients who were not terminated and continued their pregnancy had intrauterine demise and 2 (10%) had missed abortion. 13 (26%) cases resulted in live birth. It was determined that 2 (4%) cases had neonatal exitus without being able to operated, 3 (6%) cases had exitus during the intensive care unit period after the operation, and 5 (10%) cases were alive and healthy. Postnatal results of 3 (6%) cases could not be obtained.

Table 2: Relationship of cases with associating anomalies

Additional anomaly	Omphalocele n:51			Gastroschisis n: 21		Body Stalk Anomaly n:2
	Abnormal karyotype n: 10 n(%)	Normal karyotype n: 24 n(%)	Karyotype unknown n: 17 n(%)	Normal karyotype n: 17 n(%)	Karyotype unknown n: 4 n(%)	Normal karyotype n:2 n(%)
Central nervous system	1(2)	2(4)	3(6)	1(5)	-	2(100)
Respiratory system	-	1(2)	-	1(5)	-	-
Skeletal system	3(6)	1(2)	5(10)	2(9)	1(5)	2(100)
Cardiovascular system	4(8)	3(6)	14(27)	1(5)	1(5)	-
Genitourinary system	-	2(4)	2(4)	-	1(5)	-

Gastroschisis

It was observed that the mean maternal age in gastroschisis patients was 24,28 ± 7,6 years (minimum 16 - maximum 39). The mean gestational age of detection was observed to be 19,33 ± 4,88 (minimum 11 - maximum 33) weeks of gestation. It was determined that 2 (9%) cases were diagnosed in the first trimester, 18 (86%) cases in the second trimester, and 1 (5%) case in the third trimester. 12 (57%) cases were primigravida and 9 (43%) cases were multiparous.

Gastroschisis defect was located on the right in 17 (81%) cases and on the left in 4 (19%) cases. 4 (19%) cases did not accept invasive fetal karyotyping. It was observed that 17 (100%) cases who accepted karyotyping had normal karyotypes. It was determined that 16 (76%) cases had isolated gastroschisis and 5 (24%) cases had an associating anomaly.

Among the associating anomalies, the most common was the skeletal system anomaly (14%) (Table 2). 3 (14%) cases were terminated upon parental request, and these cases had additional anomalies; thoracic hypoplasia in 1 case, scoliosis and acrania in 1 case, and lymphangioma in 1 case. 1 (5%) case resulted in missed abortion (associated by cystic hygroma) and 17 (81%) cases resulted in live birth. Of the 17 cases who had live birth, 1 (5%) case had neonatal exitus, 2 (10%) cases had postoperative exitus, and 11 (52%) cases were alive and healthy. Postnatal results of 3 (14%) cases could not be obtained.

Body stalk anomaly

Maternal ages in body stalk anomaly cases were 27 and 32 (29,5 ± 3,5) years. The gestational ages that the anomaly detected were 14 and 17th (15,5 ± 2,12) gestational weeks. There were severe accompanying anomalies in all cases. Karyotype results were normal. Both cases were terminated upon the request of the parents.

Fetal and neonatal outcomes of the all cases were mentioned in the Table 3 according to being isolated or with additional anomaly/anomalies.

Table 3: Relationship between associating anomalies and fetal-neonatal outcome

	TOP n(%)	Missed abortion n(%)	Stillbirth n(%)	Neonatal exitus n(%)	Postoperative exitus n(%)	Alive n(%)	Unknown n(%)	Total n(%)
Omphalocele	31(60)	2(4)	5(10)	2(4)	3(6)	5(10)	3(6)	51(100)
• Additional anomalies	19(37)	1(2)	5(10)	1(2)	1(2)	3(6)	0	30(59)
• Isolated	12(23)	1(2)	0	1(2)	2(4)	2(4)	3(6)	21(41)
Gastroschisis	3(14)	1(5)	0	1(5)	2(10)	11(52)	3(14)	21(100)
• Additional anomalies	3(14)	1(5)	0	0	0	1(5)	0	5(24)
• Isolated	0	0	0	1(5)	2(10)	10(47)	3(14)	16(76)
Body stalk anomaly	2(100)	0	0	0	0	0	0	2(100)

TOP, termination of pregnancy

Discussion

We have retrospectively evaluated and compared the fetal and neonatal outcomes of pregnancies with prenatal diagnosis of fetal abdominal wall defects. Schmidt et al. (10) showed that from the 5th to the 12th week of pregnancy, most of the intestines develop rapidly and are physiologically located outside the abdominal cavity. Therefore, caution should be exercised when diagnosing abdominal wall defects before the 12th week. If the liver is visible outside the abdominal cavity, this usually does not regress and may be a sign of early omphalocele (11). In our study, there were two omphalocele and one gastroschisis cases diagnosed at the 11th week. The omphalocele case was accompanied by serious anomalies such as cystic hygroma and ectropia cordis, and the gastroschisis case was accompanied by serious anomalies such as hypoplastic thorax.

Goldbaum et al. (12) found that the risk of gastroschisis increased 4-fold with maternal age below 20 years. Omphalocele appears to be associated with older maternal age (13). In our study, the mean maternal age was 21 years in the gastroschisis group and 31 years in the omphalocele group. Roeper et al. (13) found that gastroschisis was associated with low parity. Most (57%) of our pregnant women with gastroschisis were primigravida, too.

Nicoloides et al. (14) didn't detect any chromosomal anomaly in any of the 26 gastroschisis cases in their study. In our study, karyotyping was performed in 12 of 21 gastroschisis cases and no chromosomal anomalies were found in any of them, including those with additional anomalies. However, the possibility of structural and chromosomal anomalies is high in omphaloceles (15). Therefore, in prenatal examination in cases of omphalocele, performing comprehensive prenatal ultrasound along with fetal echocardiography is important for the detection of structural anomalies. Fetal karyotyping should be recommended to detect associated chromosomal anomalies. The most common chromosomal anomalies are trisomies (18, 13, 21), Turner syndrome, and triploidies (16). In our study, the most common chromosomal anomalies in the omphalocele group were trisomies, and among the trisomies, trisomy 18 was seen as the most common aneuploidy.

There is at least one accompanying anomaly in 40-80% of omphalocele cases. Associated anomalies include cardiac (7-47%), gastrointestinal (3-20%), genitourinary (6-20%), musculoskeletal (4-25%), and central nervous system (4-30%), and chromosomal anomalies (3-20%) (17). In our study, 30 (59%) of the omphalocele cases were accompanied by additional anomalies. The most common accompanying anomaly in our omphalocele cases was about the cardiovascular system and compatible with the literature. The rate of accompanying anomalies in our gastroschisis group was 24% and it was lower than the rate (34%) that was reported by Heydanus et al. (18).

Fetal outcomes in omphalocele are predominantly determined by additional malformations and chromosomal anomalies (19). As the severity of the accompanying anomaly increases, prenatal and postnatal morbidity and mortality increase, too (20). Postnatal survival for isolated omphalocele can be as high as almost 100% with surgical correction (21). In our study, the postnatal survival rate was not as high as in the literature. In the omphalocele group, all patients with aneuploidy were terminated upon family request. Of the 30 (59%) patients with additional anomalies, 19 (37%) resulted in termination, 1 (2%) neonatal exitus, 5 (10%) intrauterine fetal death, 1 (2%) missed abortion, and 1 (2%) postoperative exitus. 3 patients (6%) were live and healthy postoperatively (Table 3). Additional anomalies of the healthy subjects were single umbilical artery, aberrant right subclavian artery, and pelviectasis. Of the 21 (41%) cases with isolated omphalocele, 12 (23%) resulted in termination, 2 (4%) postoperative exitus, 1 (2%) neonatal exitus, and 1 (2%) missed abortion. 2 patients (4%) were live and healthy postoperatively. The postnatal results of 3 (6%) patients could not be reached. Survival rates were similar in the groups with (6%) and without (4%) additional anomalies. Early ultrasound diagnoses, invasive prenatal diagnosis, stillbirth, and termination of pregnancy leave a small and selected population.

Gastroschisis is divided into simple and complex types according to the condition of the intestine. In simple gastroschisis, the intestine is in good condition and there are no intestinal complications. Complex gastroschisis is associated with congenital intestinal complications such as atresia, perforation, ischemia, necrosis, or volvulus. The prognosis of fetuses with gastroschisis depends largely on the condition of the intestines at birth. While the mortality rate in patients with simple gastroschisis is 3.4%, the mortality rate in patients with complex gastroschisis is 9.3% (22).

In our study, patients were not identified as divided into simple and complex gastroschisis groups. Our mortality rate was 28%, which was higher than the literature. The limitation of our study is that the choice of neonatal surgical technique, timing of surgery, timing of oral intake, and duration of parenteral nutrition, which are of critical importance in neonatal prognosis, are unknown.

Body stalk anomaly is generally characterized by major anterior body wall defect, limb deformities, kyphoscoliosis, absence or short umbilical cord, and/or the presence of craniofacial defects. Various other fetal abnormalities may be present (23). There are three different hypotheses in its development. The first theory is that fibrous bands form on the chorion surface due to the rupture of the amniotic membrane and these bands cause trauma to the fetus' body. Another theory is that the ventral body wall does not close due to impaired embryonic blood flow in the first 4-6 weeks of pregnancy and the extraembryonic coelomic cavity persists. The most accepted one is that it is caused by a defect in the germinal disc (24).

Body stalk anomaly is a rare and fatal condition. These fetuses usually have a normal karyotype. A single case of placental trisomy 16 and maternal uniparental disomy 16 has been published in the literature with this anomaly (25). No abnormal karyotype was observed in our patients, but since it was incompatible with life, termination was made upon family request for both cases.

This study had some limitations. First, the sample size was limited, and only 74 fetuses with fetal abdominal wall defects were retrospectively analyzed. Second, no information was provided regarding the omphalocele size and content of the omphalocel sac. However, the fact that our study was designed in a single center and has available long-term results constitute the strenghts of our study.

Conclusion

When a fetal abdominal wall defect is diagnosed, possible simultaneous anomalies should be investigated. Counseling is important as parents may choose to terminate the pregnancy when a severe anomaly or an abnormal karyotype is detected. The postnatal survival rate is higher in gastroschisis than in omphalocele. Although our study also supports this result, the postnatal mortality rate was found to be higher in both groups compared to the literature.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 53-58

Anesteziyoloji ve Reanimasyon Hekimlerinin Genel Anestezi Taze Gaz Akım Kullanım Alışkanlıklarının Değerlendirilmesi: Anket Çalışması

Assessment of General Anesthesia Fresh Gas Flow Usage Habits of Anesthesiology and Reanimation Doctors: Questionnaire Study

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Çalışmamız Anesteziyoloji ve Reanimasyon hekimleri arasında yapılan bir anket çalışmasıdır. Her iki yazar içinde çıkar ilişkisi bulunmamaktadır.

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Geliş Tarihi:14.02.2024
Kabul Tarihi:22.03.2024

Öz

Amaç: Türkiye'deki Anesteziyoloji ve Reanimasyon hekimlerinin inhalasyon anestezisinde taze gaz akımı tercihleri ve düşük akım anestezi (DAA) ile ilgili alışkanlıklarını değerlendirmek amaçlanmıştır.

Yöntem: Demografik veriler, genel anestezi akım tercihleri ve DAA'ya bakış açılarının değerlendirildiği 18 sorudan oluşan anket soruları internet üzerinden elektronik posta yoluyla katılımcılara iletildi.

Bulgular: Çalışmaya 245 katılımcı dahil edildi. Katılımcıların %79,60'ı uygun vakalarda DAA tercih ettiklerini belittiler. %53,06'sı çocuklarda DAA uygulamadıklarını belirtirken, %38,8'i DAA ile ilgili yeterli eğitimi aldıklarını belirtmişlerdir. Daha az volatil ajan tüketimi, maliyet etkin olması ve çevresel etkileri DAA tercih etme nedenleri olarak belirtilmektedir. Güvensizlik hissi ve dikkat gereksinimi ise tercih edilmeme nedenleri olarak öne çıkmaktadır.

Sonuç: Anesteziyoloji ve Reanimasyon hekimlerinin uygun ameliyatlarda DAA tercih ettiklerini görmekteyiz. DAA uygulaması sırasında bazı çekincelerin varlığı kullanım oranlarını azaltmakla birlikte bu durum özellikle çocuklarda daha belirgin olarak karşımıza çıkmaktadır. DAA ile ilgili yapılacak uygulamalı eğitimlerle bunun giderilebileceğini ve farkındalığının daha da artacağını düşünmekteyiz.

Anahtar Kelimeler: Düşük akım anestezi, anesteziyoloji ve reanimasyon hekimleri, anket

Abstract

Aim: To evaluate the fresh gas flow preferences of Anesthesiology and Reanimation physicians in inhalation anesthesia and their habits related to low-flow anesthesia (LFA) in Turkey.

Methods: A questionnaire consisting of 18 questions about demographic data, general anesthesia flow preferences, and perspectives on LFA was sent to the participants via electronic mail over the internet.

Results: The study included 245 participants. 79.60% of the participants stated that they preferred LFA in appropriate cases. 53.06% stated that they did not perform LFA in children, while 38.8% stated that they received adequate training on LFA. Less consumption of volatile agents, cost-effectiveness and environmental effects are stated as the reasons to prefer LFA. Feeling of insecurity and need for attention are the reasons for not preferring LFA.

Conclusion: Anesthesiology and Reanimation physicians prefer LFA in appropriate surgeries. The presence of some reservations during LFA application decreases the utilization rates. This situation is more pronounced especially in children. We think that this can be overcome with practical trainings on LFA and awareness will increase even more.

Keywords: Low flow anesthesia, anesthesiology and reanimation physicians, survey

Giriş

Düşük akım anestezi (DAA), genel anestezi sırasında ekspire edilen gazın karbondioksit (CO_2) absorbsiyonu sonrası en az %50'sinin bir sonraki inspiryumda hastaya geri verildiği inhalasyon anestezisi tekniği olarak tanımlanmaktadır. Yarı-kapalı ve yeniden solutmalı sistemler ile uygulanabilmektedir (1). Anestezi pratiğinde kullanılan taze gaz akımı (TGA), yüksek akım (2 L dk^{-1} üzeri), orta akım (1-2 L dk^{-1}), düşük akım (0.5-1 L dk^{-1}), minimal akım (0.25-0.5 L dk^{-1}) ve metabolik akım (0.25 L dk^{-1} altı) olarak sınıflandırılmıştır (2). DAA'nın fizyolojik, ekonomik ve çevresel faktörler üzerine bir çok olumlu etkisi bulunmaktadır. İnhale edilen gazın sıcaklık ve neminin korunması, hipoterminin önlenmesi, su kaybının azalması ve mukosiliyer klirensin artması gibi fizyolojik olumlu etkileri mevcuttur. Volatil ajan tüketiminin azalması ile %75 oranında tasarruf sağlayarak ekonomik olmasının yanı sıra gazların oluşturduğu sera gazı etkisinin ve ameliyathane hava kirliliğinin azalması gibi ekolojik avantajları da bulunmaktadır (3). Kaçaklar sebebiyle hipoventilasyon riski, hipoksik gaz karışımlarının hastaya verilmesi, CO_2 absorbanlarının hızlı tüketimi ve toksik maddelerin birikimi gibi durumlar da DAA ile ilgili endişeleri oluşturmaktadır (4).

Çalışmamızda anesteziyoloji ve reanimasyon hekimlerinin genel anestezi uygulamalarında TGA tercihlerini, DAA ile ilgili deneyimlerini ve bakış açılarını değerlendirmeyi amaçladık.

Gereç ve Yöntem

Çalışmamız için SBÜ Bursa Tıp Fakültesi Şehir Hastanesi Klinik Araştırmalar Etik Kurulundan onay alındı (19.07.2023 2023-12/14). Anket soruları ''Google Formlar'' web sitesi (docs.google.com/forms) aracılığıyla dijital ortamda hazırlandı. Anket çoktan seçmeli ve çok seçenekli soru teknikleri kullanılarak, hazırlandı. Soru seçeneklerinde yanıtların yönlendirilmemesi ve tarafsızlık ilkesine uygun davranıldı. Anket formları Türkiye Anesteziyoloji ve Reanimasyon Derneği (TARD) aracılığıyla derneğe asil ve yardımcı olarak üye olan doktorlara 07.08.2013 tarihinde elektronik posta yoluyla 1 kez gönderildi. Ankete katılım bağlantı linki 07.08.2013- 16.08.2023 tarihleri arasında aktifti. Ankete katılmak istemeyen kişiler çalışma dışı bırakıldı. Ankette katılımcılara toplam 18 soru yöneltildi. İlk bölümde demografik verileri içeren 7 soru, sonraki bölümde ise genel anestezi akım tercihleri ve düşük akım anesteziye bakış açılarının değerlendirildiği 11 soru yöneltildi. Belirlenen tarih aralığında anket formlarını eksiksiz olarak tamamlayan 245 katılımcının anket formundan elde edilen verileri analiz edilmiştir.

İstatistiksel analiz: Verilerin istatistiksel değerlendirmesi IBM SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) istatistiksel paket programı Package for the Social Sciences (SPSS) for Windows sürüm 22.0 kullanılarak yapıldı. Kategorik değişkenlerin tanımlayıcı istatistikleri frekans ve yüzde olarak verildi. Kategorik verilerin karşılaştırılması amacıyla ki-kare testi ve Fisher Exact testi kullanıldı. $p<0,05$ anlamlı kabul edildi.

Bulgular

Anketimize toplam 248 Anesteziyoloji ve Reanimasyon doktoru katıldı. 3 katılımcının anket sorularını eksik doldurması sebebiyle 245 katılımcı çalışmaya dahil edildi. Katılımcıların cinsiyet, yaş aralıkları, ünvan, klinik deneyim, çalıştıkları kurum ve eğitim aldıkları merkezlerin sorgulandığı demografik veriler Tablo I'de özetlenmiştir.

Tablo I: Demografik veriler

		n(245)	%
Cinsiyet	Kadın	125	51,02
	Erkek	120	48,98
Yaş (yıl)	20-35	121	49,39
	36-50	85	34,69
	51-65	36	14,69
	65 yaş üstü	3	1,22
Ünvan	Araştırma Görevlisi	81	33,06
	Uzman Hekim	121	49,38
	Dr. Öğretim Üyesi	13	5,31
	Doçent Dr.	12	4,90
	Profesör Dr.	18	7,35
Klinik deneyim (yıl)	0-5	83	33,88
	6-10	63	25,71
	11-15	34	13,88
	16-20	23	9,39
	20 yıl üzeri	42	17,14
Uzmanlık eğitiminizi hangi kurumda alıyorsunuz/aldınız ?	Üniversite Hastanesi	162	66,1
	Sağlık Bakanlığı EAH	83	33,9
Şu anda çalıştığınız kurum	Üniversite Hastanesi	75	30,61
	Sağlık Bakanlığı EAH	114	46,53
	Devlet Hastanesi	25	10,20
	Özel Hastane	31	12,65

EAH: Eğitim araştırma hastanesi

Katılımcıların DAA tercihleri sorgulandığında ünvanlara göre dağılımda araştırma görevlilerinin %82,7'si (n:67), uzman hekimlerin %72,7'si (n:88), doktor öğretim görevlilerinin %84,6'sı (n:11), doçentlerin %100'ü (n:12) ve profesörlerin %94,4'ü (n:17) DAA tercih ettiklerini belirtmişlerdir. Ünvanların kendi gruplarında tercih edenler ile etmeyenler arasındaki farklılık anlamlı bulunmuştur ***(p=0,025)***.

Hizmet verilen kurumların dağılımlarında üniversite hastanelerinde çalışanların %89,3'ü (n:67), eğitim araştırma hastanelerinde çalışanların %75,4'ü (n:86), devlet hastanelerinde çalışanların %56'sı (n:14) ve özel hastanelerde çalışanların %90,3 (n:28) kişi DAA tercih ettiklerini belirmişlerdir. Hizmet verilen kurumların kendi gruplarında DAA tercih edenler ile etmeyenler arasında anlamlı farklılık bulunmuştur ***(p=0,001)***. Yaş, klinik deneyim ve uzmanlık eğitimi alınan merkezlerin gruplar içi dağılımlarında anlamlı farklılık saptanmamıştır (Tablo II).

Tablo II: Demografik veri sınıflandırmalarına göre düşük akım anestezi tercihleri

		Düşük akım tercih edenler n, (%)	Düşük akım tercih etmeyenler n, (%)	p
Yaş (yıl)	20-35	92 (%76,6)	29 (%24,4)	0.551
	36-50	71 (%83,5)	14 (%16,5)	
	51-65	30 (%83,3)	6 (%16,7)	
	65 yaş üstü	2 (%66,7)	1 (%33,3)	
Ünvan	Araştırma Görevlisi	67 (%82,7)	14 (%17,3)	**0.025**
	Uzman Hekim	88 (%72,7)	33 (27,3)	
	Dr. Öğretim Üyesi	11 (%84,6)	2 (%15.4)	
	Doçent Dr.	12 (%100)	0 (%0)	
	Profesör Dr.	17 (%94,4)	1 (%5,6)	
Klinik deneyim (yıl)	0-5	69 (%83,1)	14 (%16,9)	0.142
	6-10	52 (%82,5)	11 (%17,5)	
	11-15	28 (%82,3)	6 (%17,7)	
	16-20	18 (%78,2)	5 (%21,8)	
	20 yıl üzeri	28 (%66,7)	14 (%33,3)	
Uzmanlık eğitiminizi hangi kurumda alıyorsunuz/aldınız	Üniversite Hastanesi	128 (%79)	34 (%21)	0.907
	Sağlık Bakanlığı EAH	67 (%80,7)	16 (%19,3)	
Şu anda çalıştığınız kurum	Üniversite Hastanesi	67 (%89,3)	8 (%10,7)	**0.001**
	Sağlık Bakanlığı EAH	86 (%75,4)	28 (%24,6)	
	Devlet Hastanesi	14 (%56)	11 (%44)	
	Özel Hastane	28 (%90,3)	3 (%9,7)	

Ki-kare ve FisherExact testi **EAH:** Eğitim araştırma hastanesi

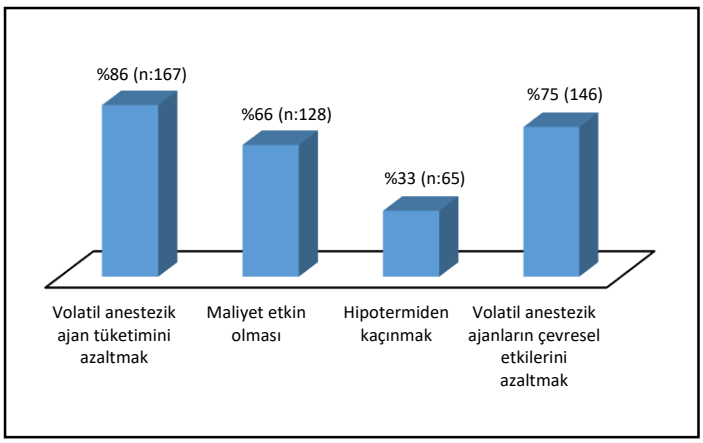
Katılımcıların %79,60'ı (n:195) uygun durumlarda DAA uyguladıklarını belirtirken, TGA tercihleri sorgulandığında %9,39'u (n:23) minimal ve metabolik akım, %38,36'sı (n:94) düşük akım, %33,87'si (n:83) orta akım ve %18,36'sı (n:45) yüksek akım uyguladıklarını belirtmişlerdir.

Çocuklarda DAA uygulayan katılımcı oranı %22,04 (n:54) iken, %24,08'i (n:59) hastaya göre tercih ettiklerini belirtmişlerdir. DAA ile ilgili olarak yeterli eğitim aldığını belirten katılımcıların oranı %38,8 (n:95) iken, eğitim organizasyonları olması halinde katılmak isteyenlerin oranı %86,9 (n:213) olarak saptanmıştır (Tablo III).

