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EGE KLİNİKLERİ TIP DERGİSİ
THE MEDICAL JOURNAL OF AEGEAN CLINICS

«EGE KLİNİKLERİ TIP DERGİMİZ HAKEMLİ BİR DERGİDİR»

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Dergimizin Kapsamı:
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On behalf of the Society of Aid to Hospitals of İzmir and Fosterage of Scientific İnvestigations

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Yönetim Adresi/ Administration address

177/7 Sok. No:1 D:1 Yeşilyurt
Tel: 0 232 244 34 38

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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 dili İngilizce'dir.

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.

İLETİŞİM

Doç. Dr. Tuncay KIRIŞ
Baş Editör
İzmir Hastanelerine Yardım ve Bilimsel
Araştırmaları Teşvik Derneği
Yeşilyurt/ İZMİR
Tel: 0507 311 46 07
e-mail. idhdergi@yahoo.com

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• Dergimizde yayınlanacak makaleler için etik kurul onayının alınması ve çalışmanın materyal-yöntem bölümünde çalışmanın etik kurul onayını aldığına dair bir açıklamanın bulunması zorunludur.

• Olgu sunumlarının dergimizde yayımlanabilmesi için hasta/hastaların onamının alınması ve olgu sunumunun giriş bölümünde 'hastadan/hastalardan onay alındığı'nı ifade eden bir cümle yer almalıdır.

• 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

TELİF HAKLARI DEVİR FORMU

Yazının Başlığı:

Sorumlu Yazarlar:

Yazarların sorumlulukları:

- Yazı(lar) (sözlü veya poster sunum şekilleri hariç) başka hiçbir yerde yayınlanmamış ve şu anda başka bir dergi veya her hangi bir yayımcıda değerlendirme altında olmamalıdır.
- Makalenin yayınlanması ile ilgili diğer yazar onaylarından gönderen yazar sorumludur.
- Belirli bir kurum tarafından desteklenen yazılar için gerekli kurum onayının alınmasından yazarlar sorumludur.
- Yazıların bilimsel ve etik sorumluluğu yazarlara aittir.

Yazar Adı Soyadı **İmza** **Tarih**

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

Klinik İzole Sendromda Multipl Skleroza Dönüşümde Manyetik Rezonans Görüntülemenin Belirleyici Rolü

Ali BİGE*0000-0212-4446-0717

* Zonguldak Bülent Ecevit Üniversitesi, Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, Zonguldak

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Yazışma Adresi: Ali BİGE

Zonguldak Bülent Ecevit Üniversitesi,

Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, ZONGULDAK

Gsm: 0532

e-mail adresi: alibige@gmail.com

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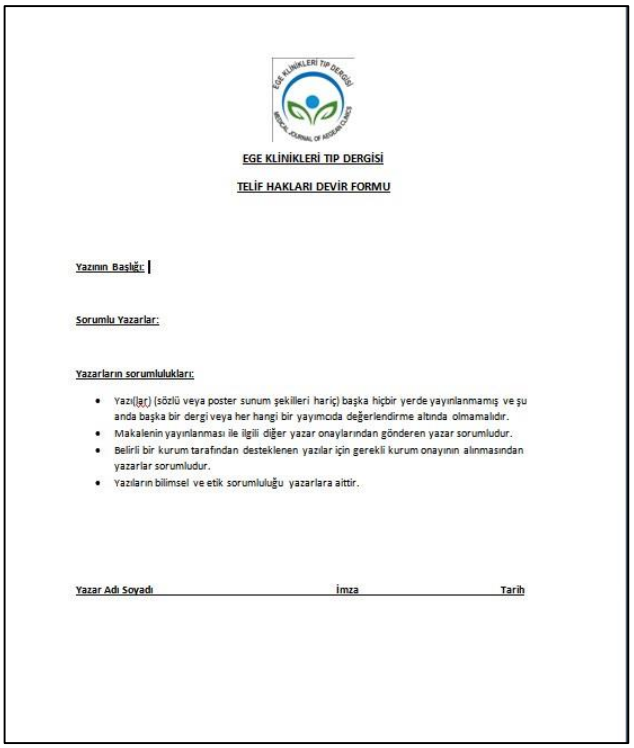

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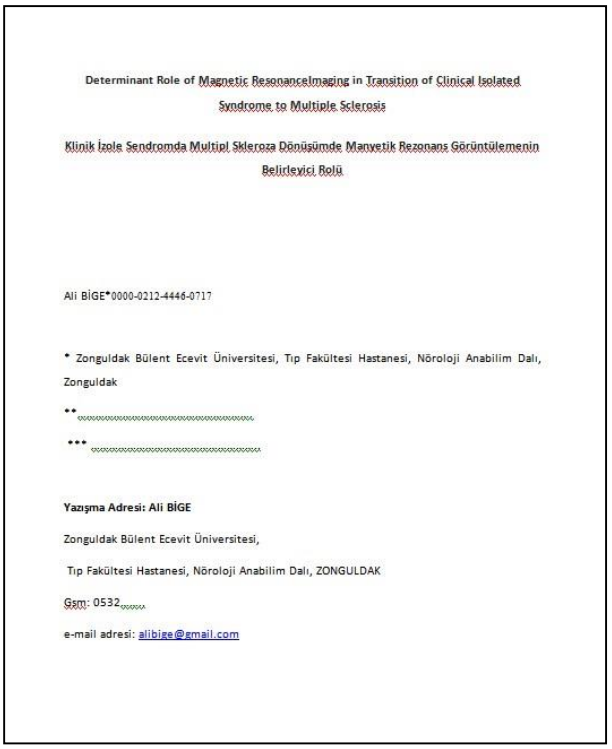

Determinant Role of Magnetic ResonanceImaging in Transition of Clinical Isolated Syndrome to Multiple Sclerosis

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Ali BİGE*0000-0212-4446-0717

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Yazışma Adresi: Ali BİGE

Zonguldak Bülent Ecevit Üniversitesi,

Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, ZONGULDAK

Gsm: 0532

e-mail adresi: alibige@gmail.com

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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Retrospective Analysis of Our Colorectal Cancer Cases: 10 Years of Experience

Kolerektal Kanser Olgularımızın Geriye Dönük Analizi: 10 Yıllık Deneyim

Cenk YAZKAN* **0000-0002-4252-8490**
Samet ŞAHİN* **0000-0003-0748-3458**
Özcan DERE* 0000-0002-2933-8983
Ilgaz KAYILIOĞLU* 0000-0002-2933-8983
Okay NAZLI*0000-0001-8500-5510
Önder ÖZCAN*0000-0001-8252-3339

*Department of General Surgery Muğla, Medicine Faculty, Muğla Sıtkı Koçman University, Muğla, Turkey

Corresponding Author: Cenk YAZKAN
Department of General Surgery Muğla, Medicine Faculty, Muğla Sıtkı Koçman University, Muğla
E-Mail: cenkyzkn@gmail.com

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Abstract

Aim: To analyze and determine the demographic, clinical, and pathological characteristics, as well as factors affecting survival, of 380 patients operated on for colorectal cancer.

Method: A retrospective study was conducted on 206 colon cancer and 174 rectal and rectosigmoid junction cancer patients operated on under emergency and elective conditions. Descriptive data regarding patient age, gender, tumor location, disease stage, average tumor size, number of excised lymph nodes, metastatic lymph nodes, ratio of the number of metastatic lymph nodes to the total number of lymph nodes dissected (LNR), whether emergency or elective surgery is performed and lymphovascular and perineural invasion (LVI, PNI) status were examined in relation to survival.

Results: In rectal cancer cases, the 2-year survival rate was 85%, the 5-year survival rate was 79%, and the overall survival rate was 65.7%. These rates were 82.9%, 71%, and 69.4%, respectively, in colon cancer cases. Tumor location in colon cancer was not associated with mortality, but tumor size greater than 5 cm, nodal metastasis, and advanced-stage disease were identified as independent factors negatively impacting survival for both colon and rectal cancers. Mortality rates were lower in rectal cancer cases without PNI and LVI compared to similar colon cancer groups. There was no difference in survival rates in patients with colon tumors in terms of emergency or elective surgery. LNR was found to be associated with survival in patients with rectal cancer.

Conclusion: Advanced stage increases mortality in colorectal cancers. While tumor location in colon cancers does not influence mortality, tumors larger than 5 cm are associated with higher mortality rates. The absence of PNI and LVI positively affects survival in rectal cancer cases. LNR is associated with survival in rectal cancer cases.

Keywords: Colon cancer, rectal cancer, survival

Öz

Amaç: Kolorektal kanser nedeniyle ameliyat edilen 380 hastanın demografik, klinik ve patolojik özelliklerinin yanı sıra sağ kalımı etkileyen faktörleri analiz etmek ve belirlemek.

Yöntem: Acil ve elektif koşullarda ameliyat edilen 206 kolon kanseri ve 174 rektal ve rektosigmoid bileşke kanseri hastası üzerinde retrospektif bir çalışma yapıldı.

Hastaların yaş, cinsiyet, tümör yerleşimi, hastalık evresi, ortalama tümör boyutu, eksize edilen lenf nodu sayısı, metastatik lenf nodu sayısı, metastatik lenf nodu sayısının diseke edilen toplam lenf nodu sayısına oranı (LNR), acil veya elektif cerrahi yapılıp yapılmadığı, lenfovasküler ve perinöral invazyon (LVI, PNI) durumu ile ilgili veriler sağ kalımla ilişkili olarak incelendi.

Bulgular: Rektum kanserli olgularda 2 yıllık sağ kalım oranı %85, 5 yıllık sağ kalım oranı %79 ve genel sağ kalım oranı %65,7 idi. Bu oranlar kolon kanseri olgularında sırasıyla %82,9, %71 ve %69,4 idi. Kolon kanserinde tümör yerleşimi mortalite ile ilişkili değildi, ancak 5 cm'den büyük tümör boyutu, nodal metastaz ve ileri evre hastalık hem kolon hem de rektum kanserleri için sağ kalımı olumsuz etkileyen bağımsız faktörler olarak tanımlandı. Perinöral ve lenfovasküler invazyonu olmayan rektum kanseri vakalarında mortalite oranları benzer kolon kanseri gruplarına kıyasla daha düşüktü. Kolon tümörlü hastalarda acil veya elektif cerrahi açısından sağ kalım oranlarında fark yoktu. Rektum kanserli hastalarda LNR sağ kalım ile ilişkili bulundu.

Sonuç: Kolorektal kanserlerde ileri evre mortaliteyi artırmaktadır. Kolon kanserlerinde tümör yerleşimi mortaliteyi etkilemezken, 5 cm'den büyük tümörler daha yüksek mortalite oranları ile ilişkilidir. Rektum kanserli olgularda perinöral ve lenfovasküler invazyonun olmaması sağ kalımı olumlu yönde etkilemektedir. LNR rektum kanseri olgularında sağ kalım ile ilişkilidir.

Anahtar Kelimeler: Kolon kanseri; rektum kanseri; sağ kalım

Introduction

Colorectal cancers are a significant public health issue due to their high rates of mortality and morbidity and their status as the most common cancers of the gastrointestinal system. According to GLOBOCAN 2020 data, colorectal cancers rank third in incidence and second in cancer-related deaths worldwide. Geographical differences in incidence and mortality rates are notable; the incidence is higher in developing countries and lower in developed ones. While the prevalence in Asia is 52.3%, it drops to 26.9% in Europe. A similar correlation is observed with mortality rates [1].

A rapid year-on-year increase in colorectal cancer cases has been observed. Data from the International Agency for Research on Cancer project a 63% increase in new colorectal cancer cases and a 73% rise in colorectal cancer-related deaths by 2040 [2].

While 70–75% of cases are sporadic, genetic factors are responsible for 25–30% [3]. Modifiable risk factors, including smoking, alcohol use, sedentary lifestyle, unhealthy diet, obesity, insulin resistance, and gut microbiota, play significant roles in sporadic cases [4].

Despite its high mortality rate and increasing prevalence, colorectal cancer is preventable by addressing modifiable risk factors. Additionally, it is a disease that can be diagnosed at an early stage through screening programs and endoscopic evaluations [4, 5].

This study aims to determine the demographic, clinical, and pathological characteristics and factors affecting survival in 380 patients operated on for colorectal cancer.

Materials and Methods

The study included 206 colon cancer and 174 rectal and rectosigmoid junction cancer patients who underwent emergency or elective surgery due to colorectal cancer between January 2013 and December 2023. The study is a retrospective, cross-sectional study in design.

For colon cancer cases, tumors in the right colon, left colon, transverse colon, and flexures were evaluated.

Promontorium was used as a landmark for surgical anatomical distinction of colon, rectum and rectosigmoid junction. Accordingly; proximal to the promontorium line was defined as colon, promontorium line as rectosigmoid junction and distal to the promontorium was defined as rectum.

Data were retrospectively obtained from patient files, archive records, and the hospital's automation system. Data on survival times and death information were obtained through the hospital automation system, the Ministry of Health death notification system and the E-pulse system.

Descriptive data regarding patient age, gender, tumor localization, disease stage, average tumor size, number of excised and metastatic lymph nodes, LNR, whether emergency or elective surgery was performed and the presence of LVI and PNI were analyzed.

The impact of age, gender, tumor localization, tumor size, disease stage, LVI, PNI, number of excised lymph nodes, LNR, whether emergency or elective surgery is performed on patient survival was investigated.

Staging was conducted using the TNM classification developed by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC), based on tumor, lymph node, and metastasis status. Modified Dukes (Astler Coller) classification was taken into account in TNM classification.

Inclusion and Exclusion Criteria:

Patients who were operated on with a diagnosis of colorectal cancer and followed up in our hospital between January 2013 and December 2023, and whose file data were completely accessible, were included in the study. Patients whose file data including the study parameters could not be accessed were excluded from the study. Patient selection is given in the flow chart (Figure 1).

Statistical Evaluation:

Data analysis was performed using SPSS 28 software. Comparative analyses were conducted using the independent sample t-test, Mann-Whitney U test, Chi-square/Fisher exact test. Survival analyses were carried out using Kaplan-Meier and Cox regression analyses. A p-value of less than 0.05 was considered statistically significant.

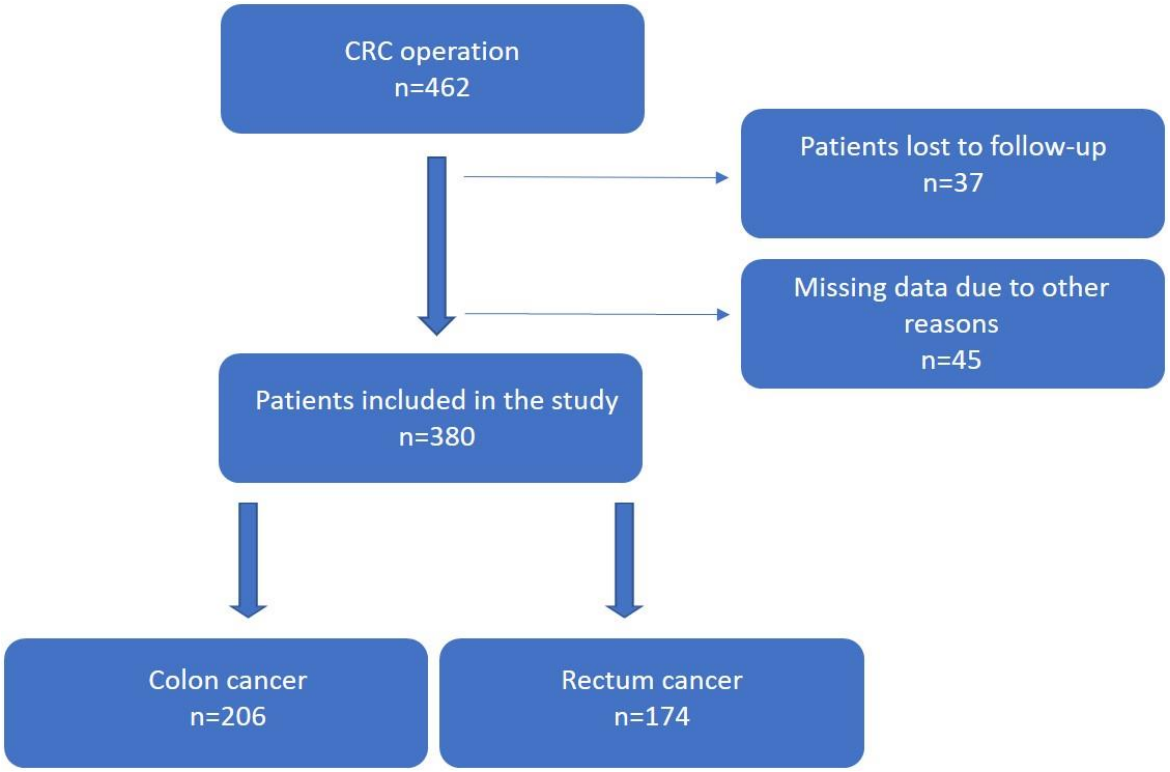

Figure 1: Patient selection flow chart

Results

The total number of patients operated on for colon cancer was 206, with 65% male and 35% female patients (mean age: 67.06 ±10.98 years). The total number of patients operated on for rectal and rectosigmoid junction cancers was 174, with 67.2% male and 32.8% female patients (mean age: 65.37 ±11.26 years). No statistically significant difference was found between colon and rectal cancer patients in terms of demographic characteristics.

In colon cancer patients, the most common tumor site was the cecum (33%), followed by the sigmoid colon (30.6%), while the least frequent site was the splenic flexure (3.9%). Among patients with rectal and rectosigmoid junction tumors, rectal cancer was approximately five times more common than rectosigmoid junction cancer.

When pathological stages of all patient groups were evaluated, both colon and rectal cancer patients had similar disease stages. In colon cancer cases, 37.4% were stage 2, and 32% were stage 3. Among rectal cancer cases, 39.1% were stage 2, and 32.8% were stage 3. Stage 1 was significantly more common in rectal cancer cases (25.9% vs. 12.6%), whereas stage 4 and metastatic disease were significantly more prevalent in colon cancer cases (18% vs. 2.3% and 5% vs. 1.1%, respectively).

The average tumor size was 5.31 cm in colon cancer cases and 3.38 cm in rectal cancer cases, with a statistically significant difference between the two groups ($p < 0.001$). The frequency of PNI and LVI was higher in patients where these features were present. The average number of excised lymph nodes was 17.5 in colon cancer cases and 12 in rectal cancer cases.

Elective surgery was performed on 64.6% of colon cancer patients and 99.9% of rectal cancer patients. Laparoscopic surgery was significantly more common in rectal cancer cases (55.7% vs. 28.2%).

Descriptive and comparative statistical data regarding demographic, clinical, and pathological results are summarized in Table 1.

Table 1. Demographic, clinical and pathologic results

		Colon (n:206)	Rectum (n:174)	P
Age (SD)		67,06 (10,98)	65,37 (11,26)	0,139
Sex	Male	134 (65)	117 (67,2)	0.665
	Female	72 (35)	57 (32,8)	
Tumor localization (%)	Cecum	68 (33)	-	-
	Outgoing column	22 (10,7)	-	
	Hepatic flexura	13 (6,3)	-	
	Transverse colon	10 (4,9)	-	
	Splenic flexura	8 (3,9)	-	
	Descending colon	22 (10,7)	-	
	Sigmoid colon	63 (30,6)	-	
	Rectosigmoid	-	28 (16,1)	
	Rectum	-	146 (83,9)	
Stage	1	26 (12,6)	45 (25,9)	<0,001
	2	77 (37,4)	68 (39,1)	
	3	66 (32)	57 (32,8)	
	4	37 (18)	4 (2,3)	
T (%)	Tis	-	5 (2,9)	0.001
	1	7 (3,4)	17 (9,8)	
	2	30 (14,6)	42 (24,1)	
	3	132 (64,1)	89 (51,1)	
	4	37 (18)	21 (12,1)	
	Tx (post-neoadj)	-	4 (2,3)	
N (%)	0	115 (55,8)	131 (75,3)	<0,001
	1	49 (23,8)	29 (16,7)	
	2	22 (10,7)	14 (8)	
	3	20 (9,7)	-	
M (%)	0	194 (94,2)	172 (98,9)	<0,001
	1	12 (5,8)	2 (1,1)	
Tumor diameter /cm (SD)		5,31 (2,31)	3,38 (2,13)	<0,001
Total number of lymph nodes removed(iqr)		17,5 (4-24)	12 (8-16)	0.040
Pathologic lymph node count (iqr)		0 (0-3)	0 (0-0.25)	0.001
PNI (%)	No	120 (58,3)	120 (69)	0.032
	There is	86 (41,7)	53 (30,5)	
LVI (%)	No	129 (62,6)	132 (75,9)	0.005
	There is	77 (37,4)	41 (23,6)	
Emergency/elective (%)	Emergency	73 (35,4)	1 (0,1)	<0,001
	Elective	133 (64,6)	173 (99,9)	
Method (%)	Conventional	148 (71,8)	77 (44,3)	<0,001
	Lap	58 (28,2)	97 (55,7)	

Survival Analyses

Survival analysis according to time was performed with Kaplan Meier analysis. Cox regression analysis was used to evaluate prognostic factors that may affect mortality.

In colon cancer cases, 2-year survival rate was found as 82.9%, 5-year survival rate as 71%, and overall survival rate as 69.4%. These rates were 85%, 79%, and 65.7% in rectal cancer cases, respectively.

Overall survival time in colon cancer cases was 36.85±29.59 (min:1, max: 108) months on average. In rectal cancer cases, it was 35.36±27.88 (min:1, max: 132).

In colon tumor patients, no statistically significant difference was found in terms of survival in patients who underwent elective surgery compared to patients who underwent emergency surgery (p=0.684).

When patients were evaluated based on tumor stages, mortality was found to be significantly higher in advanced-stage disease for both colon and rectal cancer patients ($p < 0.001$ and $p=0.019$, respectively) (Figure 2 and 3). The presence of PNI (+) and LVI (+) did not show a significant impact on mortality in either colon or rectal cancers ($p > 0.05$ for all parameters). Among colon cancer patients, tumor location, whether on the right or left side of the colon, did not significantly influence mortality ($p=0.261$).

When comparing mortality rates between colon and rectal cancer patients, it was observed that rectal cancer patients with PNI (-) and LVI (-) had lower mortality rates compared to colon cancer patients ($p=0.018$ and $p=0.020$, respectively). When comparing colon and rectal tumors by stage, no significant difference in mortality was found ($p > 0.05$) (Table 2).