Tablo III: Düşük akım anestezi genel bakış

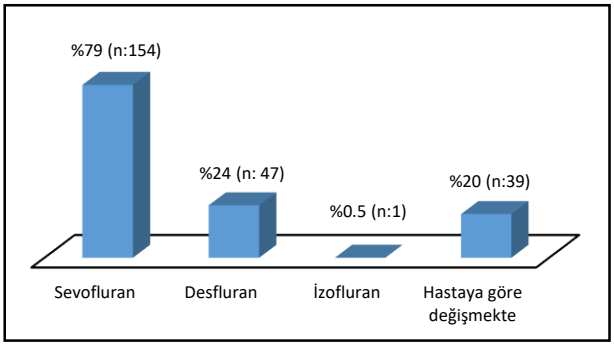
		n	%
Genel Anestezi uygulamalarında uygun durumlarda düşük akım anestezi tercih ediyor musunuz ?	Evet	195	79,60
	Hayır	50	20,40
Genel anestezi idamesinde akım tercihiniz nedir ?	0.5lt dk^{-1} ve altı	23	9,39
	0.5 lt dk^{-1}-1 lt dk^{-1}	94	38,36
	1 lt dk^{-1}-2 lt dk^{-1}	83	33,87
	2 lt dk^{-1}-4 lt dk^{-1}	45	18,36
Çocuk hastalarda düşük akım anestezi uyguluyor musunuz ?	Evet	54	22,04
	Hayır	130	53,06
	Hastaya göre tercih ediyorum	59	24,08
Düşük akım anestezi uygulaması ile ilgili yeterince eğitim aldığınızı düşünüyor musunuz ?	Evet	95	38,77
	Hayır	85	34,69
	Yeterince değil	65	26,53
Düşük akım anestezi ile ilgili eğitim organizasyonları (konu anlatım, uygulamalı eğitim) olması halinde katılmak ister misiniz ?	Evet	213	86,93
	Hayır	32	13,06

Düşük akım anestezi tercih edilme sebeplerinin sorgulandığı çok seçmeli soruya volatil ajanların tüketim miktarını azaltmak, DAA'nın ekolojik etkileri ve maliyet etkin olması en çok tercih edilme sebepleri olarak belirtilmiştir (Grafik 1).

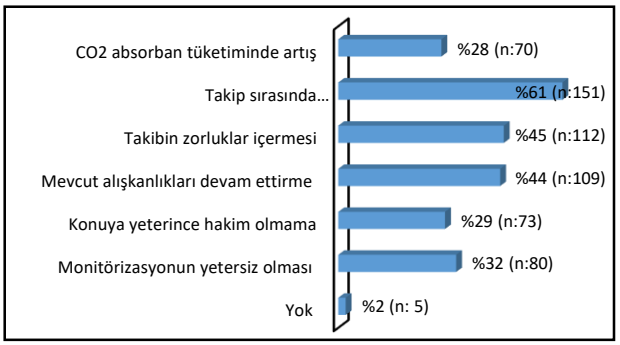


Grafik 1: Düşük akım anestezi tercih edilme sebepleri

Sevofluran DAA uygulayan katılımcılar arasında uygulama sırasında daha fazla tercih edilen volatil ajan olurken, DAA uygulaması sırasında çekincelerin sorgulandığı çok seçmeli soruya en çok güvensizlik hissi, takibin zorluklar içermesi ve mevcut alışkanlıkları devam ettirme durumları olarak belirtilmiştir (Grafik 2,3).

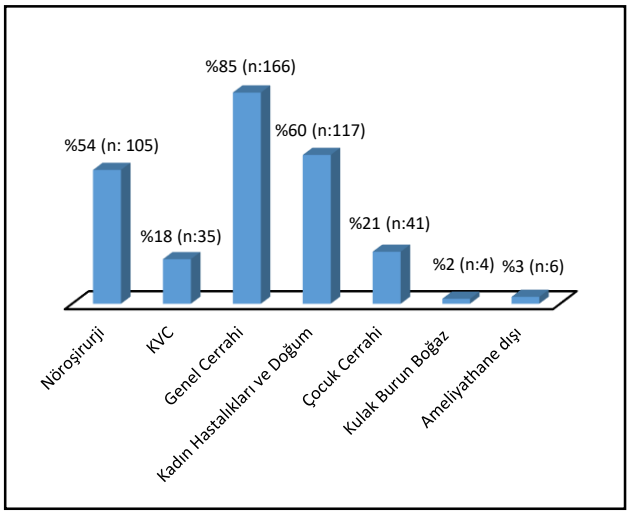


Grafik 2: Volatil ajan tercihleri



Grafik 3: DAA uygulaması ile ilgili çekinceler

Düşük akım anestezi uygulamasının en çok tercih edildiği alanların sorgulandığı çok seçmeli soruda katılımcılar genel cerrahi, jinekoloji-obstetri ve nöroşirurji ameliyatlarında daha çok tercih ettiklerini belirtmişlerdir (Grafik 4).



Grafik 4 DAA'nin en çok tercih edildiği alanlar

Tartışma

Modern anestezi cihazlarının yaygınlaşması, ekonomik nedenler ve atık anestezi gazlarının çevresel etkileri konusunda artan farkındalık sayesinde, DAA uygulamaları anestezi hekimleri arasında yaygınlaşmaktadır (5). Teknolojik gelişmeler, anestezi idamesi sırasında taze gaz akışını hastaların bazal metabolik ihtiyaçlarına göre azaltmayı mümkün kılmıştır. Monitörizasyon tekniklerinin gelişmesi ve solunum gazlarının analizi ile DAA sırasında karşılaşılabilecek sorunlar büyük ölçüde engellemiştir (6).

Volatil ajanlar küresel ısınmaya katkıda bulunma potansiyeline sahiptir. Bu ajanların karbondioksite kıyasla etkileri hakkında bazı tartışmalar vardır ancak kullanım tekniklerinin çevre kirlenme derecesini sınırlayabileceğine dair ş

üphe yoktur. Bu maddelerin çoğu neredeyse hiç metabolize edilmez ve kullanımdan sonra 1,1 ile 14 yıl arasında atmosferde kalabilmektedirler. Desfluran, izofluran ve sevofluran için 20 yıllık Küresel Isınma Potansiyeli (GWP 20) olarak kullanılan değerleri sırasıyla 6810, 1800 ve 440'tır (7). Özellikle, TGA'yı azaltmaya özen gösterilmesi ile volatil ajanlar daha verimli kullanılabilir ve hasta üzerinde aynı etkiyi sağlarken tüketim miktarları azalabilir. Tek bir vakanın ekolojik etkisi minimal olabilir, ancak kümülatif olarak düşünülünce, TGA tercihlerinin atmosfere salınan volatil anestezik ajan hacminde önemli bir fark yaratabileceği aşikardır (6,7).

İnhalasyon anestezisinde maliyetin TGA ile doğru orantılı olduğu kabul edilmektedir. Bu nedenle DAA, inhalasyon anestezisi maliyetini azaltacak bir mekanizma olarak teşvik edilmektedir (8). TGA miktarlarının azalması ile volatil ajan tüketim miktarları azalırken aynı oranda CO_2 absorbanı tüketim miktarlarında artış meydana gelir. Bu durum maliyet konusunda soru işaretleri oluştursa da Moody ve ark. yeni nesil CO_2 absorbanı kullandıkları ve farklı TGA miktarları ile maliyet analizi yaptıkları çalışmada, yeni nesil absorban kullanarak maliyet artmış olmasına rağmen sevofluran ve desfluran için TGA miktarı ile doğru orantılı olarak total maliyetlerde azalma olduğunu bildirmişlerdir. İzofluran kullanılan grupta ise paradoksal olarak maliyet artmış en uygun maliyetin 2 L dk^{-1} iken sağlandığı bildirilmiştir (8). Anketimizde katılımcıların DAA'yı en çok tercih etme sebeplerinin DAA ile volatil ajan tüketiminde azalma, bu azalma sonucunda çevresel etkilerinin azalması ve uygulamanın maliyet etkin olması olarak belirtilmesi bu konudaki farkındalığı göstermektedir.

Sevofluran, MAC değerinin düşük olması, maliyet etkinliği ve diğer volatil ajanlara kıyasla sera gazı etkisinin daha düşük olması sebebiyle tercih edilmektedir (7). Sevofluranın TGA 1L dk^{-1} altında kullanımı ile sıçanlarda nefrotoksik olan Kompound A meydana gelmektedir. Bu sebeple Amerika Birleşik Devletleri Gıda ve İlaç İdaresi tarafından onaylı prospektüsünde TGA 1L dk^{-1} altında kullanımı önerilmemektedir. Bu durum bazı anestezistlerde endişe oluştursa da DAA uygulamalarında sevofluran kullanımı kapsamlı bir şekilde araştırılmıştır ve güvenle kullanılabileceği bildirilen çok sayıda literatür verisi mevcuttur. (9-13). Bizim çalışmamızda da katılımcılar DAA uygulaması sırasında volatil ajan olarak çoğunlukla sevofluranı tercih ettiklerini belirtmişlerdir.

Anketimizde katılımcılar genel cerrahi, kadın hastalıkları-doğum ve nöroşirurji ameliyatlarında daha fazla DAA tercih ettiklerini belirtmişlerdir. Bu durumun, bu bölümlerin özellikle DAA uygulamak için gerekli uzun süreli vakalarının bir çok merkezde yapılabiliyor olması ve anestezistlerin bu vakalar konusunda tecrübeli olmaları sebebiyle kendilerini rahat hissetmelerinden kaynaklandığını düşünmekteyiz.

Anestezi uygulamaları sırasında anatomik ve fizyolojik farklılıkları sebebiyle çocukların erişkinlere kıyasla hipoksiye yatkınlıkları fazladır. Genel anestezi uygulamalarında kullanılan kafsız endotrakeal tüpler, laringeal maske kaynaklı kaçaklar ve ölü boşluk solunumu gibi durumlarda hipoksi meydana getirebilmektedir. DAA uygulaması sırasında da taze gaz akımının düşük olması ile benzer durumların meydana gelebilmesi sebebiyle çocuk hastalarda uygulama konusunda çekinceler mevcuttur. Bizim çalışmamızda da çocuk hastalarda düşük akım uygulamayan kesim çoğunluktadır (14).

Anketimizde katılımcıların %79,60'ı uygun ameliyatlarda ve hastalarda genel anestezi uygulamalarında DAA'yı tercih ettiklerini belirtirmişlerdir. Genel anestezi idamesinde TGA tercihleri sorgulandığında ise düşük veya minimal akım tercih edenlerin %47,75 olduğu görülmektedir. Genel anestezi uygulamalarında orta ve yüksek akım kullanım oranları yüksek olmasına rağmen, uygun hastalarda DAA'nın yüksek oranda tercih edilmesi bu konuda ki farkındalığın göstergesi olabilir. Yaş grupları, eğitim alınan merkezler ve klinik deneyim sürelerinin alt gruplarında DAA tercih edenler ile etmeyenler karşılaştırıldığında oransal olarak anlamlı farklılık saptanmadı. Katılımcılardan akademik kariyer yapanlar, tıp fakültelerinde, eğitim araştırma hastanelerinde ve özel hastanelerde hizmet veren gruplarda DAA'nın oransal olarak daha fazla tercih edildiğini görmekteyiz. Eğitim planlamalarının bu durumu gözeterek yapılmasının diğer gruplarda da kullanım oranlarını arttırabileceğini düşünmekteyiz.

Türkiye Anesteziyoloji ve Reanimasyon Derneği (TARD), DAA konusunda düzenli aralıklarla uygulamalı eğitim programları düzenlemektedir. Nitekim katılımcıların %38,8'inin DAA ile ilgili yeterli eğitim aldıklarını belirtmesi ve yapılması halinde uygulamalı eğitimlere katılmak isteyenlerin oranının %86,93 olması bu programları ne denli ihtiyaç olduğunun göstergesidir. Bu programlar neticesinde önümüzdeki yıllarda ülkemizdeki anesteziyoloji ve reanimasyon hekimlerinin DAA farkındalığının ve kullanım oranlarının artacağı ve çekincelerin azalacağı konusunda şüphe yoktur.

Düşük akım anestezi uygulaması sırasında gaz bileşiminde değişiklikler uzun zaman diliminde gerçekleşmektedir. Metabolizma için gerekli oksijenin sağlanabilmesi, yeterli oranda volatil anestezik ajan ve gaz karışımı verilebilmesi için yakın takip gereklidir. Bununla birlikte CO_2 absorbanlarının hızlı tüketimi, hiperkapni, CO_2'nin yeniden solunması riski, eser miktarda da olsa CO, Kompound A, etanol, aseton vb zararlı maddelerin birikimi gibi nedenler DAA ile ilgili çekinceler oluşturmaktadır (15). Çalışmamızda DAA uygularken en çok çekinilen nedenler takip sırasında olan güvensizlik hissi takibin zorluklar içermesi olarak belirtilmiştir.

Sonuç olarak Anesteziyoloji ve Reanimasyon hekimlerinin inhalasyon anestezisi uygulamalarında uygun durumlarda DAA tercih ettiklerini ve DAA'nın olumlu etkilerinin farkında olduklarını düşünmekteyiz. Uygulama sırasında bazı çekincelerin varlığı özellikle çocuklarda ve belirli cerrahilerde daha az tercih edildiği sonucuna vardık. Bunun yanında DAA yapılacak eğitimlere katılım talebinin yüksek olacağını gördük. Özellikle DAA ile ilgili çekinceleri giderecek uygulamalı eğitim programlarının arttırılarak devam etmesi gerektiğini düşünmekteyiz.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 59-72

Molecular Subtypes Of Breast Cancer: Can It Be Determinant For Preoperative MRI Planning?

Meme Kanseri Tanısı Alan Kadınlarda Operasyon Öncesi Meme MR Endikasyonu Kararında Tümörlerin Moleküler Subtiplerinin Bilinmesi Belirleyici Olabilir mi?

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Geliş Tarihi: 08.12.2023
Kabul Tarihi: 10.02.2024

Abstract

Objectives: The purpose of this study was to determine whether molecular subtype, which is an important prognostic factor for breast cancer, can be used as a determinant for preoperative breast MRI indication. Concordantly, we also searched for whether women with luminal A subtype tumors with better prognosis may not require preoperative MRI for staging.

Material and Method: A total of 150 women who underwent preoperative breast MRI with a diagnosis of breast cancer from January 2015 through December 2018 were included in the study. Subtypes were classified as luminal A, luminal B, HER-2 overexpressing, and triple negative according to immunohistochemical markers. Preoperative breast MRI findings were evaluated due to the ACR breast lexicon. Morphological, kinetic and diffusion features or the presence of additional findings on MRI were compared with molecular subtypes. Statistical analyses were performed between the luminal A subtype and the other subtypes.

Results: The subtype distribution was luminal A, 30.7%; luminal B, 50%; HER-2 over-expressing, 10%; and triple negative, 9.3%. Tumor size was significantly higher in luminal A subtype than in non-luminal A subtypes (p=0.03). There was no statistically significant difference between the two groups according to morphological, kinetic and diffusion features; the presence of multifocal, multicentric, or contralateral disease; or tumor extension. Additionally, there was no statistically significant difference between the two groups according to nipple, skin, pectoral muscle involvement or the presence of axillary and internal mammary lymph nodes.

Conclusion: The presence of additional findings and local extensive disease in women with breast cancer is seen in luminal A subtype with very high rates. In addition, luminal A subtype was found to be related to increased tumor size. Non-mass enhancements, which are less detectable in other imaging modalities, are also seen in luminal A subtype at the same rate as others. Consequently, our study showed that MRI must be performed in all molecular subtypes.

Keywords: Breast neoplasm; Subtyping, Immunologıc; Magnetic Resonance Imaging.

Öz

Giriş: Bu çalışmada, meme kanserli kadınların prognoz tayini ve tedavi yönetiminde önemli olan moleküler subtiplerin, preoperatif evreleme amaçlı meme MRG endikasyon kararında belirleyici olup olamayacağı ve bu bağlamda, en iyi prognoza sahip luminal A subtip tümör saptanan kadınlarda, evreleme amaçlı preoperatif MRG kullanılmasına gerek olup olmadığı araştırıldı.

Gereç ve Yöntemler: Ocak 2015 - Aralık 2018 tarihleri arasında meme kanseri tanısıyla preoperatif meme MRG yapılan 149 kadın çalışmaya dahil edildi. Subtipler immunohistokimyasal belirteçlere göre luminal A, luminal B, HER2 yüksek eksprese ve triple negatif olarak dört grupta incelendi. Preoperatif meme MRG bulguları ACR atlasına göre değerlendirildi. Morfolojik, kinetik ve difüzyon özellikleri ve ek bulguların varlığı moleküler subtipler ile karşılaştırıldı. İstatistiksel analizler luminal A subtipi ile diğerleri arasında karşılaştırma yapılarak elde edildi.

Bulgular: % 30.7 olguda luminal A, % 50 olguda luminal B, % 10 olguda HER2 yüksek eksprese ve % 9.3 olguda triple negatif subtipi saptandı. Luminal A subtipinde tümör boyutu luminal A olmayan subtiplere göre anlamlı olarak daha yüksekti (p=0.03). Morfolojik, kinetik, difüzyon özellikleri, multifokalite, multisentrisite, kontralateralite ve tümör uzanımı açısından iki grup arasında istatistiksel anlamlı farklılık saptanmadı. Ayrıca meme başı, cilt ve pektoral kas tutulumu, aksiller ya da internal mammariyan lenf nodu varlığı açısından da iki grup arasında istatistiksel anlamlı fark saptanmadı.

Sonuç: Meme kanserli kadınlarda ek odak ve lokal ileri hastalık varlığı gibi bulgular luminal A subtipinde de oldukça yüksek oranlarda görülmektedir. Ayrıca luminal A subtipli tümörler büyük boyutla ilişkilidir. Diğer modalitelerle saptanabilirliği daha düşük olan kitlesel olmayan kontrastlanan kanserler de luminal A subtipinde diğerleri ile aynı oranda görülmektedir. Bu nedenle çalışmamız, tüm subtipler için evreleme amaçlı preoperatif meme MRG yapılması gerekliliğini ortaya koymuştur.

Anahtar Kelimeler: Meme kanseri; İmmunolojik subtip; Manyetik rezonans görüntüleme.

Objectives

Breast magnetic resonance imaging (MRI) is the most sensitive technique for the detection of breast cancer and is increasingly being used for screening and diagnosis (1). It is mainly used for staging by evaluation of tumor size, multicentricity and multifocality, presence of in situ cancer, and involvement of skin, nipple, pectoral muscle, and axillary lymph node (1,2). As it is an expensive technique, cost-effectiveness should be kept in mind. Additionally, breast MRI is performed using intravenous (iv) gadolinium-based contrast agents, which can cause allergic reactions and nephrogenic systemic fibrosis in patients with last-stage kidney disease (3). Recent studies have shown that gadolinium-based contrast agents accumulate in the brain (4). Most importantly, glandular parenchyma can easily be affected by hormonal changes in premenopausal women. Despite its high sensitivity (98-100%) and specificity (88%), some studies support that performing preoperative MRI has no decreasing effect on the rate of local recurrence and metastasis (5,6, 7, 8, 9,10). Considering these disadvantages, it is still controversial whether preoperative breast MRI should be indicated for every breast cancer patient.

Breast cancer has many histological types and molecular subtypes with different prognoses and specific treatment approaches. The molecular subtypes of invasive carcinomas are determined by the expression of hormone receptors (estrogen receptor [ER] and progesterone receptor [PR]) and HER-2 (ERBB2) status (11,12). There are four molecular subtypes: luminal A (ER and/or PR positive, HER-2 negative and low proliferation index), luminal B (ER and/or PR positive, HER-2 positive or negative and high proliferation index), HER-2 overexpressing (ER and PR negative, HER-2 positive) and triple negative (ER and PR negative, HER-2 negative) (13). HER-2 expression (predominantly luminal B and HER-2 overexpressing subtypes) is associated with poor prognoses (14, 15). Multicentricity and multifocality, and involvement of axillary lymph nodes and skin have been shown to be associated with luminal B subtype in some radiological studies (16, 17, 18). Triple negative subtype, which has the worst prognosis, is associated with less differentiation of invasive cancer and mutation of the BRCA-1 gene (19). Of the four subtypes, luminal A has been shown to be the most common with the best prognosis.

Our aim is to investigate whether preoperative breast MRI indications may be limited by comparing the MRI findings between molecular subtypes. If it is statistically proven that these parameters are absent in luminal A group, it can be hypothesized that conventional imaging modalities may be sufficient for this subtype. Therefore, preoperative MRI may be unnecessary for luminal A group.

Methods

Patient Selection

A total of 350 women diagnosed with breast cancer were retrospectively evaluated following approval by our institutional review board in March 2019. The mean age of the women was 49.9±11.8 (between 27-80 years). All women underwent MRI for preoperative staging between January 2015 and December 2018. Of the 350, women who had surgery at another institution, received neoadjuvant chemotherapy or/and had metastatic disease were excluded. The remaining 150 women were included. MRI findings were compared with the molecular subtypes of postoperative specimens.

Breast MRI Technique

Patients were imaged on days 7-14 of the menstrual cycle in the premenopausal period. Women with known malignancy had their breast MRI without considering the day of menstruation. A 1,5 T scanner (Magnetom Aera; Siemens Medical Systems, Erlangen, Germany) MRI was used with a dedicated eight-channel breast coil in the prone position. The imaging sequence included a triplane localizer followed by a two-dimensional T1-weighted turbo spin echo (TSE) sequence without fat suppression (TR/TE, 529/11 msec; 4 mm slice thickness; matrix, 288x384; FOV, 294 mm).

This sequence was used to assess the fibroglandular tissue density of the breast parenchyma. An axial fat-suppressed T2-weighted sequence (TR/TE, 4000/85 msec; 4 mm slice thickness; matrix, 288x384; FOV, 294 mm) was then performed. Diffusion weighted images were obtained before contrast administration, using a two-dimensional EPI sequence with fat suppression (b factor: 50, 400 and 800 s/mm^2) followed by a three-dimensional T1-weighted FLASH pulse sequence (TR/TE, 4,8/2 msec; 2.1 mm slice thickness; matrix 317x352; FOV, 294 mm) with fat suppression before and after contrast administration. Gadobutrol (Gadovist, Bayer, Leverkusen, Germany) was used as the contrast agent at a dose of 0.1 mm/kg. Postcontrast images were obtained for a total of 5 minutes, repeated 5 times at 60-second intervals.

After examination, the unenhanced images were subtracted from the contrast-enhanced images on a pixel-by-pixel basis.

Kinetic curves were obtained by placing at least a 3-pixel region of interest (ROI) in the area with the most intense red color on the perfusion color map on a Siemens syngo MR D13 version workstation for the mass-enhancing lesions (Fig. 1-B,2-B and 3-B). Apparent diffusion coefficient (ADC) values were recorded from ROIs drawn freely from the entire lesion and a circular ROI from the darkest area for the mass-enhancing lesions (Fig. 1-B, 2-B and 3-B). The lowest ADC value detected after three measurements for each lesion was recorded.

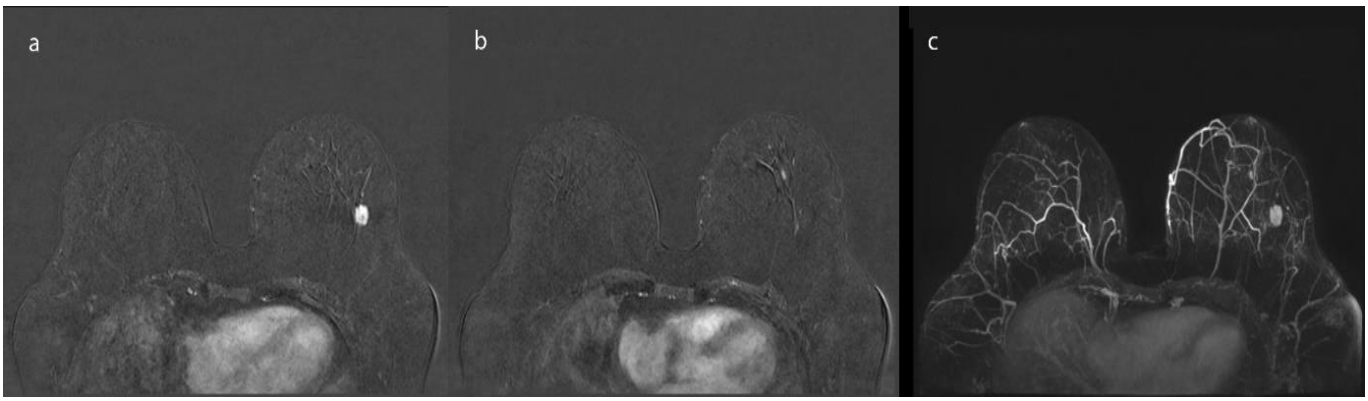

Figure 1-A. A 60-year-old woman with luminal B subtype invasive ductal carcinoma in the left breast. (a) Axial T1-weighted contrast-enhanced image with subtraction shows an irregular mass with heterogeneous enhancement. (b) A lesion located antero-inferiorly in the left breast is detected as multifocal invasive ductal carcinoma focus by core needle biopsy. (c) Both tumors are seen on contrast-enhanced MIP image.

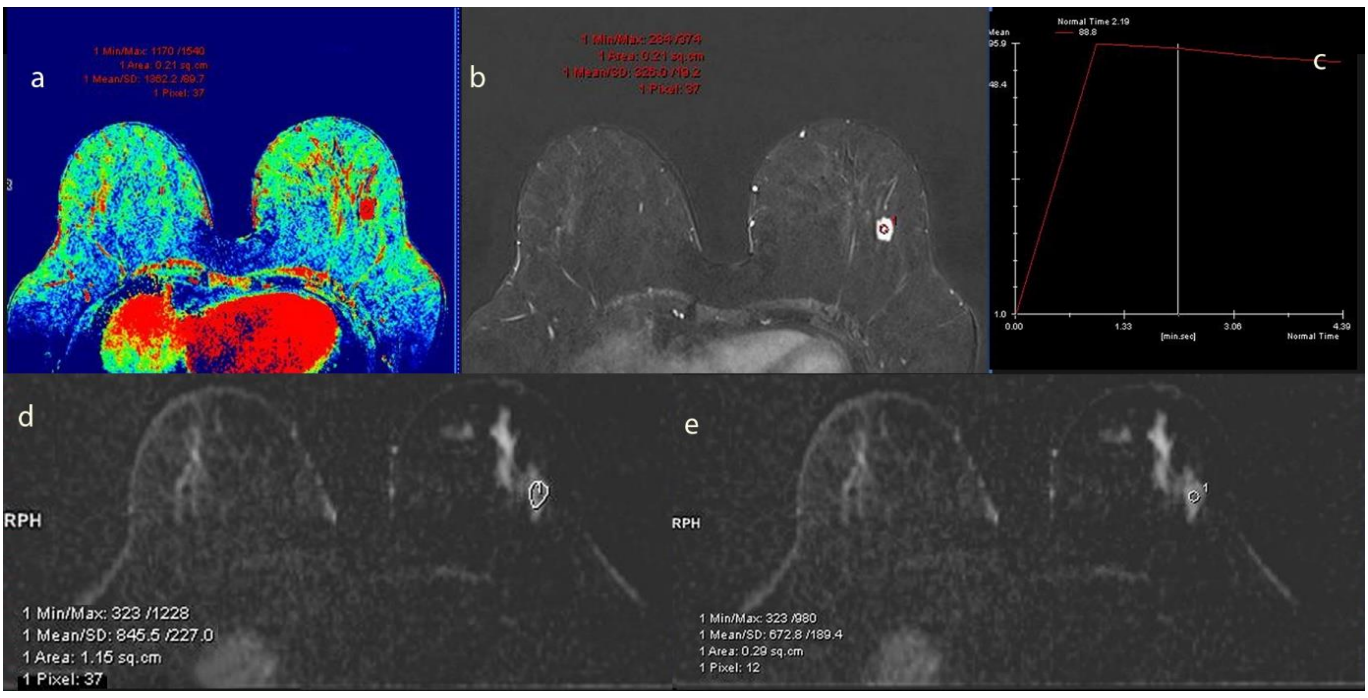

Figure 1-B. A 60-year-old woman with luminal B subtype invasive ductal carcinoma in the left breast. (a, b and c) Kinetic curve analysis of the tumor in the left breast is shown. The values for ADC of the whole lesion (d) and of the darkest area (e) are seen on ADC mapping images.

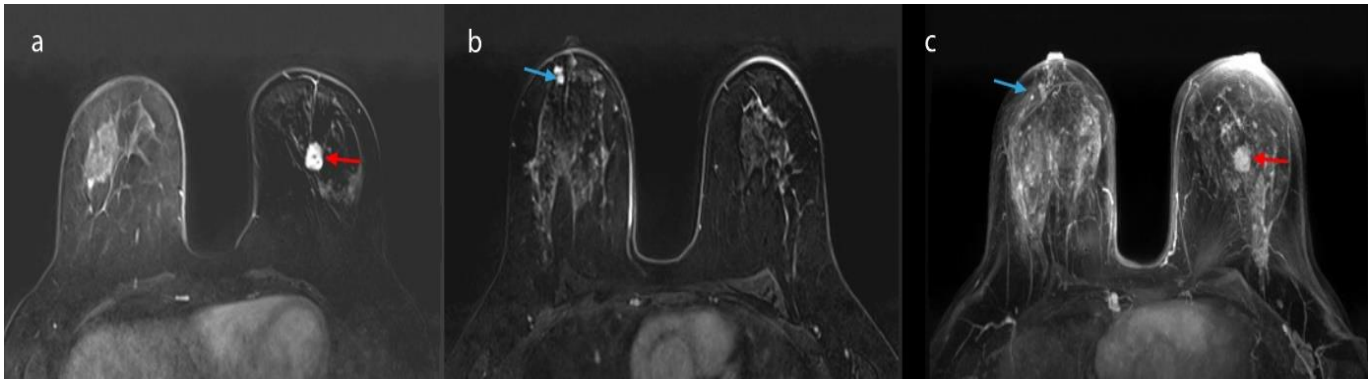

Figure 2-A. A 39-year-old woman with luminal A subtype invasive ductal carcinoma in the left breast. (a) Axial T1-weighted contrast-enhanced image with subtraction shows an irregular mass with heterogeneous enhancement (red arrow). (b) A core needle biopsy of the mass in the right breast has shown no malignancy (blue arrow). (c) Both masses are seen on contrast-enhanced MIP image.

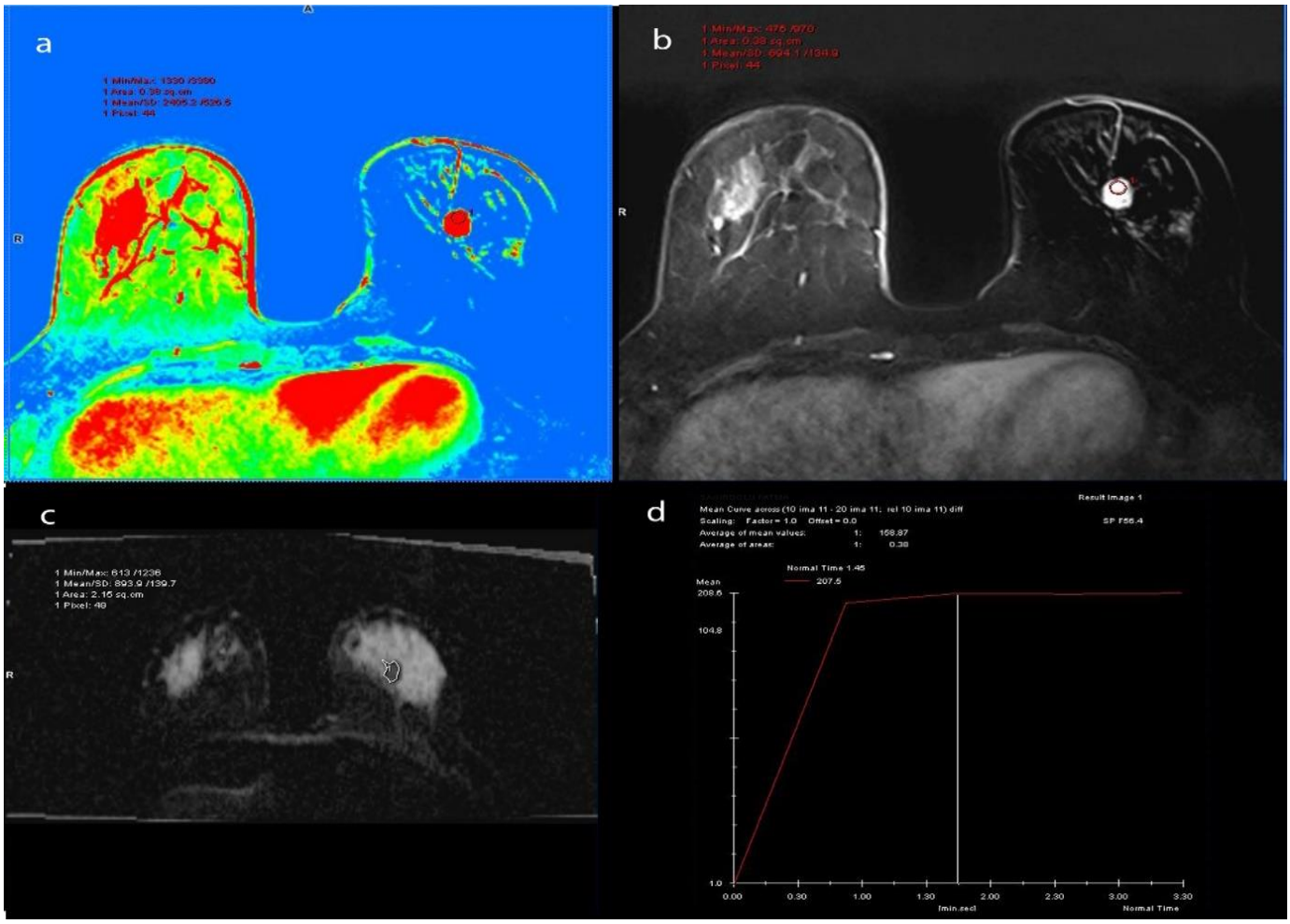

Figure 2-B. A 39-year-old woman with luminal A subtype invasive ductal carcinoma in the left breast. (a, b and d) Kinetic curve analysis of the tumor in the left breast is shown. (c) The ADC values of the whole lesion are shown on the ADC mapping image. The mass shows decreased signal intensity compared with surrounding fibroglandular tissues.

Breast MRI Findings

Two independent radiologists, one with a 10-year experience (A.K.) in breast MRI, retrospectively evaluated the images. Lesions were interpreted according to the ACR MRI breast imaging reporting and data system (BIRADS) lexicon. The amount of fibroglandular tissue (FGT), and background parenchymal enhancement (BPE) were evaluated. Lesions were categorized as focus, mass, and non-mass enhancement according to the morphological features. Analysis of kinetic curves and ADC mapping were performed for lesions presented as masses. If there was an accompanying non-mass enhancement area, it was considered tumor extension.

The maximum diameter of the lesions was recorded. In the presence of more than one mass, the largest mass was considered the index tumor. The presence of nipple, axillary lymph node, skin, pectoral muscle, and internal mammary lymph node involvement was evaluated. Multifocal, multicentric and contralateral lesions were also evaluated on the MRI and then confirmed according to the pathological report. For one woman diagnosed with Paget's disease, intraparenchymal lesion was considered index tumor. T2-weighted images with fat suppression were also evaluated. The lesions were grouped as hyperintense, hypointense, or heterogeneous signal intensity on T2-weighted images. In women who underwent mastectomy, MRI findings were compared with the surgical specimen (Fig. 3-A).

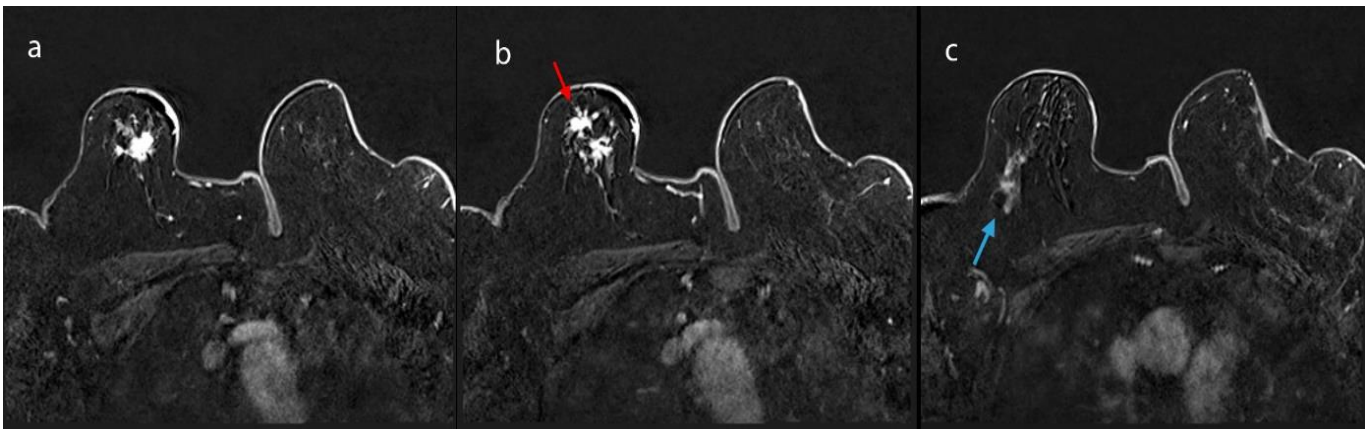

Figure 3-A. Preoperative magnetic resonance images of the right breast in a 65-year-old woman with luminal A subtype invasive ductal and lobular carcinoma. (a) Axial T1-weighted contrast-enhanced image with subtraction shows a spiculated mass with homogeneous enhancement. (b) Multifocal malignant mass in the same breast is shown (red arrow). (c) There is segmental heterogeneous non-mass enhancement located posteriorly in the upper outer quadrant of the right breast. It was proven to be benign on postoperative surgical specimens (blue arrow).

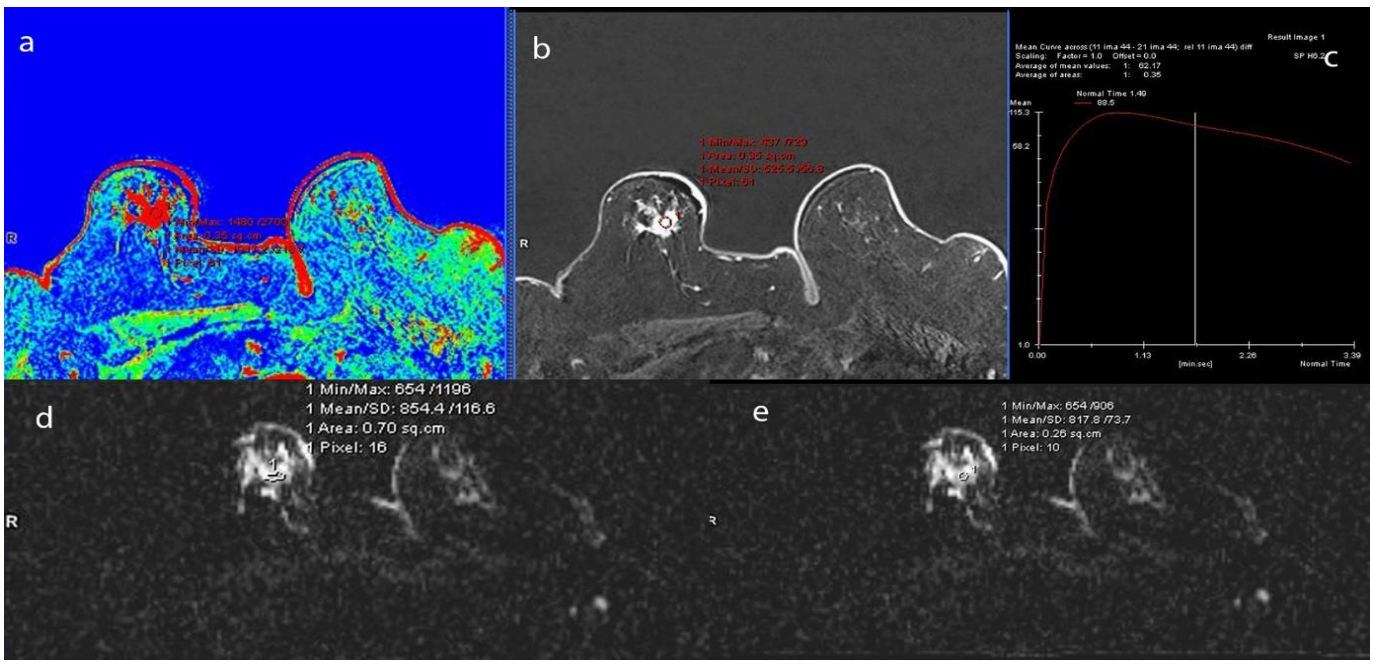

Figure 3-B. Preoperative magnetic resonance images of the right breast in a 65-year-old woman with luminal A subtype invasive ductal and lobular carcinoma. (a, b and c) Kinetic curve analysis of the index tumor in the right breast is shown. The values for ADC of the whole lesion (d) and of the darkest area (e) are seen on ADC mapping images.

If there was a lesion suspicious for multifocality, multicentricity or contralaterality in patients who underwent breast-conserving surgery, second-look ultrasound (US) was initially performed. US-guided biopsy was planned for these lesions, which were detected by ultrasound (Fig. 1-A,2-A and 4). In a few cases that presented with calcifications, mammography-guided excisional biopsy was performed. The findings detected only on MRI were histopathologically confirmed by MRI-guided vacuum biopsy.

The histopathological findings were analyzed in terms of tumor type, grade, extension, presence of additional foci and histomorphological findings in the surrounding breast tissue. According to ER and PR status, HER-2 expression and Ki-67 proliferation, tumors were classified into four molecular subtypes.

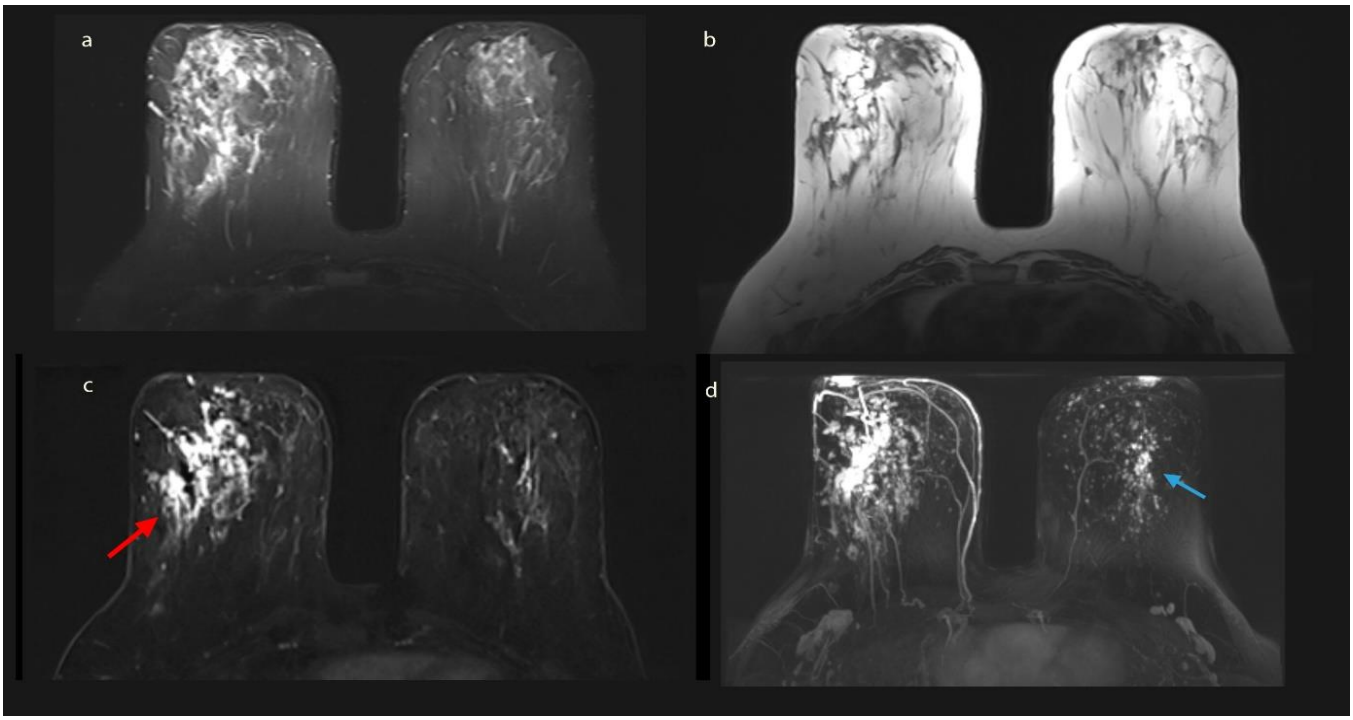

Figure 4. Preoperative magnetic resonance images of the right breast in a 35-year-old woman with luminal B subtype invasive ductal carcinoma. (a) Axial T2-weighted and (b) axial T1-weighted images show non-mass lesion of the right breast. (c) Axial T1-weighted contrast-enhanced image with subtraction and (d) contrast-enhanced MIP image of the same slice show diffuse clumped non-mass enhancement in the right breast (red arrow). There is segmental clumped non-mass enhancement in the left breast with a benign pathological result from the excisional biopsy (blue arrow).

Statistical Analysis

Numerical variables are described as the mean, standard deviation (SD), median, minimum and maximum. The distribution of variables was measured with the Kolmogorov-Smirnov test. The Mann-Whitney U test was used in the analysis of quantitative independent data. The chi-square test was used in the analysis of qualitative independent data, and Fischer's exact test was used when the chi-square test conditions were not met. All data were stored in a database for statistical analysis using SPSS v. 26.0. software. The statistical alpha significance level was accepted as $p<0,05$.

Results

A total of 150 women were included, with a mean age of 49.9 years (range 27-80 years). The most common histological types were invasive ductal carcinoma (74.7%), invasive lobular carcinoma (8%) and high-grade ductal carcinoma in situ (DCIS) (6%) (Table 1). The parenchymal composition of 17 women was entirely fatty (11.3%), 55 (36.7%) were scattered fibroglandular, 61 were heterogeneous dense (40.7%), and 17 were extremely dense (11.3%). Background enhancement (BGE) was minimal in 39 women (26%), mild in 71 women (47.3%), moderate in 32 women (21.3%), and marked in 8 women (5.3%) (Table 1)

There were 32 women (21.3%) with multifocal disease, 16 women (10.7%) with multicentric disease, and 4 women (2.7%) with contralateral disease (Table 1). Additional findings, including nipple involvement, and the presence of internal mammary lymph node, skin and pectoral muscle involvement, were observed in 53 women (35.3%) (Table 1).

Of the total, 46 (30.7%) luminal A, 75 (50%) luminal B,15 (10%) HER-2 overexpressed and 14 (9.3%) triple negative tumors were detected (Table 1).

Table 1. Frequency of evaluated findings in breast tumors

		Minimum-Maximum	Median	Mean.±sd./n-%	
Age		27 - 80	49	49.9 ± 11.8	
Breast composition	Entirely fatty			17	11.3%
	Scattered fibroglandular			55	36.7%
	Heterogeneously dense			61	40.7%
	Extremely dense			17	11.3%
Background enhancement	Minimal			39	26.0%
	Mild			71	47.3%
	Moderate			32	21.3%
	Marked			8	5.3%
Tumor diameter (mm)		5 - 153	24.5	33.5 ± 24.4	
Nipple involvement	(-)			132	88.0%
	(+)			18	12.0%
Presence of axillary lymph node	(-)			85	56.7%
	(+)			65	43.3%
Presence of internal mammary lymph node	(-)			139	92.7%
	(+)			11	7.3%
Skin involvement	(-)			133	88.7%
	(+)			17	11.3%
Pectoral muscle involvement	(-)			143	95.3%
	(+)			7	4.7%
Nipple, skin, pectoral muscle involvement and/or presence of internal mammary lymph	(-)			97	64.7%
	(+)			53	35.3%
Multifocality	(-)			118	78.7%
	(+)			32	21.3%
Multicentricity	(-)			134	89.3%
	(+)			16	10.7%
Contralaterality	(-)			146	97.3%
	(+)			4	2.7%
Multifocality, multicentricity and/or contralaterality	(-)			109	72.7%
	(+)			41	27.3%
Histological types	Apocrine carcinoma			1	0.7%
	High grade DCIS			9	6.0%
	Invasive ductal carcinoma			112	74.7%
	Invasive lobular carcinoma			12	8.0%
	Invasive breast carcinoma			2	1.3%
	Invasive and in situ carcinoma			3	2.0%
	Low grade DCIS			2	1.3%
	Medullary carcinoma			1	0.7%
	Invasive ductal and lobular carcinoma			5	3.3%
	Musinous carcinoma			3	2.0%
HER-2 over expressed				15	10.0%
Luminal A				46	30.7%
Luminal B				75	50.0%
Triple negative				14	9.3%

(+) shows that presence of finding and (-) shows that absence of finding.