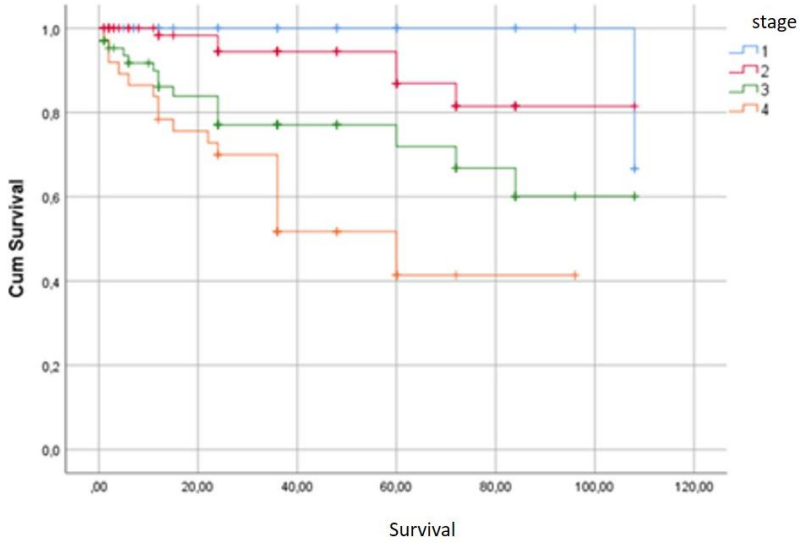

Figure 2: Kaplan Meier Survey Analysis according to stage in patients with colon cancer

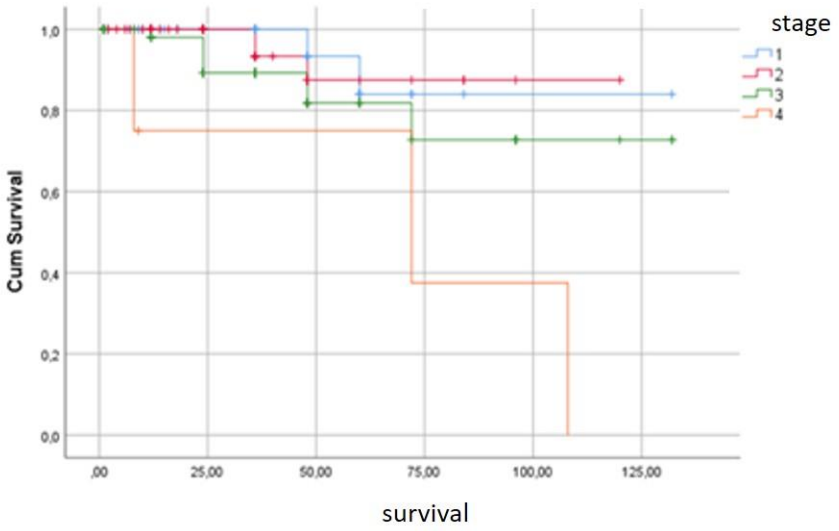

Figure 3: Kaplan Meier Survey Analysis according to stage in patients with rectal cancer

Table 2. Means and medians for survival time for colon tumors

Colon					Rectum				Comp P
	Med	SE	CI (95%)	P*	Med	SE	CI (95%)	P*	
Stage									
1	108,000	0,000	108,000-108,000	<0.001	119,680	8,069	103,865-135,495	0,019	>0,999
2	97,553	3,946	89,818- 105,287		110,200	5,445	99,528-120,872		0,502
3	80,190	6,026	68,378- 92,001		108,485	7,811	93,177-123,794		0,252
4	55,563	6,446	42,928- 68,197		69,500	24,687	21,113-117,887		0,610
PNI									
-	87,016	4,050	79,078- 94,954	0,338	111,798	6,408	99,238-124,358	0,158	0,020
+	81,452	5,205	71,251- 91,654		92,662	6,210	80,491-104,834		0,263
LVI									
-	87,142	3,907	79,485- 94,799	0,453	111,051	5,972	99,346-122,755	0,452	0,018
+	80,528	5,514	69,720- 91,336		99,046	7,773	83,811-114,280		0,223
Localization									
Right	82,279	4,698	73,071- 91,487	0,261					
Left	87,018	4,389	78,416- 95,620						

P:Log Rank (Mantel-Cox) Kaplan Meier analysis*

Tumor size measured in the specimen was found to be associated with mortality in colon cancer patients (HR: 1.097, CI 95%: 1.057–1.138, p < 0.001), but this association was not observed in rectal cancer patients (HR: 1.065, CI 95%: 0.816–1.390, p=0.643) (Figure 4). In Kaplan-Meier analysis of tumor size cutoff values in colon cancer patients, tumors measuring 5 cm or more were associated with increased mortality (p=0.001 for tumors 5, 6, and 7 cm; p < 0.001 for tumors 8, 9, and 10 cm) (Table 3). Nodal metastasis (N1,N2,N3) was found to be associated with mortality in colon cancer patients (HR: 1.106, CI 95%: 1.045–1.171, p=0.001), but no such association was observed in rectal cancer patients (HR: 1.100, CI 95%: 0.985–1.229, p=0.091).

When LNR was examined, there was no significant difference in survival in patients with colon tumors (p=0.141), while a statistically significant difference was found in patients with rectum tumors (p=0.004).

There was a significant relationship between the total number of metastatic lymph nodes and survival rate (colon p=0.032, rectum p=0.005).

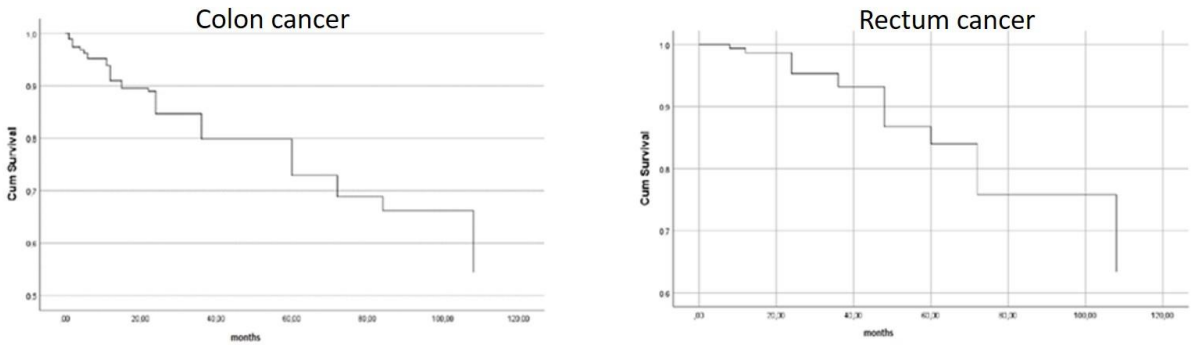

Figure 4: Cox regression analysis according to tumor size in colon and rectal cancer patients

Table 3: Survey analysis according to tumor dimension

Tm property		Est	SE	CI (95%)	P*
3 cm	<3	86.000	6,455	73,348- 98,652	0,360
	≥3	83,895	3,395	77,241- 90,549	
4 cm	<4	95,818	5,427	85,181- 106,456	0,064
	≥4	81,207	3,822	73,715- 88,699	
5 cm	<5	93,789	3,602	86,730- 100,849	0,001
	≥5	72,875	5,391	62,309- 83,441	
6 cm	<6	93,628	3,516	86,737- 100,520	0,001
	≥6	71,711	5,605	60,725- 82,696	
7 cm	<7	90,106	3,336	83,568- 96,644	0,001
	≥7	66,596	7,726	51,454- 81,738	
8 cm	<8	89,460	3,173	83,241- 95,679	<0,001
	≥8	45,084	7,242	30,891- 59,278	
9 cm	<9	88,126	3,146	81,959- 94,292	<0,001
	≥9	34,133	9,416	15,679- 52,588	
10 cm	<10	88,150	3,143	81,989- 94,311	<0,001
	≥10	33,199	9,444	14,690- 51,709	
Ln met	1	92,950	3,758	85,584- 100,316	0,004
	>1	75,149	5,206	64,946- 85,353	

P: Log Rank (Mantel-Cox) Kaplan Meier analysis*

Discussion

Colorectal cancer (CRC) is the third most common cancer type worldwide and ranks second in cancer-related mortality [5].

Demographic data revealed that the mean age of colon and rectal cancer patients was similar. However, when analyzed by gender, males were more commonly affected in both patient groups. The age and gender characteristics of our patients are consistent with the literature [6-9]. In our study, the mean age of colon cancer patients was 67.06 (±10.98) years, and it was observed that mortality rates increased with advancing age. Similarly, the literature highlights that advancing age, due to overall health status and the presence of comorbidities, increases mortality [10]. A large case series from the Aegean region, involving 117,139 patients, reported an increase in colorectal cancer incidence in individuals over the age of 60 in both genders. This relationship between age and cancer incidence emphasizes the importance of colorectal cancer screening.

Among colon cancer cases, the most common tumor site was the cecum, followed by the sigmoid colon. Unlike our findings, other studies reported higher frequencies of sigmoid and descending colon tumors [6-8]. In our study, tumor location was not found to affect survival in terms of right- or left-sided colon tumors. However, results from larger case series vary; a study involving 53,801 patients indicated no survival difference based on tumor location, whereas another study with 77,978 patients suggested poorer prognosis for right-sided colon tumors compared to left-sided ones [11, 12].

Disease stage is one of the primary parameters affecting mortality and survival in colorectal cancer [13, 14]. In survival analyses, we observed that advanced-stage disease was a poor prognostic factor across all colorectal cancer patient groups. Stage is crucial not only for influencing mortality but also for optimal treatment planning. Treatment options for colon cancer patients include surgical intervention, chemotherapy, and radiotherapy. The literature emphasizes that adjuvant chemotherapy following surgery increases survival, especially in stage II and III colon cancer patients. In rectal cancer patients, neoadjuvant chemoradiotherapy followed by surgical treatment improves local control and enhances quality of life [15, 16].

Tumor size is an independent predictive factor for survival in colorectal cancer [17-19]. A study analyzing data from the National Cancer Database of 300,386 patients highlighted that increasing tumor size was associated with higher mortality [20]. In our study, the average tumor size was 5.31 cm in colon cancer patients and 3.38 cm in rectal cancer patients. Survival analyses revealed that tumor size was a significant predictive factor in colon cancer patients but had no impact on rectal cancer survival. A recent study published in 2023 emphasized that tumors 5 cm or larger pose a risk factor for poor prognosis [21]. Our findings align with the literature.

The number of excised lymph nodes and the presence of metastatic lymph nodes significantly affect mortality in colon cancer patients. The literature indicates that patients with lymph node metastases have lower survival rates. In stage II cases, a positive correlation has been reported between the number of dissected lymph nodes and survival [22-25]. For patients with more advanced stages, lymphadenectomy is considered therapeutic as it enhances surgical success and reduces the risk of lymphatic metastasis [26, 27]. The number of excised lymph nodes is also crucial for accurate staging and planning adjuvant therapy. In our study, the average number of excised lymph nodes was 17.5 in colon cancer patients and 12 in rectal cancer patients. Nodal metastasis was identified as a critical factor affecting survival, particularly in colon cancer patients.

Our study also showed that the absence of PNI and LVI reduces mortality in rectal cancer patients. The literature similarly associates the presence of PNI and LVI with poor prognosis [28-35].

It is seen that similar rates are given in different studies regarding survival rates. In a recent study where data from 15 European countries were considered and 8785 patients were included, it was reported that 5-year survival rates varied between 60.8% and 74.5% among countries [36]. In another study where data from 11023 patients were considered, it was emphasized that survival rates varied between 65.9% and 70.5% [37].These data are similar to our study results.

In a study evaluating the data of 156 patients with stage 3 colorectal cancer, it was reported that LNR is an important prognostic factor for survival. According to the study results, no correlation was found between the total number of lymph nodes dissected and survival rates [38]. In another study evaluating 137 patients, similar results were obtained, and LNR was associated with poor prognosis [39]. According to our study results, the number of metastatic lymph nodes was found to be an important prognostic factor affecting survival in both colon and rectal cancer cases. However; it was seen that LNR only affected survival in rectal cancer cases.

Study Limitations: Colorectal surgery has been performed in our clinic for many years, with treatment protocols guided by current literature. Therefore, this study, which includes a large sample specific to our clinic, provides reliable analysis results. However, the long follow-up period includes patient groups treated before the introduction of the latest guidelines, which may have affected mortality rates.

In addition, retrospective design, variability in follow-up periods, and deficiencies in clinicopathological data may affect the accuracy of the results. In our study, data on colorectal cancer subtypes in terms of microsatellite instability (MSI) were missing. Our study covers a wide time period. Therefore, since the database for MSI evaluation could not be accessed in the old data, it was thought that this information would not reflect the entire sample of patients. Therefore, it could not be added to the study. The effects of these data on prognosis could not be evaluated. This is also an important limiting factor for our study.

The single-center nature of the study and the sample size may also be taken into account. Multicenter prospective studies with larger patient groups may allow for stronger statistical results to be obtained in the future.

Conclusion

Our study evaluated the demographic, clinical, and pathological data and mortality rates of patients operated on for colon and rectal cancer, presenting findings consistent with the existing literature. In the future, it is recommended that new treatment options and technological advancements be applied to larger patient groups and that their long-term outcomes be evaluated. Additionally, more comprehensive analyses of patient data and multicenter studies will contribute to the development of more effective and personalized approaches in colorectal cancer treatment.

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Radiological Features of Primary Neuroendocrine Breast Carcinoma and Neuroendocrine Differentiated Breast Carcinoma

Primer Nöroendokrin Meme Karsinomu ve Nöroendokrin Difeeransiyasyonlu Meme Karsinomunun Radyolojik Özellikleri

Hülya ÇETİN TUNÇEZ[*] 0000-0002-0830-0070
Zehra Hilal ADIBELLİ[**] 0000-0001-9265-8114
Levent ALTIN[*] 0000-0003-4081-8918
Demet KOCATEPE ÇAVDAR[***] 0000-0002-3278-3770
Ali Murat KOÇ[****] 0000-0001-6824-4990
Baha ZENGEL[*****] 0000-0002-1812-6846
Özlem ÖZDEMİR[******] 0000-0003-2520-5953

*Department of Radiology, Izmir City Hospital, Izmir, Turkey
**Department of Radiology, Izmir Faculty of Medicine, University of Health Sciences, Izmir, Turkey
***Department of Pathology, Izmir City Hospital, Izmir, Turkey
****Department of Radiology, Katip Çelebi University Izmir Atatürk Education and Research Hospital, Izmir, Turkey
*****Department of General Surgery, Izmir Economy University Medical Point Hospital, Izmir, Turkey
******Department of Oncology, Izmir City Hospital, Izmir, Turkey

Corresponding Author: Hülya ÇETİN TUNÇEZ
Address: İzmir City Hospital, Laka,
35040, Bornova, Izmir, Turkey
E-mail : drhulyacetintuncez@gmail.com

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Abstract

Introduction: Primary neuroendocrine breast carcinoma (NEBC) and neuroendocrine differentiated breast cancer (NEDBC) are rare subtypes of breast cancer. Our aim is to examine the radiological imaging features of this heterogeneous tumour group and to discuss histopathological findings.

Material and Methods: In this study, our hospital's data archive was reviewed and patients diagnosed with NEBC and NEDBC within 5 years were analyzed. Ultrasound, mammography and dynamic magnetic resonance imaging (MRI) features were retrospectively evaluated in accordance with Breast Imaging Reporting and Data System (BI-RADS) 5th dictionary. Estrogen receptor, progesterone receptor, Her2 expression, ki67 ratio and histological grade were recorded. Radiologic features were compared according to Ki67 ratio.

Results: The study included 51 lesions (5/51 primary NEBC, 46/51 NEDBC) of 47 patients. The most common histological type in the NEDBC group was invasive ductal carcinoma in 81% (37/46). On ultrasound, 85.7% of lesions were irregularly shaped, 52.4% were microlobulated and 92.9% had long axis perpendicular to the skin. Asymmetry and tissue distortion were seen in 77.3% (34/44) of the patients. 79.5% had microcalcification. Most of the lesions with microcalcification had a ki67 value below 20%(p=0.002). On MRI, 83.3% of the lesions showed rapid contrast uptake, while 56.3% showed washout. Diffusion restriction was observed in 93.8%. Estrogen or progesterone receptor was positive in 96% of lesions.

Discussion: NEBC and NEDBC are radiologically masses with irregular borders, long axis perpendicular to the skin, heterogeneous contrast enhancement and diffusion restriction. Histopathologically, they are often hormone positive and Her2 negative. Prospective studies with large patient series are needed in this regard.

Keywords: Breast cancer, magnetic resonance imaging, neuroendocrine carcinoma

Öz

Giriş: Primer nöroendokrin meme karsinomu (NMK) ve nöroendokrin diferansiye meme kanseri (NDBC) meme kanserinin nadir görülen alt tipleridir. Amacımız bu heterojen tümör grubunun görüntüleme özelliklerini incelemek ve histopatolojik bulgularını tartışmaktır.

Gereç ve Yöntemler: Bu çalışmada hastanemiz veri kayıt arşivi taranarak 5 yıl içerisinde NMK ve NDBC tanısı alan hastalar incelendi. Ultrasonografi, mamografi ve dinamik manyetik rezonans görüntüleme (MRG) özellikleri Meme Görüntüleme Raporlama ve Veri Sistemi (BI-RADS) 5. sözlüğüne göre retrospektif olarak değerlendirildi. Östrojen reseptörü, progesteron reseptörü, Her2 ekspresyonu, ki67 oranı ve histolojik derece kaydedildi. Ki67 oranına göre radyolojik özellikler karşılaştırıldı.

Bulgular: Çalışmaya 47 hastaya ait 51 lezyon (5/51 primer NMK, 46/51 NDBC) dahil edildi. NDBC grubunda en sık görülen histolojik tip %81 (37/46) oranında invaziv duktal karsinomdu. Ultrasonografide lezyonların %85,7'si düzensiz şekilli, %52,4'ü mikrolobüle ve %92,9'u cilde dik uzun eksenli idi. Hastaların %77,3'ünde (34/44) asimetri ve doku distorsiyonu görüldü. 79,5'inde mikrokalsifikasyon vardı. Mikrokalsifikasyon ile ki67 değeri arasında istatistiksel olarak anlamlı bir korelasyon vardı. Mikrokalsifikasyonlu lezyonların çoğunda ki67 değeri %20'nin altındaydı (p=0,002). MRG'de lezyonların %83,3'ü hızlı kontrast tutulumu gösterirken, %56,3'ü yıkanma gösterdi. Difüzyon kısıtlaması %93,8 oranında gözlendi. Lezyonların %96'sında östrojen veya progesteron reseptörü pozitifti.

Tartışma: NMK ve NDBC, radyolojik olarak düzensiz sınırlara sahip, uzun aksı cilde dik, heterojen kontrast tutulumu ve difüzyon kısıtlılığı gösteren kitleler olarak görülür. Histopatolojik olarak sıklıkla hormon pozitif ve Her2 negatiftirler. Bu konuda geniş hasta serileri ile prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Meme kanseri, manyetik rezonans görüntüleme, nöroendokrin karsinom

Introduction

Primary neuroendocrine breast carcinoma (NEBC) is an extremely rare subtype of cancer in the breast that frequently originates from the gastrointestinal or respiratory system. It represents less than 1% of all breast cancers (BC) (1). Focal neuroendocrine differentiation is more common in breast cancer and its rate in the literature is between 1% and 20% (2). One of the reasons for this wide range is that neuroendocrine markers such as chromogranin A and synaptophysin are not routinely used in the pathological evaluation of breast cancer (3). Another reason is that the diagnostic criteria of this lesion group have been changed several times by the World Health Organisation (WHO). Neuroendocrine carcinomas (NEC) were first described by Feyrter and Hartmann in 1963 and Cubilla and Woodruff in 1977 (4,5). In 2003, WHO defined NEC as more than 50% staining with neuroendocrine markers and later in 2012, this staining rate was removed and classified as well-differentiated NEBC, poorly differentiated NEBC and immunohistochemical NEC. Briefly, primary NEC and NECs were classified in a single group under the title of 'Neuroendocrine differentiated breast carcinoma' together with grade 1 or 2 breast carcinomas expressing neuroendocrine indicators. However, due to the difficulty in differentiation, a revision similar to the classification of NEC in other organs was made in 2019 and it was divided into groups as large cell NEC, small cell NEC and primary NEC (6). The 2019 WHO classification proposed that invasive breast carcinoma tumours with non-specific and specific morphology types (mucinous carcinoma, solid papillary carcinoma, etc.) and non-uniform neuroendocrine morphology and neuroendocrine marker expression be defined as 'Invasive breast carcinomas with neuroendocrine differentiation' (3).

The imaging features of breast NEC were first described by Wade et al. Until today, a limited number of studies investigating the imaging features of these tumours have been reported (7,8). The aim of this study is to examine the radiological imaging features of this rare heterogeneous tumour group and to discuss them with histopathological findings.

Material and Methods

In this study, ultrasound, mammography and dynamic contrast-enhanced magnetic resonance imaging (MRI) features of patients diagnosed with NEBC and neuroendocrine differentiated breast cancer (NEDBC) in our hospital between 2016 and 2021 were retrospectively evaluated. Patients whose images could not be accessed and those with insufficient image quality were excluded from the study. Before the study, approval was obtained from the clinical research ethics committee of our hospital on (decision date 13.01.2021 and number:08). Radiological images were evaluated blinded to clinical and pathological findings by two breast radiologists with 30 years and 8 years of experience. The findings were provided by common consensus in accordance with the Breast Imaging Reporting and Data System (BIRADS) 5. edition.

Standard craniocaudal and mediolateral oblique mammograms were obtained in all patients (Mammomat Revelation, Siemens, Erlangen, Germany). Shape, size, asymmetry, distortion, margin, breast density and calcification were evaluated on mammography. Sonographic examination was performed using a linear probe (Samsung trademark) with a frequency of 2.0-14.0 MHz. The evaluation was made from image printouts, reports and images archived in the database of our hospital. Breast composition, size, lesion shape, margin, orientation, echogenicity, posterior acoustic features, surrounding tissue changes and axillary lymphadenopathy were recorded.