There was no statistically significant difference in terms of age, parenchymal pattern, background enhancement or T2 intensity between luminal A and non-luminal A subtypes (p > 0.05) (Tables 2 and 3).

The shape, margin and internal enhancement characteristics, ADC values and kinetic curve type for masses did not differ significantly between luminal A and non-luminal A subtypes (p > 0.05) (Table 3).

There was also no statistically significant difference in terms of the distribution and internal enhancement patterns of non-mass-enhancing lesions between luminal A and non-luminal A subtypes (p > 0.05) (Table 4).

Table 2. Comparison of evaluated findings between luminal A and other subtypes

		Luminal A		non-Luminal A		p value
		Mean.±sd./n-%		Mean.±sd./n-%		
Age		50.9 ± 10.3		12.4 ± 48.5		0.280 [m]
Breast composition	Entirely fatty	5	10.9%	12	11.5%	0.065 [x²]
	Scattered fibroglandular	22	47.8%	33	31.7%	
	Heterogeneously dense	18	39.1%	43	41.3%	
	Extremely dense	1	2.2%	16	15.4%	
Background enhancement	Minimal	10	21.7%	29	27.9%	0.262 [x²]
	Mild	27	58.7%	44	42.3%	
	Moderate	8	17.4%	24	23.1%	
	Marked	1	2.2%	7	6.7%	
Side	Right	25	54.3%	48	46.2%	0.355 [x²]
	Left	21	45.7%	56	53.8%	
Quadrant	Upper outer	15	32.6%	27	26.0%	0.522 [x²]
	Lower outer	6	13.0%	18	17.3%	0.677 [x²]
	Upper middle	7	15.2%	15	14.4%	0.902 [x²]
	Upper inner	9	19.6%	15	14.4%	0.581 [x²]
	Lower inner	4	8.7%	3	2.9%	0.256 [x²]
	Lower middle	2	4.3%	5	4.8%	0.766 [x²]
	Retroareolar	2	4.3%	7	6.7%	0.846 [x²]
	Central	0	0.0%	1	1.0%	1.000 [x²]
	Upper quadrant	0	0.0%	7	6.7%	0.167 [x²]
	Lower qudrant	0	0.0%	1	1.0%	1.000 [x²]
	Diffuse	0	0.0%	3	2.9%	0.553 [x²]
	Nipple	0	0.0%	1	1.0%	1.000 [x²]
	Outer quadrant	1	2.2%	1	1.0%	1.000 [x²]

[m] Mann-whitney u test/ [x²] Ki-kare test

Table 3. Comparison of evaluated findings between luminal A and other subtypes

		Luminal A		non-Luminal A		p value
		Mean.±sd./n-%		Mean.±sd./n-%		
T2W findings	Hyperintense	8	17.4%	25	24.0%	0.394 [x²]
	Hypointense	23	50.0%	40	38.5%	
	Intermediate intensity	15	32.6%	39	37.5%	
Mass enhancement						—
Shape	Oval	0	0.0%	8	10.0%	0.060 [x²]
	Round	9	26.5%	11	13.8%	
	Irregular	25	73.5%	61	76.3%	
Margin	Circumscribed	1	2.9%	2	2.5%	1.000 [x²]
	Irregular	13	38.2%	38	47.5%	0.481 [x²]
	Spiculated	20	58.8%	40	50.0%	0.510 [x²]
Internal enhancement characteristics	Homogeneous	11	32.4%	14	17.5%	0.157 [x²]
	Heterogeneous	15	44.1%	49	61.3%	
	Ring enhancement	8	23.5%	17	21.3%	
DWI (ADC values)		837.1 ± 262.6		248.0 ± 940.5		0.162 [m]
Kinetic curve	Type 1	10	21.7%	14	13.5%	0.339 [x²]
	Type 2	15	32.6%	44	42.3%	
	Type 3	9	19.6%	22	21.2%	

[m] Mann-whitney u test/ [x²] Ki-kare test

Tumor size was significantly higher in the luminal A subtype than in the other subtypes ($p < 0.05$) (Table 4). There was no statistically significant difference in terms of multifocality (%21.7 in luminal A, %21.2 in non-luminal A), multicentricity (%4.3 in luminal A, %13.5 in non-luminal A) or contralaterality (%0 in luminal A, %3.8 in non-luminal A) between luminal A subtype and the other subtypes. In addition, the difference between luminal A and non-luminal A subtypes was not statistically significant in terms of multifocality, multicentricity and/or contralaterality (%23.9 in luminal A, %28.8 in non-luminal A) (Table 4) (Fig. 3-A).

There was also no statistically significant difference in terms of nipple, internal mammary lymph node, axillary lymph node, skin and pectoral muscle involvement or the presence of any of these findings between luminal A subtype and the other subtypes (Table 4).

The triple-negative subtype was not detected in high-grade DCIS cases (Table 5). In all low-grade DCIS cases, luminal A was the only type detected (Table 6). Luminal A subtype was not observed in medullary and mucinous carcinoma cases (Table 6). However there was no statistically significant difference in terms of these results (Table 6).

Table 4. Comparison of evaluated findings between luminal A and other subtypes

		Luminal A		non-Luminal A		p value
		Mean.±sd./n-%		Mean.±sd./n-%		
Non-mass enhancement						
Distrubition	Focal	2	4.3%	0	0.0%	0.104 $^{X^2}$
	Linear	3	6.5%	1	1.0%	0.098 $^{X^2}$
	Segmental	1	2.2%	8	7.7%	0.219 $^{X^2}$
	Regional	4	8.7%	7	6.7%	1.000 $^{X^2}$
	Multiple region	2	4.3%	3	2.9%	1.000 $^{X^2}$
	Diffuse	0	0.0%	5	4.8%	0.146 $^{X^2}$
Internal enhancement characteristics	Homogeneous	2	4.3%	1	1.0%	0.222 $^{X^2}$
	Heterogeneous	5	10.9%	13	12.5%	0.252 $^{X^2}$
	Clumped	4	8.7%	8	7.7%	1.000 $^{X^2}$
	Clustered ring	1	2.2%	2	1.9%	1.000 $^{X^2}$
Nipple involvement	(-)	41	89.1%	91	87.5%	0.777 $^{X^2}$
	(+)	5	10.9%	13	12.5%	
Presence of axillary lymph node	(-)	30	65.2%	55	52.9%	0.160 $^{X^2}$
	(+)	16	34.8%	49	47.1%	
Presence of internal mammary lymph node	(-)	43	93.5%	96	92.3%	0.800 $^{X^2}$
	(+)	3	6.5%	8	7.7%	
Skin involvement	(-)	42	91.3%	91	87.5%	0.498 $^{X^2}$
	(+)	4	8.7%	13	12.5%	
Pectoral muscle involvement	(-)	45	97.8%	98	94.2%	0.336 $^{X^2}$
	(+)	1	2.2%	6	5.8%	
Nipple, skin, pectoral muscle involvement and/or presence of internal mammary lymph node	(-)	37	80.4%	77	74.0%	0.398 $^{X^2}$
	(+)	9	19.6%	27	26.0%	
Multifocality	(-)	36	78.3%	82	78.8%	0.936 $^{X^2}$
	(+)	10	21.7%	22	21.2%	
Multicentricity	(-)	44	95.7%	90	86.5%	0.095 $^{X^2}$
	(+)	2	4.3%	14	13.5%	
Contralaterality	(-)	46	100.0%	100	96.2%	0.313 $^{X^2}$
	(+)	0	0.0%	4	3.8%	
Multifocality, multicentricity and/or contralaterality	(-)	35	76.1%	74	71.2%	0.532 $^{X^2}$
	(+)	11	23.9%	30	28.8%	
Tumor diameter (mm)		24.8 ± 15.2		26.6 ± 27.5		***0.003*** ^{m}
Tumor invasion	(-)	28	60.9%	57	54.8%	0.360 $^{X^2}$
	(+)	6	13.0%	22	21.2%	

^{m} Mann-whitney u test/ $^{X^2}$ Ki-kare test

Table 5. Evaluated age, imaging and histological features stratified by subtypes

		Luminal A		Luminal B		HER-2 Overexpressed		Triple Negative	
		Mean.±sd./n-%		Mean.±sd./n-%		Mean.±sd./n-%		Mean.±sd./n-%	
Age		50.9 ± 10.3		48.5 ± 11.7		47.5 ± 12.6		55.7 ± 14.4	
Breast composition									
Entirely fatty		5	10.9%	9	12.0%	1	6.7%	2	14.3%
Scattered fibroglandular		22	47.8%	20	26.7%	7	46.7%	6	42.9%
Heterogeneously dense		18	39.1%	32	42.7%	6	40.0%	5	35.7%
Extremely dense		1	2.2%	14	18.7%	1	6.7%	1	7.1%
Background enhancement	Minimal	10	21.7%	19	25.3%	6	40.0%	4	28.6%
	Mild	27	58.7%	32	42.7%	6	40.0%	6	42.9%
	Moderate	8	17.4%	17	22.7%	3	20.0%	4	28.6%
	Marked	1	2.2%	7	9.3%	0	0.0%	0	0.0%
T2W findings									
Hyperintense		8	17.4%	15	20.0%	6	40.0%	4	28.6%
Hypointense		23	50.0%	28	37.3%	6	40.0%	6	42.9%
Intermediate intensity		15	32.6%	32	42.7%	3	20.0%	4	28.6%
Tumor diameter (mm)		24.8 ± 15.2		± 34.2 ± 24.4		33.7 ± 19.3		56.7 ± 35.6	
Mass enhancement									
Shape	Oval	0	0.0%	7	9.3%	1	6.7%	0	0.0%
	Round	9	19.6%	6	8.0%	1	6.7%	4	28.6%
	Irregular	25	54.3%	45	60.0%	7	46.7%	9	64.3%
Margin	Circumscribed	1	2.2%	2	2.7%	0	0.0%	0	0.0%
	Irregular	13	28.3%	26	34.7%	4	26.7%	8	57.1%
	Spiculated	20	43.5%	30	40.0%	5	33.3%	5	35.7%
Internal enhancement characteristics	Homogeneous	11	23.9%	9	12.0%	3	20.0%	2	14.3%
	Heterogeneous	15	32.6%	38	50.7%	4	26.7%	7	50.0%
	Ring enhancement	8	17.4%	11	14.7%	2	13.3%	4	28.6%
DWI (ADC values)		837.1 ± 262.6		903.7 ± 212.3		1007.1 ± 222.7		751.3 ± 410.2	
Kinetic curve	Type 1	10	21.7%	10	13.3%	3	20.0%	1	7.1%
	Type 2	15	32.6%	35	46.7%	5	33.3%	4	28.6%
	Type 3	9	19.6%	13	17.3%	1	6.7%	8	57.1%
Non-mass enhancement									
Distrubition									
Focal		2	4.3%	0	0.0%	0	0.0%	0	0.0%
Linear		3	6.5%	1	1.3%	0	0.0%	0	0.0%
Segmental		1	2.2%	7	9.3%	1	6.7%	0	0.0%
Regional		4	8.7%	3	4.0%	4	26.7%	0	0.0%
Multiple region		2	4.3%	3	4.0%	0	0.0%	0	0.0%
Diffuse		0	0.0%	3	4.0%	1	6.7%	1	7.1%
Internal enhancement characteristics									
Homogeneous		2	4.3%	1	1.3%	0	0.0%	0	0.0%
Heterogeneous		5	10.9%	10	13.3%	2	13.3%	1	7.1%
Clumped		4	8.7%	6	8.0%	2	13.3%	0	0.0%
Clustered ring		1	2.2%	0	0.0%	2	13.3%	0	0.0%
Nipple involvement	(-)	41	89.1%	68	90.7%	11	73.3%	12	85.7%
	(+)	5	10.9%	7	9.3%	4	26.7%	2	14.3%
Presence of axillary lymph node	(-)	30	65.2%	43	57.3%	6	40.0%	6	42.9%
	(+)	16	34.8%	32	42.7%	9	60.0%	8	57.1%
Presence of internal mammary lymph node	(-)	43	93.5%	70	93.3%	12	80.0%	14	100.0%
	(+)	3	6.5%	5	6.7%	3	20.0%	0	0.0%
Skin involvement	(-)	42	91.3%	67	89.3%	13	86.7%	11	78.6%
	(+)	4	8.7%	8	10.7%	2	13.3%	3	21.4%
Pectoral muscle involvement	(-)	45	97.8%	73	97.3%	14	93.3%	11	78.6%
	(+)	1	2.2%	2	2.7%	1	6.7%	3	21.4%
Nipple, skin, pectoral muscle involvement and/or presence of internal mammary lymph node	(-)	37	80.4%	59	78.7%	9	60.0%	9	64.3%
	(+)	9	19.6%	16	21.3%	6	40.0%	5	35.7%
Multifocality	(-)	36	78.3%	59	78.7%	12	80.0%	11	78.6%
	(+)	10	21.7%	16	21.3%	3	20.0%	3	21.4%
Multicentricity	(-)	44	95.7%	65	86.7%	12	80.0%	13	92.9%
	(+)	2	4.3%	10	13.3%	3	20.0%	1	7.1%
Contralaterality	(-)	46	100.0%	72	96.0%	14	93.3%	14	100.0%
	(+)	0	0.0%	3	4.0%	1	6.7%	0	0.0%
Multifocality, multicentricity and/or contralaterality	(-)	35	76.1%	53	70.7%	10	66.7%	11	78.6%
	(+)	11	23.9%	22	29.3%	5	33.3%	3	21.4%
Histological types									
Apocrine carcinoma		0	0.0%	0	0.0%	0	0.0%	1	7.1%
High grade DCIS		5	10.9%	3	4.0%	1	6.7%	0	0.0%
Invasive ductal carcinoma		31	67.4%	57	76.0%	13	86.7%	11	78.6%
Invasive lobular carcinoma		3	6.5%	9	12.0%	0	0.0%	0	0.0%
Invasive breast carcinoma		1	2.2%	0	0.0%	0	0.0%	1	7.1%
Invasive and in situ carcinoma		1	2.2%	1	1.3%	1	6.7%	0	0.0%
Low grade DCIS		2	4.3%	0	0.0%	0	0.0%	0	0.0%
Medullary carcinoma		0	0.0%	0	0.0%	0	0.0%	1	7.1%
Invasive ductal and lobular carcinoma		3	6.5%	2	2.7%	0	0.0%	0	0.0%
Musinous carcinoma		0	0.0%	3	4.0%	0	0.0%	0	0.0%

(+) shows that presence of finding and (-) shows that absence of finding.

Table 6. Comparison of evaluated findings between luminal A and other subtypes

		Luminal A		non-Luminal A		p value
		Mean.±sd./n-%		Mean.±sd./n-%		
Histological types	Apocrine carcinoma	0	0.0%	1	1.0%	1.000 $^{X^2}$
	High grade DCIS	5	10.9%	4	3.8%	0.194 $^{X^2}$
	Invasive ductal carcinoma	31	67.4%	81	77.9%	0.246 $^{X^2}$
	Invasive lobular carcinoma	3	6.5%	9	8.7%	0.330 $^{X^2}$
	Invasive breast carcinoma	1	2.2%	1	1.0%	0.520 $^{X^2}$
	Invasive and in situ carcinoma	1	2.2%	2	1.9%	1.000 $^{X^2}$
	Low grade DCIS	2	4.3%	0	0.0%	0.092 $^{X^2}$
	Medullary carcinoma	0	0.0%	1	1.0%	1.000 $^{X^2}$
	Invasive ductal and lobular carcinoma	3	6.5%	2	1.9%	0.155 $^{X^2}$
	Musinous carcinoma	0	0.0%	3	2.9%	1.000 $^{X^2}$

^{m} Mann-whitney u test/ $^{X^2}$ Ki-kare test

Discussion

The use of preoperative breast MRI has emerged as an effective tool in breast cancer patients. However it is still controversial to perform breast MRI for every patient due to false positive results. In the current study, we investigated the relationship between molecular subtypes of breast cancer and MRI findings by comparing luminal subtype A with other subtypes. Although the most common subtype is luminal A according to the literature (16, 20, 21, 22, 23), we found luminal B as the most common subtype with a frequency of 50%. Bitencourt et al. also found luminal B subtype with a rate of 51.9% (17) similar to Montemezzi et al., Dilorenzo et al. and Jiang et al. (24, 25, 26). This difference might be due to the heterogeneity of the population of the study and the effect of environmental factors.

We found heterogeneous dense pattern as the most common parenchymal pattern. It has been shown that scattered fibroglandular breast tissue was less common in luminal B than other subtypes, and luminal A was significantly less common in heterogeneous dense breasts in the literature. However, in our study, there was no significant difference between luminal A and the other subtypes in terms of parenchymal pattern ($p > 0.05$). Devalapalli et al. also published a study stating that there is no significant correlation between parenchymal density and subtypes (27). There is no other study in the literature comparing luminal A and the other subtypes. However, Ozturk et al. associated the breast parenchyma pattern with ER positivity and they did not find a correlation in terms of PR positivity and HER-2 positivity (28).

Mild BGE was found most frequently in our study and was seen most commonly in luminal A subtype. In addition, it was found that HER-2 overexpressing and triple-negative subtypes were not detected in breasts with marked enhancement. However, no significant difference was observed in the comparison between luminal A and the other subtypes in terms of BGE ($p > 0.05$).

Dilorenzo et al. found that mild BGE was more common in luminal B subtype (25). They also found a statistically significant correlation between marked BGE and triple-negative subtype. This result also contradicts our study. On the other hand, Ha et al. showed no significant association between marked BPE and molecular subtypes with poor prognosis (29). In our study, no significant difference was found between the luminal A group and the other groups in terms of BGE. Kim et al. also found no significant correlation between BGE and molecular subtypes (30).

The intratumoral medium and low T2W signal intensities of the masses were associated with the luminal subtype (not specified as luminal A or B) in the study by Ozturk et al. (20). In our study, we did not find a statistically significant difference in terms of T2W image features ($p> 0.05$) between luminal A and the other subtypes. However, hyperintensity was observed commonly in luminal A subtype and hyperintensity was propotionally observed in HER-2 overexpressing subtype. Du et al. also reported that lower T2 values were associated with luminal A subtype (31). The cause of the high signal in T2W images is necrosis and is associated with high-grade tumors. The high T2W signal intensity was seen as the least common in luminal A in our study, and this result was consistent with the good prognosis of luminal A subtype.

The tumor size in luminal A group was significantly higher than in other group in our study ($p < 0.05$). This might be related to delayed diagnosis or heterogeneity in study population. It is known that MRI is the most accurate technique for determining tumor size. The presence of a larger tumor size than that detected by conventional methods can be demonstrated by breast MRI in luminal A, which has the best prognosis. In other words, it will also be an appropriate indication to use breast MRI for determining actual tumor size in cases of luminal A subtype. The data about this issue are quite controversial in the literature. Sezgin et al. found that the pathological tumor size was larger in luminal A than in luminal B and others (32).

Ozturk et al. detected a larger tumor size in HER-2 overexpressing subtype (20). However, Montemezzi et al. found that volume was significantly smaller in luminal B and larger in triple negative subtypes (24). There was no statistically significant correlation between tumor size and molecular subtype in the studies of Vilar et al. and Chen et al. (22,33). Consequently, further studies with larger series are needed.

Mass-like lesions were observed more frequently (76%) in our study. The shape, margin and internal enhancement characteristics, ADC values and kinetic curve type for mass-like lesions did not differ significantly between luminal A and the other subtypes ($p > 0.05$). It was observed that luminal A had a mostly irregular shape with spiculated margins and heterogeneous contrast enhancement. However, heterogeneous enhancement was found to be the most common enhancement type in all subtypes. Rim enhancement was proportionally more common in triple-negative subtype than in the others. Ozturk et al. associated irregular shape and non-circumscribed margin with luminal subtypes in mass-like lesions (20) They found no significant correlation between other morphological features and molecular subtypes. The circumscribed margin was associated with luminal A, and the noncircumscribed margin was associated with luminal B in a study by Montemezzi et al. (24). However, there were quite limited luminal A tumors 15%) in this study. In addition, Vilar et al. associated irregular shape with luminal A tumors (22). The results of our study showed that, when luminal A subtype was compared with other subtypes, there was no significant distinguishing feature in terms of morphological features observed in MRI. On the other hand, Grimm et al. showed that a homogeneous enhancement and a non-mass enhancement pattern have a 100% negative predictive value for luminal B subtype (21). However, in our study, 22.7% of lesions had non-mass enhancement, and 12% of them had homogeneous enhancement in luminal B tumors, and it seems that the results of these studies should be supported by larger series. Grimm et al. were unable to obtain significant results for luminal A subtype. Similarly, Long et al. could not find a significant correlation between MRI features and molecular subtypes (34).

ADC values and the kinetic curve type for masses did not differ significantly in luminal A and others. In the study by Montemezzi et al., high ADC values were associated with luminal A subtype (24). However, this study included very limited luminal A tumors. Chen et al. pointed out that ADC values are higher in hormone positive tumors (33). On the other hand, it was found that HER-2 overexpressing subtype had higher ADC values than luminal subtypes in a study (35). The results of a meta-analysis by Meyer et al. supported our findings (36). There are a few series supporting our results about kinetic curve types. All these studies have shown that there was no significant correlation between kinetic curves and molecular subtypes (20, 22, 37) In contrast, in the study of Montemezzi et al., the type 3 curve was found to be significantly lower and the type 2 curve was higher in the luminal A (24). However, it should be noted that the analysis was performed with a very limited luminal A tumors with a range of 15% in this study.

When nipple, skin and pectoral muscle involvement, and the presence of internal mammary lymph nodes were evaluated together, it was observed at a rate of approximately 20% in luminal A group and 26% in non-luminal A group. There was no statistically significant difference in the rate of these among molecular subtypes. In addition, when these features were evaluated separately, no significant difference was found between luminal A and the other subtypes. The rate of axillary involvement did not differ significantly between luminal A and non-luminal A groups in our study. Unlike our study, Richard et al. found that nipple, skin, and axillary involvement were higher in luminal B and HER-2 overexpressing subtypes compared to luminal A (16). They found no significant difference in terms of pectoral muscle involvement and the presence of internal mammary lymph nodes. On the other hand, Wu and Ma associated nipple and skin involvement with luminal A and B subtypes (23). However, they did not indicate any difference between luminal A and B. Despite all these results, we would like to point out that the subtypes were more homogeneously distributed in our study. Considering the contradictions of all this knowledge, it is quite difficult to provide consensus.

Multifocality was found at similar rates in all subtypes. Multicentricity was higher in luminal B and HER-2 overexpressing subtypes. Contralaterality was observed only in luminal B and HER-2 overexpressing subtypes. However, no statistically significant result was obtained. When looking at multifocality, multicentricity and/or contralaterality (the presence of any), it was seen in 23.9% of luminal A tumors and 28.8% of others. There was no statistically significant difference. Ozturk et al. reported that they detected multifocality and/or multicentricity more frequently in the luminal subtypes and HER-2 positive group than in triple-negative group (20). However, they did not indicate a significant p value. Similar results are also available in the study of Devalapalli et al. (27). Richard et al. found that multicentricity and/or multifocality were more common in the luminal B and HER-2 overexpressing subtypes than in the luminal A subtype. They found no significant difference in terms of contralaterality (16). Wiechmann et al. also reported a similar result (15). However, 70% of the cases were luminal A in these studies, and only 14-20% were luminal B and HER-2 overexpressing tumors. In addition, in the study of Wiechmann et al., breast MRI was not performed, and only the results of surgical specimens were evaluated (15). Bitencourt et al. and Seyfettin et al. did not find any significant correlation between multifocality and/or multicentricity and histological type or molecular subtypes in their studies (17,38). There was a more homogeneous distribution among molecular subtypes in our study. Our study shows that multifocality, multicentricity and/or contralaterality are seen in luminal A as frequently as others. In other words, the rate of additional findings in luminal A tumors cannot be neglected and preoperative breast MRI is needed. Despite false positivity rates, MRI will be beneficial in these cases.