MRI was performed with a 1.5 Tesla MRI (Magnetom Aera, Siemens, Germany) using a 4-channel breast coil. Axial T1-weighted pre-contrast images (TR: 476 ms, TE:11 ms, thickness: 4 mm, matrix 320x320, field of view 260 mm, flip angle 20°) and fat-suppressed T2-weighted images (TR:2250 ms, TE:56 ms, 4 mm thickness, matrix 320x320, field of view 300 mm, flip angle 20°) were obtained on all MRI scans. Axial diffusion-weighted images (DWI) were also obtained at b-values of 0, 500, and 1000 s/mm² (TR/TE: 5600 ms/87 ms, field of view: 5 × 35 cm; matrix 220 × 102, slice thickness: 4 mm). Apparent diffusion coefficient (ADC) maps were automatically generated on the operating console with all three images and b-values of 0, 500, and 1000 s/mm².

After intravenous injection of 0. 1 mmol/kg body weight gadolinium contrast medium (Gadoteric acid, Dotarem, Guerbet), 5 dynamic postcontrast fat suppressed T1 weighted images were obtained. Size, multifocality/multicentricity, presence of satellitic lesions, background contrast, shape, margin, T1 and T2 signal characteristics, contrast enhancement pattern, early and late phase contrast enhancement curves were evaluated. Diffusion restriction and ADC value on DWI were also recorded.

All pathology specimens were re-evaluated by a pathologist with 20 years of experience and estrogen receptor, progesterone receptor, Her2 expression, Ki-67 value and histological grade were recorded. Radiological findings were compared using a threshold of 20% for Ki-67 (9).

Data analysis was performed with IBM SPSS 26.0 programme. Descriptive statistics were presented as mean st.deviation and median (min - max) values for continuous variables and frequency numbers and percentages for categorical variables. Cross tabulations were prepared as frequency and percentage for Ki67 groups.

Differences in distribution between groups were analysed by Pearson Chi-Square Test or Fisher's Exact Test. In cases where the minimum expected values did not fulfil the test conditions, the tests were not accepted as valid and were marked as 'na'. The conformity of continuous variables to 'normal distribution' was investigated by considering graphical research (Q-Q Plot, Detrended Q-Q Plot), Shapiro Wilk test, skewness kurtosis values and sample diameter.

It was seen that the assumption of normal distribution was not met. The difference between Ki67 groups was analysed with the non-parametric method 'Mann-Whitney U Test'. median (min-max) values were presented. In all statistical comparison tests, type-1 margin of error was set as α:0.05 and two-tailed test was performed.

Results

The study included 51 lesions of 47 patients. All patients were female with a mean age of 59.1 years (SD; ±13.7, range 28-83). NEBC was found in 10% (5/51) and NEDBC in 90% (46/51) of the lesions. The most common histological type in tumours with neuroendocrine differentiation was invasive ductal carcinoma in 81% (37/46). Other histological subtypes were as follows; 10% (5/46) mucinous carcinoma, 9% (4/46) solid papillary carcinoma. Two thirds of the lesions were in the right breast and one third in the left breast. Inspection revealed nipple changes in 22.9%. With imaging methods, 54.2% of the lesions had accompanying satellites and 85.4% had multifocal/multicentric distribution. Radiological findings revealed accompanying lymphadenopathy in 54.2% (Table 1).

Table 1. Distribution of histopathological findings and additional features of patients according to Ki-67 ratio.

		Total		Ki-67 (%) ≤20		Ki-67 (%) >20		
		N	%	N	%	N	%	p
Histological Type	Invasive Ductal Carcinoma	37	73%	19	63%	18	86%	na
	Primary Neuroendocrine Carcinoma	5	10%	4	13%	1	5%	
	Solid Papillary Carcinoma	4	8%	4	13%	0	0%	
	Mucinous Carcinoma	5	10%	3	10%	2	10%	
Side	Right	32	67%	20	69%	12	63%	0.917
	Left	16	33%	9	31%	7	37%	
Nipple	Normal	37	77%	23	79%	14	74%	0.732
	Affected	11	23%	6	21%	5	26%	
Satellite Lesion	Present	22	46%	10	34%	12	63%	0.098
	Absent	26	54%	19	66%	7	37%	
Lymphadenomegaly (Radiological)	Present	22	46%	11	38%	11	58%	0.289
	Absent	26	54%	18	62%	8	42%	
Multifocality/Centricity	Present	7	15%	5	17%	2	11%	0.687
	Absent	41	85%	24	83%	17	89%	
ER/PR	Positive	46	96%	29	100%	17	89%	na
	Negative	2	4%	0	0%	2	11%	
CERB2	Positive	11	23%	3	10%	8	42%	0.016
	Negative	37	77%	26	90%	11	58%	
Histological Grade	Grade I	1	2%	1	3%	0	0%	na
	Grade II	38	79%	24	83%	14	74%	
	Grade III	9	19%	4	14%	5	26%	
Molecular Subtype	Luminal Disease	46	96%	29	100%	17	89%	na
	Her2 (+)	1	2%	0	0%	1	5%	
	Triple (-)	1	2%	0	0%	1	5%	
Age		59.3 (28-83)		57.5 (28 - 83)		57 (38 - 82)		0.625

Ultrasonographic findings;

In the retrospective review, images or reports of 42 of 51 lesions were available. Breast composition was lipomatous in 21.4% (9/42), liposclerosed type B in 42.9% (18/42), liposclerosed type C in 21.4% (9/42), and sclerosed in 14.3% (6/42). The mean sonographic size was 25.1 mm. The shape of the lesions was irregular in 85.7% (36/42). The most common margin features were microlobulation in 52.4% (22/42) and spiculated in 38.1% (16/42).

The long axis of the majority of the lesions (92.9%) was perpendicular to the skin. When echo patterns were categorised as hypoechogenic, hyperechogenic, heterogeneous and complex according to the BIRADS atlas, hypoechoic echo pattern was the most common with 43.1%. No posterior echo enhancement or shadowing was detected in 59.5% of the lesions, while no echogenicity change was observed in the surrounding tissue in 66.7%.

Mammographic findings;

Mammographic images of 44 lesions were obtained. The most common breast density was category B (43.1%, 19/44) in mammography as in ultrasound. The mean mammographic lesion size was 24.1 mm. Shape characteristics were divided into round, oval and irregular and 79.5% had irregular shape. Asymmetry and tissue distortion were seen in 77.3% (34/44) of the patients. Lesion borders were hidden by parenchyma in 3 patients (6.8%) and were sharp in only 4.5%. 21 patients (47.7%) had microlobulated, 10 (22.7%) had spiculation and 8 (18.2%) had indistinct margins.

When the mammographic lesion density was analysed, 93.2% of the lesions were equal to or higher than the parenchyma. 35 of 44 lesions (79.5%) had microcalcification. A statistically significant correlation was found between microcalcification and ki67 value and it was observed that the majority of the lesions with microcalcification had a ki67 value below 20% (p=0.002). Ultrasound and mammography features are detailed in Table 2.

Table 2. Distribution of mammography (MM) and ultrasound (US) findings of all patients according to Ki-67 ratio.

		Total		Ki-67 (%)				
				≤20		>20		
		N	%	N	%	N	%	p
MM-Patern	A-B	33	69%	24	83%	9	47%	**0.023***
	C-D	15	31%	5	17%	10	53%	
MM-Shape	Round - Ovoid	9	21%	5	19%	4	22%	1.000
	Irreguler	35	80%	21	81%	14	78%	
MM-Asymetry	Present	15	34%	6	23%	9	50%	0.126
	Absent	29	66%	20	77%	9	50%	
MM-Distortion	Present	10	23%	3	12%	7	39%	0.064
	Absent	34	77%	23	88%	11	61%	
MM-Margin	Circumscribed	2	5%	1	4%	1	6%	na
	Obscured	3	7%	2	8%	1	6%	
	Microlobulated	21	48%	12	46%	9	50%	
	Spiculated	10	23%	5	19%	5	28%	
	Indistinct	8	18%	6	23%	2	11%	
MM-Density	Low-Equal density	3	7%	16	62%	8	44%	0.417
	High density	21	48%	10	38%	10	56%	
MM-Microcalcification	Present	20	45%	25	96%	10	56%	**0.002***
	Absent	35	80%	1	4%	8	44%	
US Patern	A-B	27	64%	20	80%	7	41%	**0.024***
	C-D	15	35%	5	20%	10	59%	
US-Shape	Ovoid	6	14%	3	12%	3	18%	0.672
	Irreguler	36	86%	22	88%	14	82%	
US-Margin	Circumscribed	1	2%	1	4%	0	0%	na
	Indistinct	3	7%	2	8%	1	6%	
	Microlobulated	22	52%	13	52%	9	53%	
	Spiculated	16	38%	9	36%	7	41%	
US-Orientation	Parallel	1	2%	1	4%	0	0%	na
	Not parallel	41	98%	24	96%	17	100%	
US-Echo Patern	Complex cystic and solid	4	10%	1	4%	3	18%	na
	Hypoechoic	22	52%	15	60%	7	41%	
	Hyperechoic	4	10%	3	12%	1	6%	
	Heterogeneous	12	29%	6	24%	6	35%	
US-Posterior features	No posterior features	25	60%	16	64%	9	53%	na
	Enhancement	1	2%	1	4%	0	0%	
	Shadowing	7	17%	5	20%	2	12%	
	Combined pattern	9	21%	3	12%	6	35%	
US-Surrounding Tissue	Present	14	33%	10	40%	4	24%	0.331
	Absent	28	67%	15	60%	13	76%	

MRI findings;

MRIs of 48 patients, excluding 3 patients, were obtained and evaluated. The mean size was found to be 25.1 mm, which was the same with ultrasound. The shape was irregular in 89.6% of the MRI scans. Margins were microlobulated in 60.4%, spiculated in 25% and indistinct in 10.4%. Only 2 patients (4.2%) showed sharp contours. T1 signal was isointense with parenchyma in 81.3% of the lesions, hyperintense in 47.9% and isointense in 37.5%.

On postcontrast imaging, 79.2% showed heterogeneous contrast enhancement and 12.5% had contrast-enhancing septa. In dynamic imaging, 83.3% of the lesions show rapid contrast uptake in the initial phase and 56.3% show washout. On DWI, diffusion restriction was observed in 45 lesions (93.8%) except 3 lesions (Figure 1). The mean ADC value was 803 (range 560-1350). MRI features are detailed in Table 3.

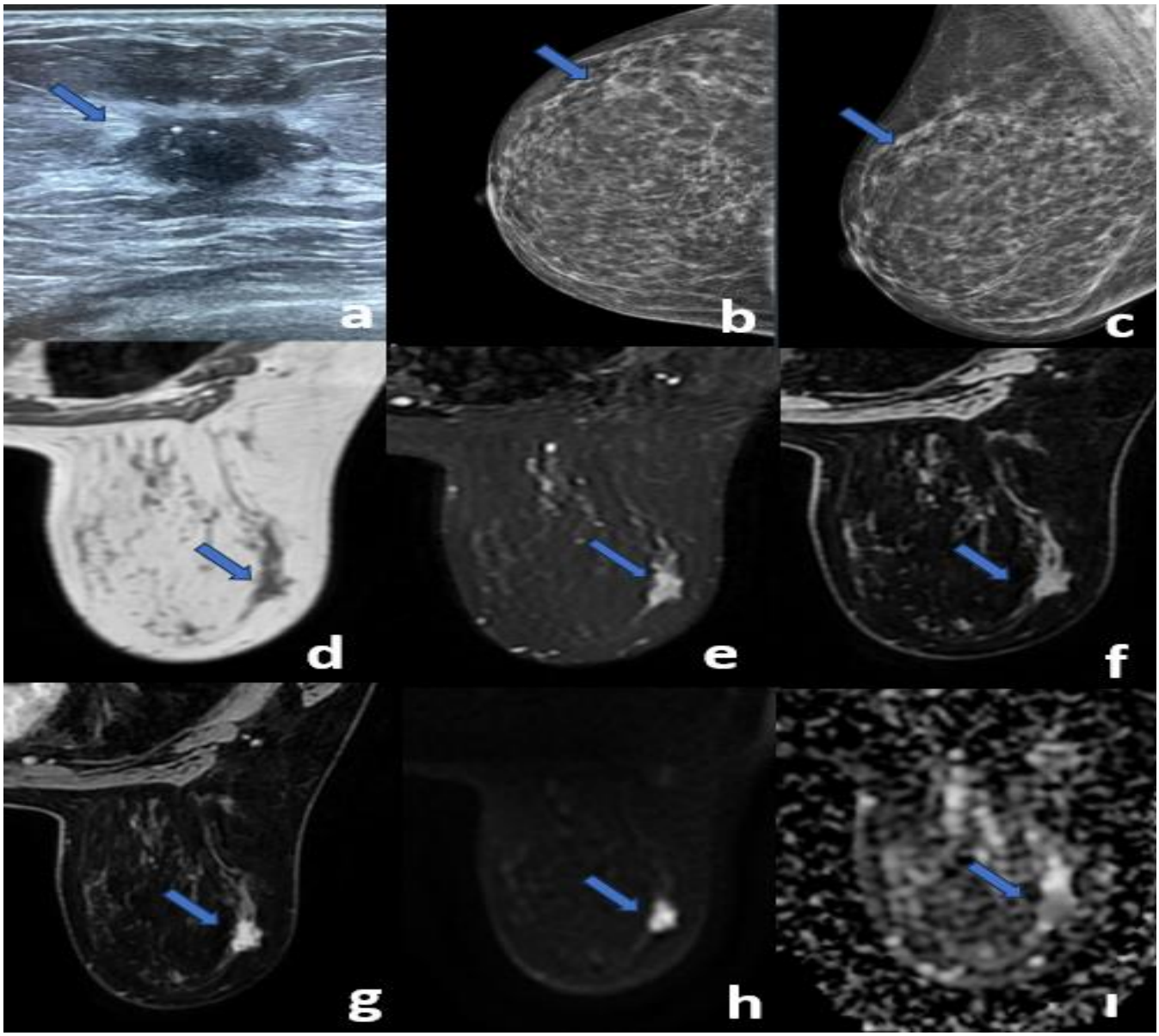

Figure 1. Ultrasound shows a solid, hypoechoic, irregularly circumscribed, ovoid-shaped mass (a) and asymmetric opacity on mammography (b, c). The tumor is hypointense on T1-weighted images (WI) (d), hyperintense on T2WI (e), and shows heterogeneous contrast enhancement on fat-suppressed precontrast (f) and postcontrast (g) images. Diffusion-weighted imaging demonstrates diffusion restriction (h) and ADC equivalent (ı).

Table 3. According to magnetic resonance imaging findings and Ki-67 ratio of patients.

		Total		Ki-67 (%) ≤20		Ki-67 (%) >20		
		N	%	N	%	N	%	p
Shape	Round- Ovoid	5	10%	2	7%	3	16%	0.372
	Irreguler	43	90%	27	93%	16	84%	
Margin	Circumscribed	2	4%	2	7%	0	0%	na
	Microlobulated	29	60%	17	59%	12	63%	
	Spiculated	12	25%	7	24%	5	26%	
	Indistinct	5	10%	3	10%	2	11%	
T1 weigheted images	Equal density	39	81%	24	83%	15	79%	na
	Low density	8	17%	4	14%	4	21%	
	High density	1	2%	1	3%	0	0%	
T2 weigheted images	Equal density	18	38%	12	41%	6	32%	na
	Low density	7	15%	4	14%	3	16%	
	High density	23	48%	13	45%	10	53%	
Enhanment Pattern	Homogenous	4	8%	3	10%	1	5%	na
	Enhancing Septa	6	13%	5	17%	1	5%	
	Heterogeneous	38	79%	21	72%	17	89%	
Initial Phase	Slow	1	2%	1	3%	0	0%	na
	Medium	7	15%	3	10%	4	21%	
	Rapid	40	83%	25	86%	15	79%	
Late Phase	Plateau	21	44%	11	38%	10	53%	0.480
	Wash Out	27	56%	18	62%	9	47%	
Diffusion Restriction	Present	45	94%	27	93%	18	95%	1.000
	Absent	3	6%	2	7%	1	5%	
Background Enhancement	1	21	44%	14	48%	7	37%	na
	2	17	35%	10	34%	7	37%	
	3	9	19%	4	14%	5	26%	
	4	1	2%	1	3%	0	0%	
ADC Value		803 (560-1350)		780 (560 - 1350)		750 (571 - 1290)		0.833

Histopathological findings;

Estrogen or progesterone receptor (ER/PR) was positive in 96% of lesions. Her2 was positive in 11 (21.5%) of the lesions, but mostly negative (Figure 2). Histological grade was grade 2 in most of the patients (78.4%), grade 3 in 19.6% and grade 1 in only 2%. In these data, the molecular subtypes of the patients were found as luminal disease in 96%, Her2 positive in 2% and triple negative in 2%. The mean Ki-67 value was 24.5 (SD; ±17.2, range 20-80).

The Ki-67 value was below 14% in 31.4% of the lesions, between 14-20% in 27.5%, and above 20% in 41.2%. The majority of the lesions with Ki-67 values below 20% were found to have type A and B breast density on ultrasound and mammography, which were statistically significant (p=0.024, p=0.023, respectively) (Table 1).

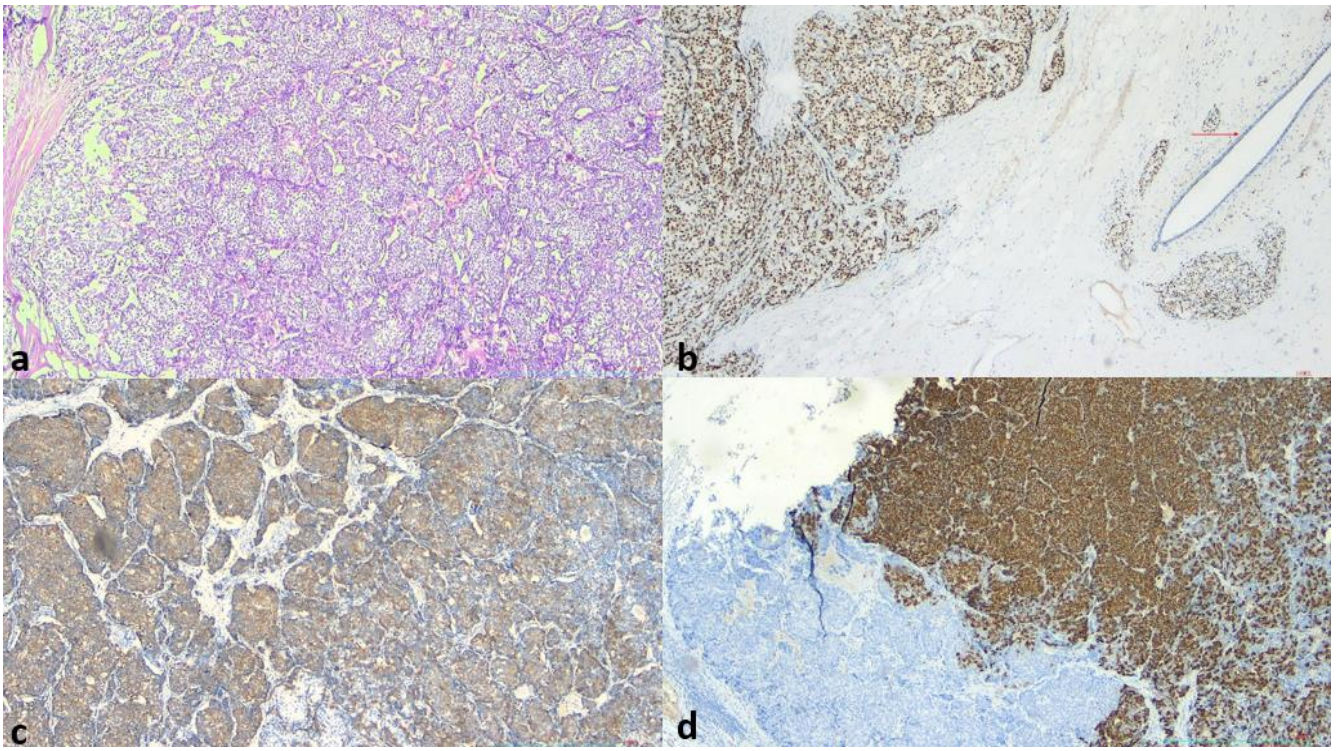

Figure 2. Tumour tissue arranged in nests separated by a thin fibrovascular stroma (a). Immunohistochemistry (IHC) shows estrogen receptor (ER) positivity in mammary duct luminal cells (arrow) and ER positivity in tumour tissue (b). Synaptophysin (c) and chromogranin (d) positivity is detected in tumour cells by IHC.

Discussion

In our study, the radiological and pathological features of NEBC and NEDBC were investigated. The typical sonographic features of this tumour group are irregular shaped, long axis perpendicular to the skin, microlobulated or spiculated contoured, hypoechoic masses. On mammography, they are often seen as irregularly circumscribed microlobulated or spiculated margin opacities accompanied by microcalcifications, tissue distortion and asymmetry. Morphological features on MRI are similar to ultrasound and mammography. In addition, diffusion restriction on DWI and heterogeneous contrast enhancement on contrast-enhanced examination are seen as tumours with early contrast enhancement and plateau or washout at later stage. In the study conducted by Kayadibi et al., it was observed that tumours with neuroendocrine differentiation had a more oval-round shape compared to those without neuroendocrine differentiation and were also most commonly irregularly shaped (10). In this study, contours were found to be well circumscribed more frequently, which is different from our study. In addition, MRI features were similar to our study and no significant difference was found when compared with the group without neuroendocrine differentiation.

Breast tissue histologically does not normally contain neuroendocrine cells; therefore, neuroendocrine tumours detected in the breast are explained by the hypothesis of neuroendocrine differentiation of epithelioid cells during carcinogenesis (11). However, the cause of the transformation of these tumour cells is currently unknown. Therefore, when a neuroendocrine tumour is detected in the breast, metastases from other organs are first excluded, and then it is considered to be the primary neuroendocrine tumour of the breast (12).

Our study showed that the majority of these lesions were ER/PR positive and Her2 negative pathologically. Hormone receptor positivity is typically associated with well-differentiated tumours and has a better prognosis. In contrast, a study by Wei et al. showed that primary NEC in the breast is an aggressive tumour and has a higher tendency for local and distant recurrence and worse overall survival compared to age, gender, race, tumour stage and nonspecific invasive ductal carcinoma cases. In this study, ER and PR positivity was found in tumours with neuroendocrine differentiation similar to our study, but neuroendocrine differentiation was shown to be a negative prognostic factor independent of hormone positivity and nuclear grade (13).