In our study, the rate of invasive ductal carcinoma was significantly higher than that of invasive lobular carcinoma. All cases of invasive lobular carcinomas were observed in luminal A and B subtypes. All mucinous carcinomas were seen in luminal B subtype, and low-grade DCIS was detected only in luminal A subtype. However, statistically significant results could not be obtained. This was attributed to the low number of noninvasive carcinoma cases. Studies with larger series are needed for significant results.

This study has some limitations. First, the number of women recruited could be higher, but it was not possible to include patients who had neoadjuvant chemotherapy since it would change the findings of the surgical specimens. Second, this was a retrospective single-institution study without a homogeneous patient population. Third, numerous parameters should be assessed according to the BI-RADS system. For this reason, the statistical precision in this study is low.

In conclusion, there have been many studies comparing preoperative breast MRI findings with molecular subtypes in breast cancer. These studies contain conflicting results.

There is no consensus on when breast MRI should be used in preoperative staging. MRI can cause false positivity and unnecessary surgery in some cases.

There is no study in the literature comparing luminal A subtype with other subtypes, as in our study. This study shows that findings such as the presence of additional foci and locally advanced disease are also seen at very high rates in the luminal A subtype. In addition, luminal A subtype is associated with a larger size. Additionally, nonmass-enhancing tumors, which are less detectable in conventional imaging methods, are also seen in luminal A as frequently as others. For these reasons, this study demonstrated that breast MRI is useful for all molecular subtypes, including luminal A, with the best prognosis. Detecting tumor size and extent more accurately by performing breast MRI preoperatively will prevent re-excisions. Future prospective and multicentric studies with more homogeneous patient populations may provide additional information and may limit indications of preoperative MRI.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 73-79

Yaşlı Hastaların İlk Vizitte Malnütrisyon Prevalansı ve Ayrıntılı Geriatrik Değerlendirme Sonuçları ile İlişkisi

Prevalence of Malnutrition at the First Visit of Elderly Patients and Its Relationship with the Results of the Comprehensive Geriatric Assessment

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Geliş Tarihi: 12.02.2024
Kabul Tarihi: 22.02.2024

Öz

Giriş: Malnütrisyon, yaşlı bireylerde yaygın olan, hastaların bağışıklık yanıtına, morbidite ve mortalitelerine etkisi kanıtlanmış bir geriatrik sendromdur. Bu çalışmanın amacı; geriatrik olguların ilk başvuru sırasında malnütrisyon durumunu tespit ederek, geriatrik değerlendirme sonuçları ile ilişkisinin araştırılmasıdır.

Gereç ve Yöntem: Bu çalışmaya Ocak 2023 - Aralık 2023 arasında Geriatri polikliniğine başvuran 290 hasta dahil edilmiştir. Hastaların nütrisyonel durumu, Mini Nütrisyonel Değerlendirme Testi-Kısa Form (MNA-KF) ile değerlendirilerek, malnütrisyonu olan (MNA≤11) ve olmayan (MNA>11) şeklinde iki gruba ayrılmıştır. Tüm hastaların demografik özellikleri, sistemik hastalıkları kaydedilmiş, demans, depresyon, ortostatik hipotansiyon (OH), üriner inkontinans, rekürren düşme, kırılganlık ve sarkopeni varlığı ayrıntılı geriatrik değerlendirme testleriyle belirlenmiştir.

Bulgular: Malnütrisyonu olan 105 hastanın yaş ortalaması 78±10, olmayan 185 hastanın ise 76±9'du. Hastaların %71,7'si kadındı, ortalama eğitim yılları 5 yıldı. Malnütre hastalarda hemoglobin (Hb), albümin ve vitamin B12 anlamlı olarak daha düşük bulundu (p<0,05). Malnütrisyon riski yüksek bireylerde geriatrik depresyon, demans, OH, rekürren düşme, kırılganlık ve sarkopeni anlamlı olarak daha yüksek oranda (p<0,05) saptanırken, üriner inkontinans ve polifarmasi görülme oranı açısından anlamlı fark izlenmedi. Binominal regresyon analizi sonrasında, karıştırıcı faktörlerden bağımsız olarak demans, geriatrik depresyon, sarkopeni ve kırılganlığın malnütrisyon riskini arttırırken (p<0,05), rekürren düşme ve OH'nin bağımsız olarak malnütrisyon riskini arttırmadığı saptandı.

Sonuç: Demans, geriatrik depresyon, sarkopeni ve kırılganlık malnütrisyon ile yakından ilişkilidir. Yaşlı hastalar malnütrisyon riski açısından taranmalı ve eşlik eden geriatrik sendromlarla birlikte gerekli müdahaleleri yapılmalıdır.

Anahtar Kelimeler: Malnütrisyon, Sarkopeni, Kırılganlık, Demans, Depresyon

Abstract

Introduction: Malnutrition is a clinical condition that is common in the geriatric population. It has a proven effect on the immune response, morbidity and mortality of patients. The aim of this study was to determine the malnutrition status of geriatric patients at initial presentation and to investigate its relationship with the results of geriatric assessment.

Materials and Methods: This study included 290 patients who applied to the Geriatrics outpatient clinic between January 2023 and December 2023. The nutritional status of the patients was evaluated with the Mini Nutritional Assessment Test-Short Form (MNA-SF) and divided into two groups as malnutrition (MNA≤11) and non-malnutrition (MNA>11).

Demographic characteristics and systemic diseases of all patients were recorded and the presence of dementia, depression, orthostatic hypotension, urinary incontinence, recurrent falls, frailty and sarcopenia were determined by comprehensive geriatric assessment tests.

Results: The mean age was 78±10 years for 105 patients with malnutrition and 76±9 years for 185 patients without malnutrition. The percentage of female patients was 71,7 and the mean years of education was 5 years. The hemoglobin (Hb), albumin and vitamin B12 were significantly lower in malnourished patients ($p<0,05$). Geriatric depression, dementia, orthostatic hypotension (OH), recurrent falls, frailty and sarcopenia were significantly higher in individuals at high risk of malnutrition ($p<0,05$), while no significant difference was observed in the incidence of urinary incontinence and polypharmacy. After binominal regression analysis, it was found that dementia, geriatric depression, sarcopenia and frailty increased the risk of malnutrition ($p<0,05$), whereas recurrent falls and OH did not increase the risk of malnutrition independently of confounding factors (age, gender, Hb, etc.).

Conclusion: Dementia, geriatric depression, sarcopenia and frailty are closely associated with malnutrition. Elderly patients should be screened for the risk of malnutrition and necessary interventions should be performed together with accompanying geriatric syndromes.

Keywords: Malnutrition, Sarcopenia, Frailty, Dementia, Depression

GİRİŞ

Dünya'da büyüme hızı en yüksek grup olan yaşlı bireylerin, fonksiyonelliklerini sürdürmeleri veya geri kazanmaları için sağlıklı yaşlanmaya yönelik müdahale ve önlemler her geçen yıl artmaktadır(1). İleri yaşla gelen fizyolojik kısıtlılıklar, eşlik eden hastalıklar, bilişsel ve zihinsel stres faktörlerinde artış biyolojik yaşlanma sürecini hızlandırmakla birlikte, Dünya Sağlık Örgütü (DSÖ) tarafından yeterli beslenme durumu, sağlıklı yaşlanmanın temel taşı olarak vurgulanmıştır(2). Yetersiz beslenmenin sonucunda gelişen malnütrisyon, dokuların ihtiyaç duyduğu miktarda makro ve mikrobesinlerin yeterince alınamaması, organ disfonksiyonuna sekonder fiziksel ve mental sağlığın bozulması olarak tanımlanmaktadır(3). Prevalansı toplumda %2 ile %32 arasında değişirken, toplumda yaşayan yaşlı bireylerde %25-60, hastanede yatan yaşlılarda ise %35-65 arasındadır(4). Malnütrisyon, yaşlı hastalarda mortalite ve morbidite artışı, fonksiyonel kapasitede azalma, enfeksiyon riskinde artış ve bası yaraları riskinde artış gibi birçok olumsuz sonuca yol açabilir. Bu nedenle erken teşhis ve tedavi edilemediği takdirde, hastaların yaşam kalitesinde azalma, hastanede yatış süresi ve yeniden yatış sayısı, bakım ihtiyacı ve ölüm riskinde artışa neden olur(5).

Geriatrik sendromlar, yaşlı hastalarda sıklıkla görülen ve birbirleriyle ilişkili bir grup klinik durumdur. En yaygın geriatrik sendromlar arasında düşme, deliryum, demans, kognitif yetmezlik, sarkopeni, osteoporoz, malnütrisyon, kırılganlık ve üriner inkontinans yer alır(6). Malnütrisyon ile aralarında çok yönlü ve kompleks bir ilişki söz konusudur. Çeşitli geriatrik sendromların malnütrisyon riskini arttırdıkları gibi malnütrisyonun da bu sendromların gelişimi üzerine etkisi mevcuttur.

Literatürde malnütrisyonla görülme sıklığı artan çeşitli sendromlar bildirilmiş olup sonuçlar toplumlara ve yıllara göre değişkenlik göstermektedir(7,8).

Bu çalışmanın amacı, yaşlı hastaların ilk değerlendirmede malnütrisyon durumunu tespit etmek ve ayrıntılı geriatrik değerlendirme parametreleri ile ilişkisini ortaya koymaktır. İkincil olarak, birbiriyle birlikteliği sık görülen geriatrik sendromların malnütrisyonu olan yaşlı hastalarla bağımsız olarak ilişkili olup olmadığını tespit etmektir.

GEREÇ VE YÖNTEM

Bu çalışmada Ocak 2023 ile Aralık 2023 tarihleri arasında Balıkesir Üniversitesi Tıp Fakültesi Geriatri Bilimdalı polikliniğine ayaktan başvurmuş olan 386 hasta incelenmiştir. Çalışma öncesinde Balıkesir Üniversitesi Tıp Fakültesi Etik Kurulu'ndan 01.11.2023 tarih 2023/145 numaralı karar ile izin alınmıştır. Bu hastaların 96'sının dışlama kriterlerine sahip olması nedeniyle, çalışma kriterlerine uygun toplam 290 katılımcı değerlendirilmiştir. Tüm katılımcıların başvuru sırasında uygulanan laboratuvar bulguları ve Ayrıntılı Geriatrik Değerlendirme testleri retrospektif olarak hasta dosyaları ve hastane veri tabanından taranmış olup, araştırmamızda kullanılmıştır.

Dışlama ve dahil edilme kriterleri

Çalışmaya katılım için onam veren ve geriatri kliniğimize ayaktan başvuran 65 yaş ve üzerinde olan hastalar dahil edildi. Gıda ulaşımına önemli ölçüde engel olabilecek nöro-müsküler hastalığı veya ileri derecede osteoartriti bulunan, akut inme/serebro-vasküler hastalık (SVO), immobilite, hemoglobin düzeyi 10 g/dL olan anemi, sepsis/septik şok, akut börek hasarı, akut karaciğer yetmezliği, akut koroner sendrom, akut solunum yetersizliği, pulmoner ödem, ciddi metabolik asidoz, dehidratasyon, elektrolit dengesizliği, muayene sırasında kalp hızında belirgin değişiklikler (bradikardi/taşikardi), akut hemoraji/hipovolemik şok gibi ciddi hastalığı olanlar, madde ya da alkol bağımlılığı olan hastalar çalışmamızdan dışlandı.

Yaş, cinsiyet ve eğitim yılını kapsayan demografik bulgular hastaların dosya bilgilerinden tarandı. Komorbiditeler olarak diabetes mellitus, hipertansiyon, kronik kalp hastalığı (konjestif kalp yetmezliği ve aterosklerotik kalp hastalığı), kronik serebro-vasküler hastalık, periferik arter hastalığı ve kronik obstruktif akciğer hastalığı varlığı açısından tüm katılımcılar sorgulandı. Ayrıca KGD kapsamında sorgulanan üriner inkontinans, noktüri (>2/gece), son bir yıl içerisinde düşme varlığı, demans, depresyon, polifarmasi ($\geq$5 ilaç kullanımı), OH ve kırılganlık durumunu içeren geriatrik sendromlar da çalışma kapsamına alındı. Geriatrik depresyon ile demansın klinik tanısı, DSM-5 tanı kriterlerine göre konuldu(9). Kırılganlık, FRIED fiziksel kırılganlık ölçeği kullanılarak tanımlandı(10). Beş maddelik kriterlerden en az üçünün birlikteliği kırılganlık olarak tanımlandı. OH, "Aktif Dikilme Testi" uygulanarak değerlendirildi, yatar pozisyondan, ayakta pozisyona geçildiğinde ilk üç dk. içerisinde sistolik kan basıncında >20 mmHg ve/veya diastolik kan basıncında >10 mmHg düşüş olması OH olarak tanımlandı(11). Türkiye'de yapılmış sarkopeni kesim değerleri çalışmaları referans alınarak, el dinamometresi ile ölçülen düşük kavrama gücü kadınlarda <14 kg, erkeklerde <28 kg olması durumu düşük kas gücü olarak tanımlanarak sarkopeni olarak değerlendirilmiştir (12).

Bilişsel açıdan değerlendirme için Mini-mental Durum Muayenesi (MMSE) kullanıldı. Nutrisyonel durum değerlendirilmesi Mini Nutrisyon Değerlendirme Testi – Kısa Form (MNA-KF) ile yapıldı (13). Toplam 14 puan üzerinden hesaplanan testin değerlendirilmesi sonucu malnütrisyon açısından riskli (≤ 11) ve normal (>11) olarak iki gruba ayrıldı. Geriatri polikliniğinde rutin uygulanan laboratuvar testlerinden tam kan sayımı, albümin, açlık kan glukozunu ve kreatinin içeren biyokimyasal parametreler, lipid profili, B12 vitamini, tiroid uyarıcı hormon (TSH) ile 25-hidroksi D vitamini düzeyleri retrospektif olarak incelendi.

İstatistiksel analiz

Araştırmada yer alan hastalar nütrisyonel açıdan, MNA skoruna göre malnütrisyon olan ve olmayan şeklinde iki gruba ayrıldı. Kategorik değişkenler yüzde (%) şeklinde belirtildi. Sürekli değişkenler için normal dağılıma uygunluğu açısından Kolmogorov-Smirnov testi uygulandı. Normal dağılıma uyan değişkenler ortalama ± standart sapma şeklinde verilirken, normal dağılıma uymayan değişkenler medyan [çeyrekler açıklığı] olarak belirtildi. Kategorik değişkenlerin karşılaştırılmasında Ki-kare veya Fisher Exact testi kullanılırken, sürekli değişkenlerin ortalama değerlerinin karşılaştırmasında veriler normal dağılıma uyuyorsa student t testi, normal dağılıma uymuyorsa Mann Whitney U testi uygulandı. Bu iki grup değişkenler için p değeri verildi. Ayrıca geriatrik sendromların nütrisyon üzerine etkisinin incelenmesi açısından binominal lojistik regresyon analizi uygulandı. İlk önce karıştırıcı faktörlerce düzeltilmemiş Odds Oranı (OO) %95 güven aralığında verildi. Daha sonra yaş, cinsiyeti, eğitim yılı, hipertansiyon ve aterosklerotik kalp hastalığını içeren komorbiditeler, laboratuvar parametrelere göre düzeltilmiş Odds Oranı (OO) hesaplandı. İstatistiksel analizin tamamı SPSS 22.0 (SPSS Inc.) paket programı kullanılarak yapıldı ve veriler için p değerinin < 0,05 olması istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Çalışmaya alınan 290 hastanın yaş ortalaması 78±10, olmayan 185 hastanın ise 76±9'du. Hastaların %71,7'si kadındı, ortalama eğitim yılları 5 yıldı. Ortalama vücut kitle indeksleri (VKI), 26.84±5.38'idi. Hastaların 105 tanesi malnütrisyon açısından riskli (MNA-KF≤11) olarak saptandı. Malnütrisyonu olan ve olmayan hastalar arasında yaş, cinsiyet, medeni durum açısından anlamlı fark izlenmedi (p>0.05).

En sık eşlik eden komorbid hastalıklar diabetes mellitus, hipertansiyon, aterosklerotik kalp hastalığı, konjestif kalp yetmezliği ve serebrovasküler hastalıklardı. Demografik verilerden istatistiksel olarak anlamlı bulunan değerlerin subgrup analizleri yapıldığında, normal grupta (MNA-KF>11) hipertansiyon (p=0.01) ve aterosklerotik kalp hastalığı (p=0.048) olanların sayısı anlamlı olarak daha yüksek bulundu. Laboratuvar parametreleri karşılaştırıldığında malnütre hastalarda hemoglobin (Hb)(p=0.02), albümin (p=0.01) ve vitamin B12 (p=0.006) anlamlı olarak daha düşük bulundu. Malnütrisyonlu ve normal beslenen grupların demografik özellikleri, komorbiditeleri ve laboratuvar parametrelerine göre karşılaştırılması gösterilmiştir (**Tablo 1**).

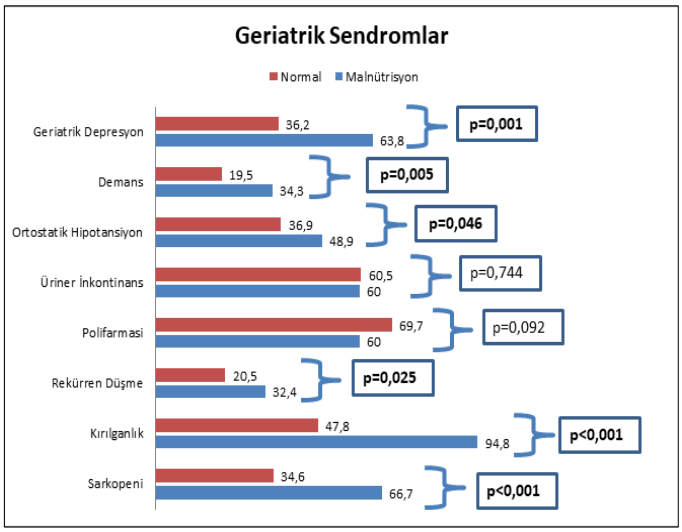
Kullandıkları ilaç sayılarına göre değerlendirildiğinde malnütrisyonu olanların %60'ında normal grubun ise % 69.7'sinde polifarmasi saptandı. İstatistiksel olarak anlamlı fark izlenmedi. Malnütrisyonu olan grupta demans (p=0.005), ortostatik hipotansiyon (p=0.046), rekürren düşme (p=0.025), geriatrik depresyon, kırılganlık ve sarkopeni (p<0.001) normal gruba kıyasla anlamlı olarak daha yüksek oranda izlendi. Üriner inkontinans ise gruplar arasında benzer oranda görüldü. Malnütrisyonlu ve normal beslenen gruplar arasında geriatrik sendromların karşılaştırılması **Şekil 1**'de özetlenmiştir

***Tablo 1**. MNA skoruna göre, malnütrisyon ve normal beslenen grupların demografik özellikleri, komorbiditeleri ve laboratuvar parametrelerine göre karşılaştırılması*

	MNA skoru ≤11 Malnütrisyon n=105	***MNA Skoru >11 Kontrol n=185***	***p değeri***
DEMOGRAFİK ÖZELLİKLER			
Yaş	78 [10]	76 [9]	0.062
Cinsiyet (Kadın;%)	73.30	70.80	0.686
Eğitim Yılı	5 [3]	5 [0]	**0.003**
Medeni Durum (Evli;%)	41.90	47.60	0.277
KOMORBİDİTELER (%)			
Diabetes Mellitus	36.20	42.70	0.277
Hipertansiyon	65.70	75.50	**0.010**
Aterosklerotik Kalp Hastalığı	11.40	20.50	**0.048**
Konjestif Kalp Yetmezliği	10.5	12.40	0.619
Serebrovasküler Hastalık	3.80	4.30	0.832
Periferik Arter Hastalığı	1.90	5.90	0.144
LABORATUVAR BULGULARI (medyan [çeyrekler açıklığı])			
Hemoglobin*(g/dL)	12.00±1.80	12.48±1.63	**0.026**
Total Kolesterol (mg/dL)	203 [76.50]	208 [84.50]	0.106
Glukoz (mg/dL)	109 [51.80]	108 [25]	0.244
Albumin (g/dL)	3.90 [0.50]	4.10 [0.40]	**<0.001**
C-reaktif protein (mg/L)	3 [17.55]	3 [4.14]	0.065
tGFH (ml/dak/1,73 m^2)	73.84 [34.72]	66.80 [29.85]	0.800
Vitamin B12 (ng/L)	315 [355]	269 [281]	**0.006**
25-OHD (mcg/L)	16.70 [14.80]	18 [15.80]	0.366
Ferritin (mcg/L)	41.40 [128.15]	27 [40.10]	0.076

** Hemoglobin düzeyi her iki grupta normal dağılıma uyduğu için veriler ortalama±standart sapma şeklinde verilmiştir.*

25-OHD: 25-hidroksi D vitamini; MNA: Mini-nütrisyonel değerlendirme; tGFH: tahmini Glomerüler Filtrasyon Hızı



Şekil 1. *Malnütrisyon ve normal beslenen grupların geriatrik sendromlar açısından karşılaştırılması*

MNA-SF testi kullanılarak yapılan nütrisyon sınıflamaları üzerinde geriatrik depresyon, demans, ortostatik hipotansiyon, rekürren düşme, kırılganlık ve sarkopeninin tahmini rölatif risk katsayıları hesaplandı. Yaş, cinsiyet, eğitim yılı, hipertansiyon, aterosklerotik kalp hastalığı durumu, hemoglobin, albümin ve vitamin B12 düzeylerine göre düzeltme yapıldığı zaman normal nütrisyona sahip grup ile malnütrisyon risk grubu arasında sarkopeni [OR: 4.24 (%95 CI)], kırılganlık [OR: 4.56 (%95 CI)], demans [OR: 1.94 (%95 CI)] ve depresyon [OR: 2.06 (%95 CI)] riskinin anlamlı olduğu saptandı (p< 0.05) (Tablo 2)

Tablo 2. Binominal regresyon analizinde geriatrik sendromlar ile malnütrisyon arasındaki ilişkinin değerlendirilmesi

Geriatrik Sendromlar		***Odds Oranı***	***%95 Güven Aralığı***	***p değeri***
Sarkopeni				
	Düzeltilmemiş	3,78	2,27-6,27	**<0,001**
	Düzeltilmiş*	4,24	2,33-7,73	**<0,001**
Kırılganlık				
	Düzeltilmemiş	4,46	2,59-7,69	**<0,001**
	Düzeltilmiş*	4,56	2,46-8,44	**<0,001**
Rekürren Düşme				
	Düzeltilmemiş	1,85	1,07-3,18	**0,026**
	Düzeltilmiş*	1,75	0,95-3,24	0,072
Ortostatik Hipotansiyon				
	Düzeltilmemiş	1,69	1,02-2,72	**0,047**
	Düzeltilmiş*	1,44	0,82-2,53	0,194
Demans				
	Düzeltilmemiş	2,15	1,25-3,71	**0,005**
	Düzeltilmiş*	1,94	1,04-3,62	**0,037**
Geriatrik Depresyon				
	Düzeltilmemiş	2,26	1,38-3,70	**0,001**
	Düzeltilmiş*	2,06	1,19-3,58	**0,010**

Tartışma

Yaşlı hastalarda ilk vizitte beslenme durumu ve geriatrik sendromlarla ilişkisini inceleyen bu çalışmada bulgular, malnütrisyon riski yüksek hastaların düşme, kırılganlık, sarkopeni, OH, demans ve depresyon gibi geriatrik sendromlarla ilişkili olduğunu, özellikle sarkopeni, kırılganlık, demans ve geriatrik depresyonun etkisinin daha belirgin olduğunu göstermiştir.

Malnütrisyon, yaşlı hastalarda kolay farkedilemeyen ya da atlanılabilinen bir geriatrik sendromdur. Ancak beslenme durumunun ve malnütrisyon riskinin belirlenip gerekli müdahalelerde bulunulması eşlik eden komorbid hastalıkların yönetiminde de önemli rol oynamaktadır. Yaşlı hastaların, diğer erişkinlerden daha sık olarak, birinci basamak sağlık kuruluşlarına başvurduğu bildirilmiştir(14). Bu nedenle yeterli/yetersiz beslenmenin derecesini belirlemede kullanılan nütrisyonel değerlendirme testleri aile hekimleri ve evde bakım birimlerinde çalışan hekimlerin de kullanabileceği şekilde pratik, etkili ve uygulanabilir olmalıdır. MUST (Malnutrition Universal Screening Tool), NRS2002 (Nutritional Risk Screening), GLIM (Global Leadership Initiative on Malnutrition), Mini Nutrisyonel Değerlendirme (MNA) tarama hedefine en uygun testlerdir (15–17). Çalışmamızda MNA testinin toplam puanı analiz edilmiş, soru sayısı daha az ve benzer etkinlikte olacak şekilde geliştirilen kısa form (MNA-SF) kullanılmıştır. MNA-SF, malnütrisyon durumunu göstermede MUST ve NRS2002 nütrisyonal değerlendirme testleri ile benzer bulunmuştur(18,19). Özellikle yaşlı hastalarda nütrisyonel değerlendirme testlerinin karşılaştırıldığı bazı çalışmalarda GLIM, malnütrisyona bağlı mortalite artışı ve hastanede yatış süresine etkisini göstermede daha etkili bulunmuştur. GLIM kriterleri iki aşamalı yaklaşım ile hastaların değerlendirildiği bir tarama testidir (20). İlk aşamada malnütrisyon açısından riskli hastalar onaylanmış tarama testlerinden biriyle belirlendikten sonra, malnütrisyon şiddetinin teşhisi ve derecelendirilmesi için, istemsiz kilo kaybı, düşük VKİ, kas kütlesinde azalma, gıda alımında azalma, sindirim sistemi hastalığı açısından değerlendirme yapılır (17). Tanı için fenotipik ve etiyolojik birer kriterin olması beklenen GLIM, nitel değerlendirme içermesi, pratikte uygulanabilirliğinin güç ve soruların yoruma açık olması nedeniyle tercih edilmemiştir.

Çalışmamızda malnütrisyon açısından riskli hastalar ve malnütrisyonu olan hastaların toplam prevalansı %56.7 olarak saptanmış olup literatür ile benzer orandadır. Ülkemizde, 2010 yılında İç Hastalıkları polikliniğine başvuran yaşlı hastalar üzerinde yapılan bir çalışmada malnütrisyon riski yüksek ve malnütre hastalar %44 oranında tespit edilirken, yakın zamanda 60 yaş ve üzeri 2816 hastanın alındığı tek merkezli çalışmada MNA-KF ≤7 olanların oranı %13 olarak tespit edilmiştir (4,21).

Geriatrik malnütrisyonda nütrisyon durumunu gösteren, pratikte yaygın kullanılabilen laboratuvar parametreleri arasında hemoglobin, albumin, total kolesterol, lenfosit yer alır(22). Bu çalışmada da malnütrisyon açısından riskli hastalarda daha düşük hemoglobin, albumin düzeyi ve vitamin B12 eksikliği izlenmiş olup total kolesterol ve diğer parametrelerde anlamlı fark izlenmemiştir.

Kırılganlık, fizyolojik rezervlerin azaldığı, minör stres faktörlerine karşı direncin düşmesi, gelişen olumsuz sağlık sonuçlarıyla vücudun kendine yetemediği bir durumdur. Anormal kilo kaybı, halsizlik, fiziksel aktivitede azalma, yürüme hızında yavaşlama, el kavrama gücünde azalmadan en az üç tanesinin varlığı ile tanı konur (10). Ülkemizde ve Dünya'da kırılganlık prevalansı üzerine yapılan çalışmalarda kadınlarda görülme sıklığı erkeklerden daha fazla bulunmuştur (23). Ülkemizde 13 farklı merkezden 1126 yaşlı bireyin değerlendirildiği FRAIL-TURK çalışmasında katılımcıların %39.2'sinde kırılganlık, %43.3'ünde kırılganlık riski saptanmıştır (24). Malnütrisyonu olan yaşlı bireylerde kötü beslenmenin sonucunda %90 kırılganlık ve ya kırılganlık riski (pre-fail) gelişmektedir (25). Çalışmamızda literatürle uyumlu olarak malnütrisyon açısından riskli bireylerin %94.8' inde kırılganlık ve kırılganlık riski saptanmıştır.

Tanı kriterlerinin, sarkopeni başta olmak üzere diğer geriatrik sendromlarla benzer özellikleri içermesi, bir çalışmada 'Kırılganlığın geriatrik ağı' olarak adlandırılmıştır (26). Sarkopeni de kırılganlığa benzer şekilde fiziksel aktivitede azalma, kavrama gücü kaybı, fiziksel aktivitede azalma ile seyreden, yağsız kas kütlesinde azalmaya bağlı gelişen bir geriatrik sendromdur (27). Yaşlılığa bağlı fizyolojik değişikliklerin sonucunda gelişen tat ve duyu kaybı, yemeklere duyulan ilgide azalma, gastrik boşalmada yavaşlama, yetersiz protein alımı, komorbid hastalıklar, polifarmasi ve fiziksel aktivitede azalma sarkopeni gelişiminden sorumlu tutulmaktadır (28). Ülkemizde 2008 yılında, ayaktan hastalarda geriatrik sendrom prevalansının değerlendirildiği bir çalışmada sarkopeni prevalansı %25 olarak bulunmuştur (6). Huzurevinde kalan yaşlılarda malnütrisyon ve sarkopeni ilişkisi üzerine yapılan bir çalışmada sarkopeni durumu el dinamometresi ile kas gücü ölçümüne dayanılarak yapılmış ve 349 hastanın 274'ünde (%78.5) düşük bulunmuştur. Çalışmamızda sarkopeni tanımlaması için dinamometre ile düşük kas gücü ölçümünden faydalanılmış olup, kas kütlesi ölçülememiştir. Malnütrisyonu olmayan hastalarda %34.6, malnütrisyon riski yüksek ve malnütre olanlarda ise %66.7 oranında kas gücü düşük saptanmıştır. Literatürde ayaktan başvuran hastalarda saptanan sarkopeni oranlarına göre çalışmamızda yüksek oran saptanması, kas kütlesi değerlendirme komponentindeki kısıtlılık nedenli olarak değerlendirilmiştir.

Hem kırılganlığın hem de sarkopeninin düşme ve kırık riskinde artış, günlük yaşam aktivitelerinde ve yaşam kalitesinde azalma, morbidite ve mortalitede artışa yol açtığı bilinmektedir (29). Geriatrik hastalarda düşme, fizyolojik ve fonksiyonel kapasitede azalma, polifarmasi, kronik hastalıklar, denge ve postür bozuklukları gibi etkenler sonucunda gelişir. Yaş artışıyla ve malnütrisyon ile birlikte görülme sıklığında da artış olup 70 yaşta %25, 75 yaş ve üzerinde %35 oranında izlenmektedir (30). Çalışmamızda da prevalansı literatürle benzer oranlarda bulunmuştur.

Malnütrisyonu olmayanlarda OH %36.9 oranında görülürken, riskli grupta %48.9 olarak izlenmiştir. OH prevalansı yapılan çalışmalarda her geçen yıl artmakta olup genel nüfusta %30 civarında görülürken, malnütrisyon riski yüksek bireylerde %45 dolaylarında seyretmektedir (31,32). Bulgular literatür ile uyumlu izlenmiştir.

Geriatrik depresyon, malnütrisyonla ilişkili olabileceği bilinen bir diğer geriatrik sendromdur. Çalışmamızda malnütrisyon riski yüksek bireylerde %63.8, malnütrisyonu olmayanlarda ise %36.2 oranında bulunmuştur. Ülkemizde daha önce yapılan çalışmalarda, 65 yaş üzeri kişilerde depresyon sıklıkları huzurevinde yaşayanlarda %10.2–68.9, kendi evlerinde yaşayanlarda %29 olarak bildirilmiş olup bulgularımız literatürle uyumludur (33,34).

Geriatrik sendromların birbiriyle ilişkili olabileceği ve malnütrisyonun da diğer geriatrik sendromlar için tek başına risk faktörü olduğu ve demografik özellikler, komorbid durumlardan etkilendiği bilinmektedir (21). Yaş, cinsiyet, eğitim yılı, hipertansiyon, aterosklerotik kalp hastalığı durumu, hemoglobin, albümin ve vitamin B12 düzeylerine göre düzeltmeyle yapılan regresyon analizi sonrası, sarkopeni, kırılganlık, demans ve geriatrik depresyonun malnütrisyon riskiyle ilişkili olduğu görülmüştür. Literatürde Saka ve ark. malnütrisyon ile demans, düşme ve depresyonu ilişkili bulmuş olup bulgular regresyon analizi ile değerlendirmemiştir (21). 2008 yılında yapılan ve malnütrisyonun diğer geriatrik sendromlarla ilişkisinin incelendiği bir diğer çalışmada ise malnütrisyon ile geriatrik depresyon ilişkili bulunmuş, demans ile nütrisyonel durum arasında ilişki gözlenmemiştir (35). Ülkemizde yapılan bir diğer çalışmada ise geriatrik depresyon, üriner inkontinans, demans, OH, sarkopeni ve kırılganlık normal gruba göre, malnütrisyon ve malnütrisyon riski olan yaşlılarda daha yüksek gözlenmiş olup çalışmamızdaki bulgularla benzerdir (36).

Sarkopeni ve kırılganlığın, demans ve depresyona göre etkisi daha yüksek saptanmıştır. Yapılan bazı çalışmalarda malnütrisyon sarkopeni öncülü, sarkopeni ise kırılganlığın bir komponenti olarak değerlendirilmektedir (37). Ayrıca sarkopeni ve kırılganlıkta ortak fizyopatolojik mekanizmaların varlığı birbirleriyle ilişkili olmalarını desteklemektedir (38). Sarkopeni tanısında kullanılan düşük kas kütlesinin, kırılganlık gelişiminde bağımsız bir risk faktörü olduğu çalışmalarda gösterilmiştir (38,39).

Çalışmamızın bazı güçlü yönleri vardır. Birincisi, malnütrisyon ile geriatrik sendromlar ve AGD parametrelerinin ilişkisini geniş kapsamda inceleyen bir çalışma olmasıdır. İkincisi, kötü nütrisyonel durum ile bu parametrelerin ilişkisinin yaş başta olmak üzere karıştırıcı faktörlerden bağımsız olarak gösterilmesidir. Çalışmamızın kısıtlılıkları ise örneklem büyüklüğünün küçük olması, retrospektif ve kesitsel bir çalışma olmasıdır. Bir diğer kısıtlılığımız sarkopeni tanısı için kas kütlesi kaybının değerlendirilememiş olmasıdır. Hastalarımızın önemli bir kısmında biyoimpedans analizi yapılamaması nedeniyle dahil edilmemiştir. Çalışmamız retrospektif olduğundan rutin tetkiklerde istenmeyen ayrıntılı vitamin ve mineral düzeyleri değerlendirilememiştir.

Sonuç

Yaşlı hastalarda malnütrisyon, yaygın görülen bir geriatrik sendromdur. Birinci basamak hekimleri, aile hekimleri, iç hastalıkları uzmanları tarafından malnütrisyon tarama farkındalığı arttırıldığında erken tanı ve müdahaleler ile mortalite ve morbiditenin azalmasına katkı sağlanabilir. Demans, geriatrik depresyon, sarkopeni ve kırılganlık malnütrisyon ile yakından ilişkilidir. Yaşlı hastalar malnütrisyon riski açısından taranmalı ve eşlik eden geriatrik sendromlarla birlikte bütüncül yaklaşılarak gerekli müdahaleleri yapılmalıdır.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 80-86

Relationship Between Heart Rate Variability and Premature Ventricular Contractions

Kalp Hızı Değişkenliği ile Ventriküler Erken Atımlar Arasındaki İlişki

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Geliş Tarihi: 07.02.2024
Kabul Tarihi:22.03.2024

Abstract

Background: Premature ventricular contraction (PVC) is the most often type of ventricular arrhythmias. Heart rate variability (HRV) is an efficient noninvasive methods for assessing autonomic effects on the heart. This study aimed to investigate the relationship between HRV and PVC.

Methods: 80 patients with frequent PVCs and 108 patients without PVC as control group included in this study. Rhythm holter was performed in all participants. Frequent PVCs defined as more than 30 times PVCs in 1 hour, according to the Lown classification. The HRV evaluated by time domain analysis included the standard deviation of all NN intervals (SDNN), standard deviation of the average NN intervals (SDANN), the square root of the mean of the squares of successive differences between adjacent NN intervals (rMSDD), the percentage of normal RR intervals that differ by more than 50 millisecond (PNN50).

Results: Patients with frequent PVCs were older ($p<0.001$) and they had more coronary artery disease ($p<0.001$), hypertension ($p=0.026$) and diabetes mellitus ($p<0.001$). Their ejection fraction ($p=0.001$) and estimated glomerular filtration rate levels ($p=0.001$) were lower. Patients with frequent PVCs had lower levels of SDNN ($p<0.001$) and SDANN ($p<0.001$). PNN50 ($p=0.802$) and rMSDD ($p=0.572$) were not statistically different between groups.

Conclusion: Patients with frequent PVCs have been shown to have impaired HRV, indicated by low SDNN and SDANN levels associated with sympathetic overactivity. HRV measurements in patients with PVCs are a simpler and noninvasive method for the assessment of cardioneural regulation using rhythm holter monitoring.

Keywords: Heart rate variability, premature ventricular contraction, sympathetic system

Öz

Amaç: Ventriküler kaynaklı aritmilerin en sık kaşılaşılan tipi ventriküler erken atımlardır (VEA). Kalp hızı değişkenliği, kalp üzerindeki otonomik etkileri değerlendirmek için en etkili noninvaziv yöntemlerden biridir. Bu çalışmada kalp hızı değişkenliği ile ventriküler erken atımlar arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Sık VEA'sı olan 80 hasta ile VEA izlenmeyen 108 hasta çalışmaya dahil edildi. Tüm katılımcılar ritm holter ile değerlendirildi. Lown sınıflandırmasına göre ritm holterde 1 saat içinde 30'dan fazla VEA izlenmesi sık VEA olarak tanımlandı. Kalp hızı değişkenliği, tüm NN aralıklarının standart sapmasına (SDNN), ortalama NN aralıklarının standart sapmasına (SDANN), bitişik NN aralıkları arasındaki ardışık farkların karelerinin ortalamasının karekköküne (rMSDD) ve 50 milisaniyeden fazla farklılık gösteren normal RR aralıklarının yüzdesine (PNN50) göre değerlendirildi.

Bulgular: Sık VEA'sı olan hastalar daha yaşlı (p<0.001), daha fazla koroner arter hastası (p<0.001), hipertansif (p=0.026) ve diyabetik (p<0.001) idi. Ejeksiyon fraksiyonları (p=0,001) ve glomerüler filtrasyon hızları da daha düşüktü (p=0,001). Sık VEA izlenen hastalarda SDNN (p<0.001) ve SDANN (p<0.001) değerleri daha düşük saptandı. PNN50 (p=0.802) ve rMSDD (p=0.572) değerleri ise gruplar arasında anlamlı farklılık göstermiyordu.

Sonuç: Çalışmamızda sık VEA'lı hastalarda, aşırı sempatik aktiviteyle ilişkili düşük SDNN ve SDANN değerlerinin izlendiği bozulmuş kalp hızı değişkenliği saptadık. Sık VEA izlenen hastalarda ritm holter ile kalp hızı değişkenliği kardiyonöral regülasyonun değerlendirilmesinde faydalı ve invaziv olmayan bir yöntemdir.

Anahtar Kelimeler: Kalp hızı değişkenliği, sempatik sistem, ventriküler erken atım.

Introduction

Premature ventricular contraction (PVC) is the most frequent type of ventricular arrhythmias. The autonomic nervous system is an important regulatory mechanism in arrhythmias, including PVCs and ventricular tachycardia (1). The autonomic nervous system, including sympathetic and parasympathetic system, plays a prominent role in the occurrence of ventricular and atrial arrhythmias (2,3)**.**

Heart rate variability (HRV) shows the influence of the parasympathetic and sympathetic systems on the heart. The balance between parasympathetic and sympathetic activity regulates the cardiac cycle from beat to beat. Heart rate variability is a noninvasive marker for cardiac autonomic modulation. It is also used for assessment of cardiac adaptation mechanisms and cardiac autonomic status (4). HRV is calculated based on oscillations between R-R intervals of the ECG. HRV is associated with cardiovascular diseases, metabolic diseases, age, exercise, circadian rhythm and respiratory rate (5-7)**.** Also, HRV is associated with higher cardiovascular mortality (8). Rhythm holter systems is a noninvasive and basic method to assess HRV.

Whereas, the relationship between PVC and HRV in the population still remains controversial (9,10). This study aimed to investigate the relationship between HRV and PVC.

Materials and methods

80 patients with frequent PVCs and 108 patients without PVC as control group included in this study. Frequent PVCs defined as more than 30 times in 1 hour, according to the Lown classification (10). The exclusion criteria were patients aged <18 years old, incomplete 24 hour rhythm holter datas and patients with atrial fibrillation.

All participants underwent a 24 hour rhythm holter monitoring by using a validated three channel device (Borsam Holter ECG BS6930, Borsam Biomedical Instruments Co., Ltd, China) and the datas were analysed on iTengo Analysis System. All participants were suggested to maintain their regular activities during the rhythm holter examination.

The HRV evaluated by time domain analysis included the standard deviation of all NN intervals (SDNN), standard deviation of the average NN intervals (SDANN), the percentage of normal RR intervals that differ by more than 50 millisecond (PNN50) and the square root of the mean of the squares of successive differences between adjacent NN intervals (rMSDD) (11,12).

This retrospective study was approved by the local ethics committee according to the declaration of Helsinki.

Statistical Analysis

SPSS 13.0 (SPSS Inc., IBM, Chicago, IL, USA) was used for statistical analyses. Kolmogorov-Smirnov test was used to analyze the distribution of the parameters. Categorical variables were expressed as percentages and frequencies. Abnormally distributed parameters are expressed as median and percentiles (25–75) and normally distributed variables as mean±SD. Categorical variables were tested with the Chi-square or Fisher's exact test. Normally distributed continuous parameters were evaluated with 2-tailed Student's t-test and abnormally distributed parameters with Mann-Whitney U test. A p value <0.05 was accepted as statistically significant.

Results

80 patients with frequent PVCs and 108 patients without PVC were included in this study. Patients with frequent PVCs were 61±17 years of age and control group was 56.7±5.5 years of age. Patients with frequent PVCs were older compared to the control group (p<0.001). 55% of the patients with frequent PVCs and 43.5% of the control group was male. There was no significant difference in gender between the groups (p=0.079). BMI was 28.2±3.8 kg/m^2 of the patients with frequent PVCs and 26.2±5.3 kg/m^2 of the control group. The BMI was not statistically significant between groups (p=0.069).

36.3% of the participants were diabetic, 47.5% of the participants were hypertensive and 23.8% of the participants had coronary artery disease in patients with frequent PVCs. 12% of the participants were diabetic, 32.4% of the participants were hypertensive and 6.5% of the participants had coronary artery disease in control group. Diabetes mellitus (p<0.001) and HT (p=0.026) and coronary artery disease (p<0.001) rates were significantly higher in patients with frequent PVCs compared to the control group.

Ejection fraction (EF) was 60 (55-65) % in the patients with frequent PVCs and 60 (60-65) % in the control group. E ussu was 7 (6-9) in the patients with frequent PVCs and 9 (8-11) in the control group. LVEDD was 48 (46-50) mm in the patients with frequent PVCs and 46 (44-48) mm in the control group. LVESD was 32 (29-36) mm in the patients with frequent PVCs and 31 (28-34) mm in the control group. Left atrium was 36 (32-40) mm in the patients with frequent PVCs and 32 (30-36) mm in the control group. Ascending aorta was 33.1±3.2 mm in the patients with frequent PVCs and 31.4±4.6 mm in the control group. EF (p=0.001), E' (p=0.003) were significantly lower and left ventricular end diastolic diameter (LVEDD) (p<0.001), left ventricular end systolic diameter (LVESD) (p=0.047), left atrium (p=0.001), ascending aorta (p=0.004) were higher in the patients with frequent PVCs compared to the control group.

E wave (p=0.407), A wave (p=0.547), and pulmonary artery systolic pressure (PAsP) (p=0.137) were similar between groups. Baseline characteristics and echocardiographic parameters of the groups were given in Table 1.

ACE-I/ARB (p=0.014), beta-blocker (p<0.001), thiazide diuretic (p=0.026), acetylsalicylic acid (p=0.001), diltiazem (p=0.031) and statin (<0.001) usage were higher in the patients with frequent PVCs compared to the control group. Calcium channel blocker (p=0.510) usage was similar between groups.

Glucose was 108 (90-130) mg/dl in the patients with frequent PVCs and 95 (90-105) mg/dl in the control group. HbA1c was 6 (5.6-6.9) in the patients with frequent PVCs and 5.6 (5.3-6) in the control group. eGFR was 79.3±24.2 ml/min in the patients with frequent PVCs and 91.9±20.4 ml/min in the control group. Creatinine was 1.08±0.8 mg/dl in the patients with frequent PVCs and 0.89±0.32 mg/dl in the control group. Urea was 40±22.4 mg/dl in the patients with frequent PVCs and 31.3±12.5 mg/dl in the control group.

Table 1. Baseline characteristics and echocardiographic parameters of the groups

	Patients with Frequent PVCs (n=80)	**Control Group (n=108)**	**P**
Age (years)	61±17	54±19	**<0.001**
Male/female	44/36 (55%-45%)	47/61 (43.5%-56.5%)	0.079
Body mass index (kg/m^2)	28.2±3.8	26.2±5.3	0.069
Hypertension	38 (47.5%)	35 (32.4%)	**0.026**
Diabetes mellitus	29 (36.3%)	13 (12%)	**<0.001**
Coronary artery disease	19 (23.8%)	7 (6.5%)	**<0.001**
Echocardiographic parameters			
Ejection fraction (%)	60 (55-65)	60 (60-65)	**0.001**
E wave	82±26	86±21	0.407
A wave	78±22	67±22	0.547
E' wave	7 (6-9)	9 (8-11)	**0.003**
LVEDD (mm)	48 (46-50)	46 (44-48)	**<0.001**
LVESD (mm)	32 (29-36)	31 (28-34)	**0.047**
Left atrium diameter (mm)	36 (32-40)	32 (30-36)	**<0.001**
PASP (mmHg)	20 (15-30)	20 (15-20)	0.137
Ascending aorta (mm)	33.1±3.2	31.4±4.6	**0.004**

LVEDD: Left ventricular end diastolic diameter, LVESD: Left ventricular end systolic diameter, PASP: Pulmonary arterial systolic pressure

Total Cholesterol was 198±42mg/dL in the patients with frequent PVCs and 190±45mg/dL in the control group. LDL was 120±37mg/dL in the patients with frequent PVCs and 116±36mg/dL in the control group. HDL was 45 ±11mg/dL in the patients with frequent PVCs and 49±12mg/dL in the control group. Triglyceride was 157±63mg/dL in the patients with frequent PVCs and 122±74mg/dL in the control group. Glucose (p=0.001), HbA1c (p=0.002), creatinine (p=0.001), urea (p=0.001) and triglyceride (p=0.002) were higher and eGFR (p=0.001), HDL (p=0.024) were lower the patients with frequent PVCs compared to the control group. Hemoglobin (p=0.459), hematocrit (p=0.601), platelet (p=0.091), WBC (p=0.075), AST (p=0.629), ALT (p=0.999), total cholesterol (p=0.329) and LDL (p=0.539) were similar between groups. Medications and hematological/biochemical parameters of the groups were given in Table 2.