Ki67 value is a marker of tumour proliferation and in our study, type A and B breast density and presence of microcalcification on mammography were found to be associated with low Ki-67 values.

Data on the prognosis of NEBC are still controversial. Previous studies have shown that neuroendocrine differentiated lesions do not show a significant difference in terms of prognosis compared to other invasive breast cancers without this feature (14-16). However, later studies have shown that these tumours have a poor prognosis in long-term follow-up and are associated with local and distant recurrence (17,19). Due to their rarity, the lack of randomised controlled trials means that the most appropriate treatment method is controversial. In general, surgery and chemotherapy regimens remain the treatment of choice for ductal type breast cancer.

Our study has some limitations. Some of them are as follows; firstly, due to the retrospective nature of the study, ultrasound, mammography and MRI images of all patients were not available. Secondly, there was no comparison group. The lack of information about the survival of the patients also led to the inability to determine the imaging features affecting the prognosis.

In conclusion, our study showed that primary neuroendocrine carcinoma of the breast and breast cancers with neuroendocrine differentiation are diffusion-restricted masses with irregular margins, microlobulated-spiculated contours, microcalcifications, heterogeneous contrast and kinetic curves showing plateau and washout in the late phase. These tumours are mostly hormone receptor positive and Her2 negative histopathological features but have a worse prognosis than other hormone receptor positive tumours of the breast. Prospective studies involving larger, multicentre comparative cohorts of patients may provide more information on treatment approaches, survival and how to improve clinical practice.

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Clinical Characteristics and Medium-Term Outcomes of Patients Exposed to a Wildland-Urban Interface Fire: A Retrospective Cohort Study from İzmir, Türkiye

Wildland-Kentsel Ara Yüz Yangınına Maruz Kalan Hastaların Klinik Özellikleri ve Orta Vadeli Sonuçları: İzmir, Türkiye'den Retrospektif Bir Kohort Çalışması

İbrahim KORKMAZ* 0000-0001-6874-5277
Özge EREN KORKMAZ 0000-0002-9476-4938**
Duygu Gizem YILDIRIM* 0009-0001-0549-0382
Naz EREN* 0009-0001-4156-5388
Safiye Dilan TAHTASIZ* 0009-0005-9106-9218
Fatmana SARAÇ* 0009-0006-5440-9778

* İzmir Şehir Hastanesi, Acil Tıp Kliniği, İzmir
**İzmir Dokuz Eylül Üniversitesi Tıp Fakültesi, Epidemiyoloji Bilim Dalı, İzmir

Yazışma Adresi: İbrahim KORKMAZ
İzmir Şehir Hastanesi, Acil Tıp Kliniği, İzmir
E-mail adresi: abrahamkorkmaz11@gmail.com

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Abstract

Objective: In 2024, we aimed to evaluate the clinical and laboratory characteristics of individuals admitted to the emergency department during the forest fire that occurred in Izmir Yamanlar region and to determine the risk factors associated with hospital readmission during the 6-month follow-up period. We also aimed to reveal the prevalence of short- and medium-term health effects in individuals exposed to fire and biomarkers that can be used to predict these effects.

Methods: This single-center, retrospective cohort study included 98 patients who presented with fire-related symptoms between August 13-18, 2024. Demographic and clinical data and laboratory results were obtained retrospectively from hospital records and the national health system.

Results: The median age of the patients was 33.0 years and 66.3% were male. The most common reasons for presentation were dyspnea (37.8%), trauma (25.5%), nausea (14.3%), headache (13.3%) and conjunctival hyperemia (13.3%). Within six months, 19.4% were readmitted to the hospital. Multivariate analysis identified advanced age (Adjusted OR (AOR): 1.04; p = 0.023) and low pH levels at admission (AOR: 0.09; p = 0.029) as independent predictors of hospital readmission. Respiratory reasons (dyspnea 26.4%, cough 15.8%) accounted for 72.7% of readmissions. No significant correlation was found between pH, lactate, COHb, HCO3 and troponin levels and the duration of readmission (p > 0.05).

Conclusion: Exposure to fire smoke causes medium-term health problems, especially in elderly individuals and those presenting with low pH. These findings emphasize the importance of early detection and regular follow-up of at-risk groups.

Keywords: Emergency Service, Hospital ; Environmental Exposure; Wildfires

Öz

Amaç: 2024 yılında İzmir Yamanlar bölgesinde meydana gelen orman yangını sırasında acil servise başvuran bireylerin klinik ve laboratuvar özelliklerini değerlendirmek ve 6 aylık izlem sürecinde hastaneye tekrar başvuru ile ilişkili risk faktörlerini belirlemek amaçladık. Ayrıca, yangına maruz kalan bireylerde kısa ve orta vadeli sağlık etkilerinin yaygınlığını ve bu etkileri öngörmede kullanılabilecek biyobelirteçleri ortaya koymayı hedefledik.

Yöntem: Tek merkezli, retrospektif kohort tasarımında yürütülen bu çalışmaya, 13–18 Ağustos 2024 tarihleri arasında yangına bağlı semptomlarla başvuran 98 hasta dahil edildi. Demografik ve klinik veriler ile laboratuvar sonuçları hastane kayıtları ve ulusal sağlık sisteminden retrospektif olarak elde edildi.

Bulgular: Hastaların median yaşı 33,0 yıldı ve %66,3'ü erkekti. En sık başvuru nedenleri dispne (%37,8), travma (%25,5), mide bulantısı (%14,3), baş ağrısı (%13,3) ve konjonktival hiperemi (%13,3) idi. Altı ay içinde, %19,4'ü hastaneye tekrar başvurdu. Çok değişkenli analizde ileri yaş (Düzeltilmiş OR (AOR): 1.04; p = 0.023) ve başvuru sırasındaki düşük pH seviyeleri (AOR: 0.09; p = 0.029) hastaneye tekrar başvurunun bağımsız belirleyicileri olarak tanımlandı. Solunumsal nedenler (dispne %26,4, öksürük %15,8) tekrar başvuruların %72,7'sini oluşturdu. pH, laktat, COHb, HCO3 ve troponin düzeyleri ile tekrar başvuru süresi arasında anlamlı bir ilişki bulunmadı (p > 0.05).

Sonuç: Yangın dumanına maruz kalmak, özellikle yaşlı bireylerde ve düşük pH ile başvuranlarda orta vadeli sağlık sorunlarına yol açmaktadır. Bu bulgular, riskli grupların erken tespiti ve düzenli takibinin önemini vurgulamaktadır.

Anahtar Kelimeler: Acil Servis; Çevresel Maruziyet; Orman Yangınları

Introduction

Forest fires are one of the major disasters that threaten public health and are becoming more frequent worldwide due to global climate change and increasing urbanization. Turkey, which is located in the Mediterranean basin, is at high risk of forest fires due to its geographical and climatic characteristics. In recent years, especially in the summer months, fires affecting large areas in various regions of our country have been occurring and causing economic and ecological losses. According to the records of the General Directorate of Forestry for the last ten years between 2014 and 2023, records show that approximately 2,569 forest fires occur on average every year and approximately 23,229 hectares of forest area are burned in these fires (1).

The smoke released during forest fires contains many harmful substances such as carbon monoxide, nitrogen oxides, sulphur dioxide, particulate matter (PM10, PM2.5) and volatile organic compounds. These toxic substances can cause acute and chronic effects, especially on the respiratory and cardiovascular systems. In the literature, an increase in asthma, COPD exacerbations, pneumonia, and other respiratory infections after fire exposure has been reported (2). In addition, cardiovascular events, eye irritation, headache, and psychological stress are among the common health problems (3-5).

It has been shown that there is a 9% increase in emergency room visits and a 4% increase in the risk of hospitalization following exposure to fire smoke (6).

A Brazilian study showed that wildfire waves were associated with a 23% increase in hospitalizations for respiratory diseases and a 21% increase in hospitalizations for cardiovascular diseases (7). The increase in these two hospital-based indicators suggests significant health risks associated with exposure to fire smoke. The most common causes of ED admission after exposure are asthma, exacerbation of chronic obstructive pulmonary disease, pneumonia, acute bronchitis, cardiopulmonary symptoms, and heart failure (8). It has also been reported that there is an increase in emergency department (ED) visits due to headaches and migraines even after short-term forest fires (9).

Between August 13 and 18, 2024, a total area of 4,300 hectares was burned in the forest fire that occurred in the Yamanlar region of Izmir. The fire spread beyond the forest area and affected the residential areas in the region, and many people sought medical attention with complaints related to smoke exposure. The aim of this study was to determine the demographic and clinical characteristics of the patients admitted to our hospital during the fire, to analyze their laboratory parameters, and to evaluate their readmission status in a 6-month period. Our study will contribute to a better understanding of the short- and medium-term health outcomes of patients exposed to forest fires and shed light on future disaster management planning.

Material and Methods

Study Design and Scope

In this single-center retrospective cohort study, we evaluated the clinical characteristics of patients admitted to the ED of a tertiary care hospital during the forest fire that occurred between August 13-18, 2024, in the Yamanlar region of Izmir, and their readmission to the hospital within 6 months. The study protocol was approved by the ethics committee (Decision no: 2025/135 Date: 19.03.25). Informed consent was not obtained as patients were not involved in the design, recruitment, or conduct of the study.

Since there is no direct data in the literature on the frequency of readmission to hospital within 6 months in individuals exposed to forest fire, studies examining similar environmental exposures were used for sample size calculation. In a systematic review by Reid et al. it was reported that the effects of exposure to forest fire smoke on respiratory diseases were consistent and the effect sizes were moderate (2). Therefore, the assumption of medium effect size (Cohen's d = 0.3) was adopted in our study. With this assumption, a total of 88 individuals were aimed to be reached in the calculation using G-Power 3.1 for 80% statistical power and 5% significance level. In our study, the targeted sample size was exceeded by reaching 98 patients.

Participants and Data Collection

Patients who were admitted to the hospital with symptoms related to exposure to forest fires between August 13-18, 2024. Patients whose medical records were incomplete and whose 6-month follow-up data could be accessed were included in the study. Patients admitted for non-fire-related reasons, pregnant patients, pediatric patients, and patients whose data could not be accessed during the follow-up period were excluded from the study.

Re-admission with fire-related complaints was defined as patients re-admitted to hospital with symptoms (such as dyspnea, cough, eye irritation, headache, chest pain, sore throat, skin irritation) attributable to wildfire exposure within 6 months of initial presentation. Whether these complaints were fire-related was determined by the clinician evaluating the patient, taking into account the patient's medical history, the time of onset of symptoms and the results of clinical assessment, and recorded in the patient file. To ensure standardization, patient records were reviewed by two independent investigators during the retrospective evaluation and a third investigator was consulted in doubtful cases.

Demographic information, complaints at admission, vital signs, laboratory values (pH, lactate, carboxyhemoglobin levels, bicarbonate, troponin), hospitalization status and duration, and reasons for readmission were obtained retrospectively from patient files, hospital automation system, and e-Nabız system, which is a centralized system for recording health data in Turkey. The readmissions of all patients to the hospital within a six-month period after their initial admission were evaluated. Patients with ongoing complaints due to fire exposure who were readmitted to the hospital for this reason were identified and the timing of admission, reasons for admission, departments consulted, and clinical outcomes were recorded. Both initial and repeat admission times were calculated in days.