Table 2. Medications and hematological/biochemical parameters of the groups

	Patients with Frequent PVCs (n=80)	**Control Group (n=108)**	**P**
ACE-I/ARB	26 (32.5%)	19 (17.6%)	**0.014**
Beta-blocker	35 (43.8%)	15 (13.9%)	**<0.001**
Thiazide diuretic	22 (27.5%)	15 (13.9%)	**0.026**
Acetylsalicylic acid	28 (35%)	16 (14.8%)	**0.001**
Diltiazem	4 (5%)	0 (0%)	**0.031**
Statin	20 (25%)	5 (5.6%)	**<0.001**
Calcium Channel Blocker	17 (21.3%)	24 (22.2%)	0.510
Hematological and biochemical parameters			
Glucose (mg/dl)	108 (90-130)	95 (90-105)	**0.001**
HbA1c	6 (5.6-6.9)	5.6 (5.3-6)	**0.002**
Hemoglobin (g/dl)	13.4±2.1	13.6±1.8	0.459
Hematocrit (%)	40±5.8	40.5±5	0.601
Platelet (x1000/uL)	240±63	259±74	0.091
WBC (x1000/mm³)	7.3±2.4	6.7±2	0.075
eGFR (ml/min)	79.3±24.2	91.9±20.4	**0.001**
Creatinine (mg/dl)	1.08±0.8	0.89±0.32	**0.035**
Urea (mg/dl)	40±22.4	31.3±12.5	**0.001**
AST (U/L)	19 (17-25)	20 (20-24)	0.629
ALT (U/L)	16 (12-25)	17 (12-23)	0.999
Total Cholesterol (mg/dL)	198±42	190±45	0.329
LDL (mg/dL)	120 ±37	116±36	0.539
HDL (mg/dL)	45 ±11	49±12	**0.024**
Triglyceride (mg/dL)	157 ±63	122±74	**0.002**

ACE-I: Angiotensin converting enzyme inhibitors, ARB: Angiotensin receptor blockers, WBC: White blood cell count, eGFR: Estimated glomerular filtration rate, AST: Aspartate transaminase, ALT: Alanine transaminase, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

SDNN was 138.1±55 ms in the patients with frequent PVCs and 176.3±50.9 ms in the control group. SDANN was 136.5 (96.5-190.3) ms in the patients with frequent PVCs and 203.5 (149.3-280) ms in the control group. PNN50 was 28.6±23.5 % in the patients with frequent PVCs and 27.8±18.6 % in the control group. rMSDD was 76 (48-137) ms in the patients with frequent PVCs and 86.5 (54-124.8) ms in the control group.

PVC was 2015 (1031-5283) in the patients with frequent PVCs and 0 (0-0) in the control group (p<0.539). SDNN (p<0.001) and SDANN (p<0.001) were significantly lower in the patients with frequent PVCs compared to the control group. PNN50 and RMSDD were similar between groups. Heart rate variability parameters of the groups were given in Table 3.

Table 3. Heart rate variability parameters of the groups

	Patients with Frequent PVCs (n=80)	Control Group (n=108)	P
SDNN (ms)	138.1±55	176.3±50.9	<**0.001**
SDANN (ms)	136.5 (96.5-190.3)	203.5 (149.3-280)	<**0.001**
PNN50 (%)	28.6±23.5	27.8±18.6	0.802
rMSDD (ms)	76 (48-137)	86.5 (54-124.8)	0.572
PVC	2015 (1031-5283)	0 (0-0)	<**0.001**

SDNN: Standard deviation of all NN intervals, SDANN: Standard deviation of the average NN intervals, PNN50: Percentage of normal RR intervals that differ by more than 50 millisecond, rMSDD: Square root of the mean of the squares of successive differences between adjacent NN intervals. PVC: Premature ventricular contraction

Discussion

PVC is the most frequent type of ventricular arrhythmias. Although PVC has a benign character, it has been found to be associated with mortality (8). The parasympathetic and sympathetic systems plays an important role in modulation of ventricular arrhythmias (13).

The main findings of the present study are heart rate variability calculated by SDNN and SDANN related with sympathic system activation were lower in patients with frequent PVC compared to the control group. Also, patients with frequent PVCs were older and they had more coronary artery disease, hypertension and diabetes mellitus. Their ejection fraction and estimated glomerular filtration rate levels were lower compared to the control group. HRV, a noninvasive and basic marker for assessing the cardiac autonomic function, describes the oscillations between R–R intervals of ECG. High levels of HRV usually indicate efficient autonomic function in a healthy individuals, while low levels of HRV often indicate an autonomic nervous system dysfunction (14). SDNN and SDANN reflect a more contribution of sympathetic activity to HRV, and lower levels of SDNN and SDANN show an increased sympathetic tone. Whereas, pNN50 and rMSSD are reliable indicators of parasympathetic tone (15-17).

Dong et al evaluated 4754 patients who received 24 hour rhythm holter for palpitation. Patients with PVC ≥1 and patients without PVC were compared. SDNN, SDANN, rMSSD and pNN50 were lower in patients with PVC ≥1 group (18). Zhang et al studied with 106 patients with frequent outflow tract PVCs and 106 healthy individuals. Patients underwent radiofrequency catheter ablation for drug resistant symptoms and intolerant caused by PVCs. These patients had either PVC burden >10% or PVC counts >10 000 beats/24 hour assessed by rhythm holter monitoring.

Significantly lower levels of SDNN and SDANN were observed in the patients with PVCs compared to the healthy individuals. However, there was no statistically significant difference in the levels of pNN50 and rMSSD between groups (19). Askin et al comprised 50 patients with occasional PVCs (5–10 PVCs/hour) and 50 patients with frequent PVCs (>10 PVCs/hour) . HRV parameters of SDANN, SDNN, RMSSD and PNN50 were similar between groups (20). Barutcu et al compared to the 43 patients with frequent PVCs and control group. Frequent PVCs are defined as occurrence at least 30 times during a 1 hour recording according to the Lown classification or at least once during a standard ECG recording. HRV parameters of SDNN, SDANN, PNN50 and RMSSD levels were similar between groups (10). In the present study, patients with PVCs had lower SDNN and SDANN indicating that enhanced sympathetic activity than patients without PVC. PNN50 and rMSSD were lower but not statistically significant between groups. The reason why Zhang et al (19) and Askin et al (20) results were insignificant may be the lower sample size.

Age was similar between groups and not related with PVCs in Askin et al's study (20). By contrast, an analysis of the ARIC study cohort demonstrated that older age associated with the presence of PVC (21,22). Similarly, patients with frequent PVCs were older in our study.

Nowadays, there is no consensus about whether the incidence of PVC is higher in women or men. Dong et al (18) demonstrated that men had a higher incidence of PVC than women. Haruta et al studied with 5685 individuals, indicated no significant difference in the incidence of PVC between the genders (23). Sirichand et al showed that the incidence of symptomatic idiopathic PVCs were higher in women (24). There was not statistically difference between the genders in the present study.

Sympathetic neural factors are important in the initiation and maintenance of a blood pressure (25). In hypertensive patients, the arrhythmogenic substrate of left ventricular hypertrophy may induce the reentry mechanism. The ventricles are sensitive higher blood pressure. Fibrosis, subendocardial ischemia and higher blood pressure stress can trigger abnormal rhythm (26). In our study, patients with frequent PVCs were more hypertensive.

An analysis using the ARIC study cohort showed that a history of coronary artery disease was associated with the presence of PVCs (21,22). The arrhythmogenic substrate of ischemic or fibrotic myocardial area may stimulate the reentry mechanism. Patients with frequent PVCs had more coronary artery disease in our study.

Agarwal et al demostrated that type 2 diabetes mellitus is related with higher prevalence of ventricular arrhythmias independent of chronic heart failure or coronary artery disease. Patients with frequent PVCs were more diabetic in our study (27).

Barutcu et al (10) found that the left ventricular EF was lower and the LVEDD, LEVESD were higher in patients with frequent VPCs compared with the control group. Left ventricular systolic dysfunction may induce sympathetic activation as a compensatory mechanism resulting in frequent PVCs.

Conclusion

Our findings support that the sympathetic overactivity indicated by lower SDNN and SDANN levels is related with frequent PVCs. HRV measurements in patients with PVCs are a simpler and noninvasive method for the assessment of cardioneural regulation using rhythm holter monitoring.

Limitations

The limitations of this study were relatively small sample size and retrospective design. Further, larger and prospective studies are warranted to support our results. Also, we did not evaluated with HRV frequency domain analysis evaluated by high frequency and low frequency power.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1):87-93

Single Center Experience with Radiofrequency and Cryoballoon Ablation in Patients with Atrial Fibrillation

Atriyal Fibrilasyon Hastalarında Radyofrekans ve Kriyobalon Ablasyon İle Tek Merkez Deneyimi

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Geliş Tarihi: 24.03.2024
Kabul Tarihi: 31.03.2024

Abstract

Objective: This retrospective study evaluates the efficacy and safety of pulmonary vein isolation (PVI) using radiofrequency ablation (RFA) and cryoballoon ablation (CBA) in patients with symptomatic persistent or paroxysmal atrial fibrillation (AF) resistant to at least one antiarrhythmic drugs (AAD) at a single center. It aims to identify predictors of AF recurrence post-treatment, thereby informing clinical decision-making and improving patient management strategies.

Methods: This retrospective, single-center study analyzed 119 patients who underwent PVI via RFA or CBA. The patients were categorized into two groups based on the recurrence of AF at long-term follow-up [Recurrence (-), n = 95; Recurrence (+), n = 24]. The primary outcome measured was the recurrence of any documented AF episode following a 3-month blanking period.

Results: During the median follow-up of 2.1 years (range: 1.5-3.6 years), 79.8% of participants remained free from AF recurrence post-procedure, while 20.2% experienced recurrence. Our analysis showed that body mass index (BMI) (OR:1.18, 95%CI: 1.05-1.33, p = 0.005), left atrial (LA) diameter (OR:1.22, 95%CI:1.01-1.36, p <0.001), and estimated glomerular filtration rate (eGFR) (OR:0.96, 95%CI:0.93-0.99, p = 0.016) as independent predictors of AF recurrence.

Conclusion: Our findings showed that BMI, LA diameter and eGFR were significant predictors of AF recurrence after PVI. These results highlight the potential for personalized treatment approaches in AF care, suggesting areas for further research to optimize treatment outcomes.

Keywords: Atrial Fibrillation, Cryoballoon Ablation, Radiofrequency Ablation.

Öz

Amaç: Bu retrospektif çalışma, tek merkezde yapılan, en az bir antiaritmik ilaca (AAİ) dirençli semptomatik, persistant veya paroksismal atriyal fibrilasyonu (AF) olan hastalarda radyofrekans ablasyonu (RFA) ve kriyobalon ablasyonu (KBA) ile yapılan pulmoner ven izolasyonunun (PVI) etkinliğini ve güvenliğini değerlendirmektedir. Ablasyon sonrası AF rekürrensinin öngördürücülerini belirleyerek, klinik karar verme sürecine katkıda bulunmayı ve hasta yönetim stratejilerini geliştirmeyi amaçlamaktadır.

Yöntem: Çalışmamızda, RFA veya KBA ile PVI uygulanan 119 hasta retrospektif olarak analiz edilmiştir. Hastalar, uzun dönem takipte AF rekürrensi gelişmesine göre iki gruba ayrılmıştır [Rekürrens (+), n = 24; Rekürrens (-), n = 95]. Birincil sonlanım noktası ilk 3 aylık kör dönemden sonra ortaya çıkan dökümente edilmiş AF atağıdır.

Bulgular: Ortalama 2,1 yıl (1,5-3,6 yıl) takip süresi boyunca, hastaların %79,8'inde işlem sonrası AF rekürrensi gelişmemiş, %20,2'sinde rekürrens gelişmiştir. Analizimiz, vücut kitle indeksi (VKİ) (OR:1.18, 95%CI: 1.05-1.33, p = 0.005), sol atrium (LA) çapı (OR:1.22, 95%CI: 1.01-1.36, p<0.001) ve tahmini glomerüler filtrasyon oranının (eGFR) (OR:0.96, 95%CI: 0.93-0.99, p = 0.016) AF rekürrensinin bağımsız öngördürücüleri olduğunu göstermektedir.

Sonuç: Bulgularımız, VKİ, LA çapı ve eGFR'nin PVI sonrası AF rekürrensinin önemli öngördürücüleri olduğunu göstermektedir. Bu sonuçlar, AF bakımından kişiselleştirilmiş tedavi yaklaşımlarının önemini vurgulamakta ve daha fazla araştırma yapılması gerektiğini göstermektedir.

Anahtar Kelimeler: Atriyal Fibrilasyon, Kriyobalon Ablasyonu, Radyofrekans Ablasyonu

Introduction

Atrial fibrillation (AF), the most prevalent sustained cardiac arrhythmia in clinical practice globally, affects approximately 1-3% of the adult population, with prevalence rates climbing to about 9%, aged ≥65 and above 17%, aged ≥ 80 years (1-3). The association between AF and consequential health complications, such as stroke, heart failure, dementia, and heightened morbidity and mortality risks, underscores the imperative for efficacious management and treatment strategies (4-7).

Pulmonary vein isolation (PVI) via radiofrequency ablation (RFA) and cryoballoon ablation (CBA) has emerged as a pivotal treatment modality, demonstrating promise for patients with both persistent (PeAF) or paroxysmal atrial fibrillation (PAF) (8,9). The inherent complexity of AF and its varied clinical manifestations necessitate a thorough evaluation of these treatment options to optimize patient care.

The advent of RFA and CBA technologies has significantly transformed therapeutic approaches to AF, promising reductions in recurrence rates and improvements in quality of life (10). Despite widespread adoption, the comparative effectiveness and safety of these modalities, particularly across different AF subtypes, continues to be a subject of active research. In this study, we aimed to show our clinic's experience of electrical isolation through RFA and CBA of pulmonary veins in AF patients.

Material and Method

Study Population

In this retrospective study, we enrolled a total of 119 patients with symptomatic AF referred to our arrhythmia center from January 2015 to December 2022. All participants, aged 18 years and older had a history of AF resistant to at least one antiarrhythmic drugs (AAD). Patients were classified into PAF or PeAF groups based on the clinical diagnosis from electrophysiological studies and medical history. PAF was defined as episodes that resolved on their own or with treatment within 7 days, while episodes lasting beyond 7 days were deemed PeAF. Patient records were obtained from electronic medical records, including electrocardiograms (ECGs), echocardiography, 24-hour Holter monitoring, and blood tests.

Exclusion Criteria

Individuals were excluded if they had previously undergone ablation, presented severe valvular heart disease, congenital heart abnormalities, a predisposition to bleeding, contraindications to anticoagulant therapy, or evidence of thrombi on transesophageal echocardiography (TEE).

Ethical Considerations

Informed consent was obtained from all participants after providing comprehensive details about the ablation procedures, their effectiveness, and potential risks. The study was approved by the Clinical Research Ethics Committee of İzmir Kâtip Çelebi University Atatürk Training and Research Hospital on 21 March 2024, with approval number 0174 ensuring compliance with ethical standards and the Declaration of Helsinki.

Pre-procedural Preparation

Prior to ablation, patients ceased AADs for a period equivalent to at least five half-lives of the drug, except for amiodarone, which was discontinued for a minimum of 14 days. Stroke risk was assessed using the CHA_2DS_2-VASc score to guide anticoagulation therapy. Individuals on warfarin achieved target International Normalized Ratio (INR) levels ranging from 2.0 to 2.5, while those on non-vitamin K antagonist oral anticoagulants (NOACs) continued their regimen without interruption. Cardiac structure and function were evaluated using transthoracic echocardiography (TTE), and TEE was used to exclude left atrial thrombosis prior to the procedure.

Ablation Procedure

Ablation procedures were tailored individually to each patient based on the underlying AF characteristics and the patient's specific anatomical and clinical profile. For RFA, a catheter was introduced via the femoral vein and advanced into the left atrium (LA) after a transseptal puncture. The 3D mapping system created real-time images of the heart's electrical activity to guide the ablation catheter to the pulmonary veins' antral regions. RF energy was then applied in a point-by-point fashion around the pulmonary vein ostia to create continuous lesions, ensuring complete electrical isolation.

A CBA was performed by The Artic Front Advance PRO (AFA-Pro, Medtronic-) system and The Polarx (Boston Scientific) system. In the case of CBA, a cryoballoon catheter was advanced over a guidewire into the LA, again following transseptal puncture. The balloon was then inflated and positioned at the pulmonary vein ostia. Once optimal contact was confirmed, the balloon delivered a freezing temperature to create circumferential lesions, leading to pulmonary vein isolation. The use of a second-generation cryoballoon allowed for enhanced cooling and more uniform lesion formation. For both methods, pulmonary vein isolation was confirmed via exit block (loss of electrical signals from the pulmonary veins to the atrium) and entrance block (lack of electrical signals from the atrium to the pulmonary veins). Complications were monitored for and managed according to current clinical guidelines.

The choice of ablation technique was at the discretion of the operating physician, who considered factors such as the size and shape of the atria and the patient's specific AF history.

Postprocedural Management

After the procedure, every patient was monitored in the cardiology ward for 24 hours. To ensure their heart rhythm remained stable, control ECG were conducted in the morning following the procedure and again immediately before discharge. Patients whose conditions were stable were then permitted to leave the hospital. Provided that no pericardial effusion was detected, oral anticoagulation therapy was initiated on the evening of the ablation day. This treatment was continued for at least three months post-procedure to prevent potential complications.

Follow-up

Patients underwent systematic follow-up evaluations with ECG and if they had symptomatic episodes with 24-hour Holter monitiring at 1, 3, 6, and every 6 months after post-ablation. A diagnosis of recurrence of AF was defined as AF were confirmed on 12-lead ECG or AF with lasting at least 30 seconds were documented on 24-hour Holter monitoring three months after the index ablation procedure (blanking period). The primary endpoint of the study was defined as the recurrence of any documented AF episode after a 3-month blanking period.

Patient Grouping Based on AF Recurrence

For analysis, patients were divided into two groups: those who experienced a recurrence of AF and those who did not, Recurrence (-) (n = 95) and Recurrence (+) (n = 24). This approach allowed for an extensive evaluation of the long-term outcomes of the ablation procedure.

Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were presented as mean ± standard deviation or median with interquartile range depending on their distribution, while categorical variables were presented as frequencies and percentages.

The Chi-square test was chosen for the analysis of categorical variables, given its effectiveness in determining whether there are statistically significant differences between the expected and observed frequencies in one or more categories. For continuous variables, the t-test or Mann-Whitney U test was applied depending on the data distribution, enabling comparison of means between two groups. Multivariate logistic regression analysis was conducted to identify independent predictors of AF recurrence, incorporating variables that demonstrated a p-value <0.10 in univariate analyses. A two-sided p-value <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS 26 (SPSS Inc., Chicago, IL, USA).

Results

We presented the demographic and clinical features of the study in Table 1. Average age was 56.9 years (SD ± 10.6) for the recurrence (-) group and 60.2 years (SD ± 10.0) for the recurrence (+) group, with no statistically significant difference (p = 0.173). Participants aged ≥ 65 years were more prevalent in the recurrence (+) group (38%) compared to the recurrence (-) group (20%), though not reaching statistical significance (p=0.071). Gender distribution was similar across groups (45% male inrecurrence (-) vs. 33% in recurrence (+), p = 0.291). No significant differences were found in the prevalence of diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), hyperlipidemia, chronic obstructive pulmonary disease (COPD), stroke, and smoking habits, with each p-values> 0.05. The median CHA_2DS_2VASC score and the history of electrical cardioversion did not significantly differ between groups (p = 0.077 and p = 0.672, respectively). There was no difference between groups regarding mortality.

Table 1. Demographic and clinical features of the study population

Variables	Recurrence (-) (n = 95)	Recurrence (+) (n = 24)	p-value
Age	56.9 ± 10.6	60.2 ± 10.0	0.173
Age ≥ 65 n (%)	19 (20)	9 (38)	0.071
Male gender n (%)	43 (45)	8 (33)	0.291
Diabetes Mellitus n (%)	22(23)	9(8)	0.153
Hypertension n (%)	51(54)	12(50)	0.747
Coronary artery disease n (%)	15(16)	3(13)	0.688
Hyperlipidemia n (%)	12(13)	4(17)	0.605
Chronic obstructive pulmonary disease n (%)	4(4)	0(0)	0.307
Stroke n (%)	5 (5)	1(4)	0.826
Smoking n (%)	15 (16)	4 (17)	0.933
Heart failure with n (%)			0.161
Preserved EF n (%)	2(2)	3 (13)	
Mid-range EF n (%)	4 (4)	1 (4)	
Reduced EF n (%)	9 (10)	2 (8)	
AF type			0.751
Persistent n (%)	42(44)	12(50)	
Paroxysmal n (%)	53(56)	12(50)	
AF ablation type			0.649
RFA n (%)	11 (12)	2 (8)	
CBA n (%)	84 (89)	22 (92)	
CHA_2DS_2VASC score n (%)	2(1-3)	2.5(1.25-3)	0.077
History of cardioversion n (%)	39(41)	11(46)	0.672
Medical treatment at admission n (%)			
ASA n (%)	17 (18)	4 (17)	0.888
Clopidogrel n (%)	6(6)	1 (4)	0.689
VKA n (%)	19 (20)	5 (21)	0.928
NOAC n (%)	41(43)	8 (33)	0.382
ACE-I n (%)	20 (21)	6 (25)	0.676
ARB (%)	16 (17)	4 (17)	0.984
CCB n (%)	16 (17)	5 (21)	0.647
Digoxin n (%)	7(7)	1 (4)	0.576
Amiodarone n (%)	16 (17)	3 (13)	0.604
BB n (%)	64 (67)	12 (50)	0.114
Moderate MR n (%)	4 (4)	3(13)	0.123
Moderate TR n (%)	7 (7)	3 (13)	0.418
Medical tretament at discharge n (%)			
Amiodarone n (%)	58 (61)	15 (63)	0.896
Propafenon n (%)	22 (23)	7 (29)	0.540
BB n (%)	34 (36)	6 (25)	0.317
Mortality n (%)	1 (1)	0 (0)	0.614

Abbreviations: EF:ejection fraction, AF:Atrial fibrillation, RFA:radiofrequency ablation, CBA:cryoballoon ablation, ASA:asetil salicylic acid, VKA: vitamin K antagonist, NOAC: non-VKA oral anticoagulant, ACE-I:angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, CCB: calcium channel blockers, BB:beta-blockers, MR: mitral regurgitation, TR: tricuspid regurgitation

Laboratory findings of the patients were provided in Table 2. A significant difference in body mass index (BMI) was observed between groups, with the recurrence (+) group showing higher BMI (32.3 ± 3.3 kg/m²) compared to those without (26.6 ± 3.2 kg/m², p <0.001).

No significant differences were found in left ventricular ejection fraction (LVEF), However, the LA diameter was significantly larger in the recurrence (+) group (45.7 ± 4.0 mm) compared to the recurrence (-) group (39.5 ± 4.8 mm, p < 0.001).

Table 2. Laboratory findings of the study population

Variables	Recurrence (-) (n = 95)	Recurrence (+) (n = 24)	p-value
BMI (kg/m^2)	26.6 ± 3.2	32.3±3.3	< 0.001
LVEF %	56.6 ± 9.4	55.2 ± 11.2	0.538
LVEDD (mm)	46.9± 4.4	45.8± 3.8	0.256
LVESD (mm)	30.3± 5.4	31.2± 7.9	0.540
LA diameter (mm)	39.5 ± 4.8	45.7 ± 4.0	< 0.001
PASP (mmHg)	29.8 ± 7.2	32.3 ± 9.8	0.172
Hemoglobin (g/dl)	13.4 ± 1.6	13.7 ±1.4	0.173
WBC (x10^3 /μL)	7.9 ±1.9	8.1 ±1.9	0.064
eGFR (mL/min/1.73 m^2)	77.8 ± 18.0	76.3± 19.9	0.081
TSH (mU/L)	2.1 ± 2.4	2.3 ± 2.0	0.094

Abbreviations: BMI: body mass index**,** LVEF: left ventricular ejection fraction, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, LA: left atrium, IVS: interventricular septum, LVPW: left ventricular posterior wall, RA: right atrium , PASP: pulmonary artery systolic pressure WBC; white blood cell, eGFR: estimated glomerular filtration rate, TSH: thyroid-stimulating hormone.

After adjusting for confounders, eGFR (OR = 0.96, 95% CI: 0.93-0.99, p=0.016), BMI (OR = 1.18, 95% CI: 1.05-1.33, p = 0.005), and LA diameter remained significant predictors of recurrence (OR = 1.22, 95% CI: 1.01-1.36, p <0.001). These were presented in Table 3.

Table 3. Recurrence predictors in univariate and multivariate analysis.

Variables	Univariate		Multivariate	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Age ≥ 65	2.82 (1.20-6.62)	0.017		
CHA_2DS_2VASC score	1.51 (1.11-2.06)	0.009		
BMI	1.26 (1.14-1.39)	< 0.001	1.18 (1.05-1.33)	0.005
LA diameter	1.27(1.16-1.39)	< 0.001	1.22(1.01-1.36)	< 0.001
WBC	1.05 (0.83-1.33)	0.694		
eGFR	0.96 (0.94-0.99)	0.002	0.96 (0.93-0.99)	0.016
TSH	1.05 (0.87-1.26)	0.641		

Abbreviations: CHA_2DS_2VASC score: congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category, BMI: body mass index, LA: left atrium, WBC; White blood count, eGFR: estimated glomerular filtration rate, TSH; thyroid-stimulating hormone.

After the procedure, 1 patient (0.8%) developed hematoma in the femoral region, which resolved without intervention. A haemodynamically relevant pericardial effusion necessitating drainage during the same hospital stay occurred in 1 patient (0.8%). Four patients (3.3%) with phrenic nerve palsy recovered within 24 hours. There were no death, major bleeding, or strokes as a consequence of the ablation.

Discussion

This study revealed that after a CBA and RFA procedure, 79.8% of patients were had no AF recurrence in the long-term follow-up. The current study's identification of BMI, LA diameter, and eGFR as significant predictors of AF recurrence post-PVI provides valuable insight into the nuanced interplay of physiological factors influencing AF outcomes.

These findings are particularly relevant in light of the ongoing debate over the optimal management strategies for AF patients undergoing ablation. Our observation that an increased BMI is associated with higher AF recurrence rates corroborates the findings of Liu F et al. who demonstrated a linear relationship between BMI and AF recurrence in a meta-analysis of 26,450 patients (11). However, the magnitude of risk associated with BMI in our study is slightly higher, which could be attributed to our cohorts demographic differences, suggesting that individual patient characteristics might modulate the impact of BMI on AF recurrence.

Consistent with our results, the LA diameter's role as a predictor for AF recurrence was highlighted in the study by Liao YC et al. and Kim YG et al. , which found that LA enlargement was independently associated with AF recurrence following ablation (12,13). The similarity in findings underscores the importance of atrial remodeling in AF pathophysiology, further advocating for the inclusion of LA diameter in the risk assessment models for AF recurrence post-ablation.

eGFR, like previous studies such as the one conducted by Boyalla V et al. find a significant association between eGFR levels and AF recurrence (14), our study suggests that higher eGFR serves as a protective factor against AF recurrence . The similar recurrence rates observed between RFA and CBA in our study as shown study by Vaishnav AS et al., which found no significant difference in AF recurrence rates between RFA and CBA (15).

Despite the latest technological advances such as CBA and RFA in the treatment of AF, recurrence rates are still high (16). Our study which primarily utilized ECGs and symptom focused rhythm Holter monitoring for all patients, may not fully detect asymptomatic recurrences of AF. This selective approach could lead to an underestimation of recurrence rates, as suggested by the comparative lower incidence reported herein. Studies have shown poor correlation between symptoms and occurrence of AF (17). This perspective is supported by the study of Verma A et al. who highlighted the critical role of comprehensive rhythm monitoring in detecting AF episodes post-ablation (18). Symptoms alone are insufficient to estimate the post-ablation AF burden, as 12% of patients experience asymptomatic recurrences. This significant discrepancy underscores the possibility that our methodology might contribute to an underestimation of the true recurrence rate.

The study by Neuman T et al. showed that the perception of AF by patients after PVI leads to an underestimation of the recurrence of AF (19). These studies acknowledged the limitations of intermittent monitoring in capturing transient or asymptomatic episodes, aligning with our concerns regarding potential underreporting. This significant discrepancy underscores the possibility that our methodology might contribute to an underrepresentation of the true recurrence rate. The differences in follow-up practices emphasize the need for a standardized approach in Holter monitoring post-ablation outcomes and may explain the variations in reported recurrence rates across

Our study's observation that catheter ablation complications are generally non-severe and self-resolving aligns with the broader research showing low complication rates, underscoring the procedure's overall safety. The specific rates of pericardial effusion and phrenic nerve palsy reported here are within the ranges observed in wider studies, including a systematic review, which reinforces the necessity of vigilant post-ablation monitoring (20).

As a limitation; the retrospective, single-center design of our study may limit the generalizability of the results. A broader, more heterogeneous population would be ideal to strengthen the validity of our findings. Furthermore, retrospective data may introduce information bias, potentially impacting the accuracy of the results. In this study, we did not use Holter monitoring in all patients for the detection of AF at follow-up, except when symptomatic episodes were reported. Future studies should consider multicenter, randomized trials with extended follow-up to more robustly ascertain the roles of BMI, LA diameter, and eGFR as predictors of AF recurrence.

Conclusion

This study confirms that BMI, LA diameter, and eGFR are key predictors of AF recurrence following PVI. Incorporating these indicators in pre-ablation assessments can help personalize treatment plans and may improve outcomes. Additionally, targeting modifiable factors like obesity could further reduce recurrence risks. Ongoing research, particularly prospective studies, is crucial to validate these findings and refine ablation strategies.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2024;62 (1): 94-98

Trigliserit/Glukoz İndeksinin Koroner By-pass Uygulanan Non Diabetik Hastalarda Postoperatif Şeker Kontrolüne Etkisi

The Effect of Triglyceride/Glucose Index on Postoperative Sugar Control in Non-Diabetic Patients Undergoing Coronary By-pass Surgery

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Öz

Amaç: Trigliserit/Glukoz indeksi son dönemlerde insülin direncini belirlemede etkin olarak kullanılmaya başlanan bir formüldür. Çalışmamızda normoglisemik olup koroner arter hastalığı nedeniyle koroner arter bypass greft operasyonu olan hastalarda hiperglisemi oluşumuna etkisini araştırmayı amaçladık.

Yöntem: Non- diabetik olup koroner arter hastalığı nedeniyle elektif olarak izole KABG ameliyatı uygulanan 98 hasta çalışmaya dâhil edildi. Tüm hastaların demografik ve klinik verileri ile birlikte preoperatif dönemde Trigliserit/glukoz İndeksleri hesaplandı ve yüksek indeks ve düşük indeks olarak iki grup oluşturuldu. İşlem sırasında ve postoperatif dönemde insülin ihtiyacı olacak şekilde kan şekeri yükselen hastalar değerlendirildi.

Bulgular: Koroner by-pass işlemi sırasında ve sonrasında insüline ihtiyaç olan şeker yüksekliği oranı yaklaşık % 25 olarak görülmüştür. Trigliserit/glukoz indeksi hesaplanıp yüksek skora sahip hastalarda düşük olanlara göre insülin ihtiyacı anlamlı olarak daha fazla görülmüştür ($p<0.001$).

Sonuç: Çalışmamızda yüksek trigliserit/glukoz indeksi değerleri olan hastalarda koroner arter bypass operasyonlarında ve sonrasında insülinle kontrol altına alınabilen hipergilsemi oluşturan bir öngördürücü olabileceğini belirledik.

Anahtar Kelimeler: Koroner Arter Hastalığı, Hiperglisemi, Trigliserit/Glıkoz İndeks

Abstract

Purpose: Triglyceride/Glucose index is a formula that has recently begun to be used effectively in determining insulin resistance. In our study, we aimed to investigate the effect of trigliceride/glucose index on postoperative hyperglycemia in normoglicemic patients who underwent coronary artery bypass graft surgery due to coronary artery disease

Method: 98 non-diabetic patients who underwent elective isolated CABG surgery due to coronary artery disease were included in the study. Triglyceride/glucose Indexes were calculated in the preoperative period along with the demographic and clinical data of all patients, and two groups were created: high index and low index. Patients whose blood sugar increased, requiring insulin during the procedure and in the postoperative period, were evaluated.

Results: The rate of high blood sugar requiring insulin during and after the coronary bypass procedure was observed to be approximately 25%. Insulin requirement was found to be significantly higher in patients with high trigliseride/glucose index scores than in those with low scores ($p<0.001$).

Conclusion: In our study, we determined that patients with high triglyceride/glucose index values may be a predictor of hyperglycemia, which can be controlled with insulin, during and after coronary artery bypass operations.

Keywords: Coronary Artery Disease, Hyperglisemia, Trigliseride/Glucose Index

Giriş

Koroner arter bypass greft (KABG) cerrahisi, ateroskleroz nedeniyle perfüzyonu bozulan miyokardın arter ve ven greftler aracılığıyla re-perfüze edilmesini sağlamaktadır. Bu yöntemle başta hastalardaki göğüs ağrısı gibi iskemiye bağlı semptomlar giderilir, miyokard infarktüsü, ani ölüm gibi komplikasyonların riskleri azaltılır (1). Kalp ameliyatı sırasında kardiyopulmoner bypass a bağlı yüksek stres yanıt, insülin direnci, eksojen katekolaminlerin fazla salınımı ve hipotermi gibi sebeplerden dolayı diyabet varlığından bağımsız olarak da kan şekeri yükselir. Kan şekeri seviyesindeki bu akut yükseliş serbest oksijen radikallerinin, enflamatuvar ve proenflamatuvar sitokinlerin üretiminde artışa neden olur (2).

Kan şekeri yükselmesi diyabet tanısı olmasa bile kalp cerrahisinde sıklıkla gelişir. Hasta normoglisemik olsa bile cerrahi sırasında ve sonrasında gelişen kan şekeri yükseklikerinin morbidite ve mortaliteyi artırmaktadır (3). Hipergliseminin, miyokard enfarktüsü olan hastalarda miyokarddaki enfarkt alanını genişlettiği, iskemik - reperfüzyon hasarını artırdığı gösterilmiştir (4).

Kan şekeri yüksekliği ve ameliyat sonrası sağkalım arasındaki ilişkiye yönelik çalışmalar çoğunlukla diyabetik hastalar ve kritik hastalarda uygulanmıştır ve bu çalışmalarda ameliyat sırası hipergliseminin morbiditeyi artırıcı önemli bir faktör olduğu bildirilmiştir (5). Ancak normoglisemik hastalarda kalp cerrahisine bağlı intraoperatif ve cerrahi sonrasında kontrolsüz kan şekeri artışını gösteren çalışmalar daha sınırlı sayıdadır. İşlem öncesi diyabetik olmayan ve insülin rezistansı olan hasta gurubunda cerrahi strese bağlı postoperatif şeker regülasyonu bozulmaktadır. Bilindiği üzere insülin direnci metabolik sendromun bir varyantı olup diabetes mellitus tanısına yatkınlık oluşturan bir antitedir (6).

Trigliserit-glukoz indeksi, son dönemde Homeostatic Model Assessment (HOMA-IR)**,** glikosile edilmiş hemoglobin (HbA1c) ve trigliserit/yüksek yoğunluklu lipoprotein (HDL) gibi belirteçlerle birlikte insülin rezistansını belirlemede daha iyi performansla kullanılabilen bir yöntem haline geldi (7).

Çalışmamızın amacı normoglisemik olup KABG operasyonu uygulanan hastalarda ameliyat sırası ve sonrası dönemde bozulan kan şekeri regülasyonu için insülin ihtiyacının oluşmasında trigliserit/glukoz indeksinin etkili olup olmadığını ve diğer predispozan faktörleri belirlemektir.

Gereç Ve Yöntemler

Bu araştırmada fakülte etik komitesinin izni (0160/21.03.2024) alındıktan sonra non diabetik olup koroner arter hastalığı nedeniyle elektif olarak izole KABG ameliyatı geçiren 98 hasta dosyası retrospektif olarak incelendi. Diabetes mellitus tanısı olanlar, kronik böbrek yetmezliği tanısı olanlar unstabil olarak cerrahiye giden hastalar çalışmaya dahil edilmedi. Tüm operasyonlar median sternotomi ile kardiyolpulmoner by-pass kullanılarak ve X-Klemp ile kardiyak arrest sağlanarak full revaskülarizasyonla gerçekleştirildi.

Ameliyat öncesine ait veriler her hasta için yaş, cinsiyet, vücut kütle indeksi (VKİ), gibi demografik verilerin yanı sıra sigara kullanımı, hipertansiyon, periferik arter hastalığı (PAH), miyokard enfarktüsü, aritmi öyküsü, kronik obstrüktif akciğer hastalığı (KOAH) varlığı kaydedildi. Hastaların preoperatif alınan açlık kan değerlerinden hemogramda WBC, hemoglobin ve platelet değerleri ile biyokimyada kreatinin, albümin, CRP, HDL, LDL, glukoz ve trigliserid değerleri kaydedildi. Bununla birlikte preoperatif yapılan ekokardiyografilerden sol ventrikül ejeksiyon fraksiyonu değerleri ayrıca hastaların New York kalp sınıflamasına ait NYHA skorları kaydedildi.

Ameliyat sırasında ve sonrası veriler olarak tüm hastaların kardiyopulmoner bypass (KPB) ve kros klemp süreleri, ameliyat sırasında ve sonrası yoğun bakım ünitesindeki insülin ihtiyacı, inotrop ve vazapressör ihtiyacı, intraaortik balon pompası kullanım ihtiyacı, inme öyküsü ve kanama nedeniyle revizyon ihtiyacı idi.

Tg-glukoz indeksi ln (açlık tg X açlık glukoz/2) formülü ile hesaplandı (8). Konvansiyonel US Trigliserit/Glukoz index hesaplamaya göre ≤4,77 değerinden küçük olanlar düşük Trigliserit/Glukoz index 4,77 değerinden büyük olanlar yüksek trigliserit/glukoz index olarak değerlendirildi ve yüksek ve düşük olarak gruplandırıldı (9).

Kan şekeri kontrolü ameliyat sırasında ve yoğun bakım döneminde kan şekeri düzeylerine alınan kan gazları ölçümleriyle değerlendirildi. Kan şekeri kontrolünde kristalize insülin (Humulin R®, Lilly,Indianapolis, USA) uygulandı. Kan şekeri >200 mg/dL olmadıkça insülin verilmedi, insülin dozları kan şekeri yükseklik düzeyine göre belirlenip intravenöz kristalize insülin şeklinde ve yakın takiple uygulandı ve gereğinde hastalara Portland protokolüne göre insülin infüzyonu uygulandı.(10)

İstatistiksel analiz, Çalışma verileri değerlendirilirken niceliksel değişkenlerin gruplar arasındaki karşılaştırmalarında One-way ANOVA ve Kruskal-Wallis testi, niteliksel verilerin karşılaştırılmasında ise Pearson ki-kare testi kullanıldı. Trigliserit/glukoz indeksi yüksek olanlar ve düşük olan hastaların veri farklılıkları t-testi, Man-Whitney U, ki-kare veya Fisherin kesin testi ile değerlendirildi. Sürekli değişkenler ortalama ± standart sapma, nominal değişkenler ise sayı ve yüzde (%) veya ortanca (IQR) olarak bildirildi. P<0.05 değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular

Çalışmaya katılan hastaların yaş ortalaması 66,6olup %74,2 si erkek idi. Hastaların 25' inde (% 25,5) işlem sırasında veya sonrasında kan şekeri regülasyonu için insülin ihtiyacı olmuştur.

Hastaların ameliyat öncesi özellikleri Tablo 1'de verilmiştir. Tg-glukoz indeksi ≤4,77 (düşük grup) olan hasta sayısı 72 (%77) iken 26 hastada (%26,5) Tg index 4,77 (yüksek grup) den büyüktü. İndexin yüksek olduğu grupta hipertansiyon daha sık olmasına rağmen istatistik açıdan fark gözlenmemiştir (p=0.129).

Tablo 1: Ameliyat Öncesi Değişkenler

Değişkenler	TG index ≤4,77(Grup0-72 kişi)	TG index ≥4,77 (grup1-26 kişi)	p-Değeri
Yaş	67.5 (60-71)	68(62-75)	0.356
Cinsiyet-erkek	57 (79.2%)	18(69.2%)	0.222
VKI	22.1 (21-23.8)	22.1(22.1-23.9)	0.701
HT	15(20.8%)	9(34.6%)	0.129
KOAH	16(22.2%)	1(3.8%)	0.026
PAH	8(11.1%)	2(7.7%)	0.474
Sigara	15(20.8%)	3(11.5%)	0.230
NYHA Klas	1 (1-1)	1(1-1.25)	0.637
MI	11(15.3%)	3(11.5%)	0.460
Aritmi	4(5.6%)	5(19.2%)	0.053
LVEF	50(45-55)	50(45-54)	0.807
Kreatinin	0.92 (0.78-1.09)	0.86(0.77-1.04)	0.440
Albumin	3.3 (3.02-3.5)	3.3(2.98-3.5)	0.691
Hemoglobin	12 (11-13)	12.3(11.1-13.5)	0.347
CRP	4(2-5)	3(2-5)	0.373
Trigliserit	129 (112-138)	169(152-193)	<0.001
Glukoz	90(87-95)	97(94-100)	<0.001
HDL	57 (49-65)	58(53-62)	0.557
LDL	128 (101-145)	123(98-141)	0.418
WBC	8400(7500-9900)	7950(7075-9000)	0.184
Tg_İndex	4.68 (4.62-4.73)	4.86(4.79-4.93)	<0.001

Kısaltmalar: CRP: c reaktif protein; HDL: high density protein; HT: hipertansiyon; KOAH: kronik obstrüktif akciğer hastalığı; LDL: low densitiy protein; LVEF: left ventrikül ejeksiyon fransiyonu; MI:miyokard infarktüsü; NYHA: New york heart association; PAH: periferik arteryel hastalık; VKI:vücut kitle indeksi; WBC: white blood cell

KOAH düşük indeksli grupta daha sık görülmüştür (p=0.026). Trigliserit ve glukoz değerleri yüksek indexli grupta istatistik olarak daha yüksek idi (her ikisi için p<0.001). Ameliyat sırası ve postoperatif dönemdeki özellikler tablo 2 de verilmiştir. Buna göre yüksek Tg indeksli gruptaki hastalarda işlem sırasında ve sonrasında insülin ihtiyacı düşük indeksli gruptaki hastalara göre anlamlı olarak daha yüksek gözlenmiştir (p<0.001).

Tablo 2: Ameliyat sonrası değişkenler

Değişkenler	TG index ≤4,77	TG index ≥4,77	p-Değeri
CPB zamanı	60 (53-67)	62(55-68)	0.726
X-Klemp zamanı	40 (32-43)	43(34-48)	0.248
İABP ihtiyacı	3(4.2%)	1(3.8%)	0.714
Vazopresör ihtiyacı	20(27.8%)	6(23.1%)	0.426
Kanama için Revizyon	3(4.2%)	1(3.8%)	0.714
İnme	4 (5.6%)	0(0%)	0.285
İnsulin ihtiyacı	8(11.1%)	17(65.4%)	<0.001

Kısaltmalar: CPB: Kardiyopulmoner by-pass; İABP: intra aortik balon pompası, X: kros

Tartışma

Kalp ameliyatı sırasında ve sonrasında yükselen kan şekeri düzeylerinin mortalite ve morbiditeyi artırdığı bilinmektedir (11). Buna neden olan etkenler cerrahiye bağlı hipermetabolik stres yanıt, insülin direnci, kardiyopulmoner by-pass a bağlı yoğun inflamatuvar yanıt, yüksek eksojen katekolamin salınımları ve hipotermi gibi nedenlerle diyabet varlığından bağımsız olarak kan şekeri yükselmesine neden olmaktadır. Cerrahi sırasında kan şekeri seviyesindeki ani yükselişler serbest oksijen radikallerinin ve sitokinlerin üretiminde artışa neden olur. İnsülin ise tam ters etkiyle enflamatuvar yanıtı azaltır, miyokardın glikoz kullanımını artırır ve koroner by-pass cerrahisi sonrasında aerobik metabolizma etkisindeki artışa sekonder olarak serbest yağ asidi seviyelerini düşürüp, serbest oksijen radikallerini, adezyon moleküllerini ve C-reaktif protein seviyelerini düşürdüğü klinik çalışmalarda gösterilmiştir (12). Çalışmalarda normoglisemik hastalarda Koroner by-pass işlemlerinde gelişen hiperglisemi oranı % 50 nin üzerinde belirtilmiştir. Koroner arter by-pass greft ameliyatı uygulanan hastanın değerlendirildiği çok merkezli prospektif gözlemsel bir çalışmada ise postoperatif dönemde maksimum kan şekeri değeri 200 mg/dL'nin üzerinde olan hasta oranının diyabetik olmayan hastalarda %36, diyabetik olanlarda ise %84.5 olduğu bildirilmiştir (13). Bizim çalışmamızda işe insülin ihtiyacı olacak şekilde bozulan şeker regülasyonunun oranı yaklaşık %25 olarak gözlenmektedir.

Daha önceki çalışmaların çoğu postoperatif dönemde gelişen hiperglisemin mortalite ve morbidite üzerine olan etkileri üzerine odaklamış durumdayken özellikle normoglisemik hastalarda gelişen postoperatif hiperglisemiye neden olan değişkenlere daha az vurgulandığı gözlenmiştir. Bunu göz önüne alan az sayıda çalışma ise gelişen hipergliseminin özellikle insülin direnci ve metabolik sendrom eğilimi üzerine vurgu yapmaktadır (14).

İnsülin direnci (IR), kardiyometabolik hastalıklar için önemli bir risk faktörüdür ve Tip 2 Diabet Mellitus'un tanımlayıcı bir özelliğidir. İnsülin direncini klinikte hesaplamak için HOMA-IR, HbA1c (glycosylated hemoglobin) ve triglyceride/high density lipoprotein oranı gibi modeller kullanılsa da son dönemde yeni bir geliştirilen bir model olan Trigliserit/glukoz İndexinin insülin direncini ölçmede diğer yöntemlere göre daha basit ve daha kullanılışlı bir formül olduğu bildirilmiştir.

Yakın dönem çalışmalarda Trigliserit/glukoz İndexin diabetes mellitus açısından risk taşıyan hastaların erken belirlenmesinde faydalı bir yöntem olduğu bildirilmiştir (15). Özellikle de bu indeksin Tip 2 diabet mellitus gelişmesi riskini hesaplamada oldukça önemli olduğu vurgulanmıştır. Bunun yanında TyG indeksi koroner arter hastalığı prognozunun güvenilir bir göstergesidir. Ergani ve arkadaşlarının yakın dönemde gebelerde gestasyonel diyabet gelişimi üzerine yaptığı çalışmada da yine trigiserit/glukoz indeksinin iyi bir öngördürücü olduğu savunulmuştur. Bu bilgiler ışığında biz de çalışmamızda normoglisemik hastalarda uygulanan koroner bypass cerrahisi sonrası aşırı bozulan şeker regülasyonunun etkilerini araştırmayı amaçladık. Çalışmamızda preoperatif dönemde yüksek trigliserit/glukoz indeksi değerleri olan hastalarda KABG operasyonlarında ve sonrasında şeker regülasyonuda ciddi bozulmaya neden olabilecek bir öngördürücü olabileceğini belirledik. Çalışmamızı sınırlayan bazı faktörler bulunmaktadır. Verilerimiz retrospektif olup örneklem büyüklüğü nispeten küçüktür ve tek merkez çalışmasıdır. Hastalar taburcu edildikten sonra uzun süreli glikoz takibine ilişkin verimiz yok. HbA1c, çalışma döneminde hastaların rutin protokolünde olmadığından çalışmaya dâhil edilen pek çok hastada ölçülmemişti, bu nedenle de çalışma kapsamına alınmadı.

Çalışmamızda normoglisemik hastalarda preoperatif Trigliserit/Glukoz indeks değerinin koroner by-pass ameliyatları sonrasında daha fazla hiperglisemi oluştuğunu gözlemledik ancak bu indeksin postoperatif hiperglisemi oluşumu üzerine bağımsız bir değişken olduğunu öngördüren ve destekleyen çok merkezli ve randomize kontrollü çalışmalara ihtiyaç olduğunu belirtmeliyiz

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