Statistical analysis

Data were analyzed using R software (version 2024.12.0+467). Median [IQR] or mean ± standard deviation (SD) were used for descriptive statistics, and categorical variables were expressed as number (n) and percentage (%). Compliance with normal distribution was evaluated by the Shapiro-Wilk test; the Mann-Whitney U test was used for data that did not fit the normal distribution; and the Chi-square or Fisher's exact test was applied for categorical variables.

Multivariate logistic regression analysis was performed with the "ENTER" method using the independent variables found to be statistically significant. The fit of the model was assessed by Likelihood test, multicollinearity was examined by Variance Inflation Factor (VIF) test and variables with values < 5 were included in the model.

Univariate survival analyses were performed using the Cox regression model ("survival", "survminer" packages) to examine potential influencing factors on hospital readmission time. In this analysis, the effect of each independent variable on event duration (time to readmission) was assessed separately. The limit of statistical significance was set at $p < 0.05$.

Results

A total of 98 patients were included in the study. The median age of the patients was 33.0 years (IQR 18.0), and 66.3% were male. Smoking was present in 45.9% of the patients. The most common presenting symptoms were dyspnea (37.8%), trauma (25.5%), nausea (14.3%), headache (13.3%), and conjunctival hyperemia (13.3%). In laboratory results, the median pH value was 7.39 [IQR: 0.50], lactate was 1.30 [IQR: 0.80], COHb was 1.60 [IQR: 1.80], HCO3 was 25.8 [IQR: 3.9], and troponin was 6.00 [IQR: 5.90] (Table 1).

While 99.0% of the patients were discharged, 1.02% were hospitalized in the intensive care unit. During the 6-month follow-up period, 19.42% of patients were readmitted to the hospital. Reasons for readmission included check-up (31.5%), dyspnea (26.4%), cough (15.8%), headache (10.5%), and dry eye (10.5%). 11.2% Of patients presented repeatedly, but further context is needed to clarify in what manner or frequency this occurred. The median time to first presentation was 20.0 (IQR: 57.0) days and the median time to second presentation was 44.5 (IQR: 55.8) days (Table 2).The most preferred clinical units were pulmonology (36.8%), orthopedics (21.1%), ED (15.8%), and neurology (10.5%) (Table 1).

Table 1: Baseline characteristics and clinical features of patients

Parameters	median [IQR] n(%)
Age	33.0 [18.0]
Gender	
Male	65 (66.3%)
Female	33 (33.7%)
Current smokers	45 (45.9%)
Presenting complaints	
Dry cough	11 (11.2%)
Productive cough	3 (3.06%)
Conjunctival hyperemia	13 (13.3%)
Sore throat	5 (5.10%)
Headache	13 (13.3%)
Dyspnea	37 (37.8%)
Nausea	14 (14.3%)
Vomiting	11 (11.2%)
Anxiety	1 (1.02%)
Trauma	25 (25.5%)
Burn	1 (1.02%)
Fracture	5 (5.1%)
Laboratory findings:	
Heart Rate	80.0 [5.0]
Systolic blood pressure (SBP)	130 [5.0]
Diastolic blood pressure (DBP	80.0 [4.0]
Respiratory rate (RR), mean±SD	16.2 ± 1.34
pH	7.39 [0.50]
Lactate	1.30 [0.80]
Carboxyhemoglobin (COHb)	1.60 [1.80]
Bicarbonate (HCO3)	25.8 [3.9]
Troponin	6.00 [5.90]
Hospitalization status:	
Discharged	97 (99.0%)
ICU admission	1 (1.02%)
Revisit	19 (19.4%)
Reasons for revisit (n=19):	
Follow-up examination	6 (31.5%)
Headache	2 (10.5%)
Dyspnea	5 (26.4%)
Dry eyes	2 (10.5%)
Cough	3 (15.8%)
Syncope	1 (5.3%)
Repeated visits:	11 (11.2%)
First admission duration (days):	20.0 [57.0]
Second admission duration (days):	44.5 [55.8]
Admission department:	
Emergency Department	3 (15.8%)
Pulmonology	7 (36.8%)
Ophthalmology	2 (10.5%)
Neurology	2 (10.5%)
Orthopedics	4 (21.1%)
Burn unit	1 (5.26%)
SD: Standart deviation	

The median age of patients readmitted to the hospital within 6 months was significantly higher (40.0 [IQR: 19.0] vs. 31.0 [IQR: 17.0], p = 0.006). There was no statistically significant difference between the groups in terms of gender, smoking, and most clinical symptoms. However, readmitted patients had a significantly lower initial pH value (7.36 [IQR: 0.03] vs. 7.40 [IQR: 0.05], p = 0.008). In multivariate logistic regression analysis, older age and low pH levels at admission were found to be independent predictors of readmission within six months.

Each one-year increase in age increased the probability of hospital readmission by 4% (AOR: 1.04; 95% CI: 1.00-1.08; p = 0.023). Furthermore, each 0.1 unit decrease in pH level increased the risk of readmission by approximately 91% (AOR: 0.09; 95% CI: 0.00-0.61; p = 0.029) (Table 2).

Table 2: Comparison of Baseline Characteristics and Factors Associated with 6-Month

	Revisit Patient	**None**			
	N=19	***N=79***			
	N(%) / median [IQR]	**N(%) / median [IQR]**	**p**	**Adjusted OR (95% CI)**	**p**
Age, year	40.0 [19.00]	31.0 [17.00]	**0.006**	1.04 (1.00-1.08)	**0.023**
Gender			0.551		
Male	11 (16.9%)	54 (83.1%)			
Female	8 (24.2%)	25 (75.8%)			
Smoking status	11 (24.4%)	34 (75.6%)	0.363		
Dry cough	2 (18.2%)	9 (81.8%)	1.000		
Productive cough	2 (66.7%)	1 (33.3%)	0.095		
Conjunctival hyperemia	3 (23.1%)	10 (76.9%)	0.712		
Sore throat	0 (0.00%)	5 (100%)	0.580		
Headache	4 (30.8%)	9 (69.2%)	0.272		
Dyspnea	9 (24.3%)	28 (75.7%)	0.484		
Nausea	2 (14.3%)	12 (85.7%)	1.000		
Vomiting	1 (9.09%)	10 (90.9%)	0.686		
Anxiety	0 (0.00%)	1 (100%)	1.000		
Trauma	7 (28.0%)	18 (72.0%)	0.245		
Heart rate (HR)	80.0 [0.0]	80.0 [5.80]	0.873		
Diastolic blood pressure (DBP)	80.0 [0.0]	80.0 [5.00]	1.000		
Respiratory rate (RR), mean $\pm$ $\boldsymbol{SD}$	16.4 $\pm$ 1.67	16.0 $\pm$ 1.20	0.657		
pH*	7.36 [0.03]	7.40 [0.05]	**0.008**	0.09 (0.00-0.61)	**0.029**
Lactate	1.70 [1.15]	1.30 [0.68]	0.575		
Carboxyhemoglobin (COHb)	1.60 [1.10]	1.60 [2.20]	0.603		
Bicarbonate (HCO3)	25.3 [4.10]	26.0 [3.90]	0.251		
Troponin	4.70 [1.70]	8.50 [5.60]	0.245		

*pH (per 0.1 unit), OR:Odds Ratio, CI: Confidence Interval, SD: Standart Deviation
Nagelkerke R^2: 0.50, Likelihood Ratio Test p<0.001

According to the results of univariate Cox regression analysis, no statistically significant correlation was found between the duration of readmission and age, pH, lactate, carboxyhemoglobin (COHb), bicarbonate (HCO3) and troponin levels (p > 0.05). HR: 0.98 (95% CI: 0.94-1.02) was found for the age variable and it was observed that age had no significant effect on the time to readmission.

Similarly, pH (HR: 0.91; 95% CI: 0.24-3.48; p = 0.901), lactate (HR: 1.05; 95% CI: 0.69-1.59; p = 0.818), COHb (HR: 1.24; 95% CI: 0.69-2.23; p = 0.467), HCO3 (HR: 1. 01; 95% CI: 0.93-1.10; p = 0.750) and troponin (HR: 0.99; 95% CI: 0.92-1.08; p = 0.948) levels did not significantly affect readmission time (Table 3).

Table 3: Univariate Cox Regression Analysis of Risk Factors Associated with Length of Hospital Readmission

Variables	HR (exp(coef))	95% CI	p
Age	0.98	0.94 – 1.02	0.322
pH*	0.91	0.24 – 3.48	0.901
Lactate	1.05	0.69 – 1.59	0.818
Carboxyhemoglobin (COHb)	1.24	0.69 – 2.23	0.467
Bicarbonate (HCO3)	1.01	0.93 – 1.10	0.750
Troponin	0.99	0.92 – 1.08	0.948
HR: Hazard Ratio, Cl: Confidence Interval, *pH (per 0.1 unit)			

Discussion

This retrospective cohort study evaluated the clinical characteristics and 6-month follow-up outcomes of patients admitted to the ED of a tertiary hospital during the forest fire in the Yamanlar region of Izmir. The most important finding of our study was that 19.4% of the patients were readmitted to the hospital with complaints related to fire exposure during the 6-month period, and these patients had significantly higher mean age and lower baseline pH values. These findings demonstrate that wildfires have not only acute but also medium-term health effects and highlight the importance of developing strategies for early identification and follow-up of individuals at risk.

Respiratory symptoms are the leading health effects on fire. In our study, the most common presenting complaint was shortness of breath. In the literature, it has been reported that respiratory complaints are the most common reason for admission after forest fire exposure (6,10-12). Wah et al. emphasized that inflammatory processes developing after fire exposure may cause irritation and airway reactivity, especially in the respiratory tract, and may increase asthma and COPD exacerbations (13). The majority of the readmissions in our study were due to respiratory complaints (dyspnea, cough), confirming the clinical reflection of this pathophysiologic process.

It has been shown in many studies that exposure to fire smoke causes an increase in hospital admission rates. Liu et al. reported that health effects after exposure to wildfire smoke may not be limited to the acute period, and respiratory symptoms, espically, may last for weeks (14). Wah et al. reported that respiratory symptoms due to fire exposure persisted for a long time, and new asthma diagnoses were even made in some cases (13). In our study, the rate of readmission within 6 months was found to be 19.4%, which is consistent with the data in the literature and demonstrates the importance of medium-term effects, especially in communities directly exposed to fire.

In our study, the mean age of the individuals who were re-admitted to the hospital was significantly higher among those exposed to fire, revealing that elderly individuals are more vulnerable to the health effects of forest fires. In the literature, it has been stated that this situation is related to multidimensional physiopathological and environmental reasons. Liu et al. (2017) and Chen et al. (2021) reported that the effects of fire smoke may be more pronounced in elderly individuals due to decreased respiratory reserve, susceptibility to inflammation and low physiological tolerance to toxic gases such as carbon monoxide (15,16). Requia et al. (2021) showed that elderly individuals had a higher rate of post-fire health service application because they usually have more comorbidities (7). However, Sorensen et al. (2021) emphasised that fire-related symptoms in the elderly may not be evident in the acute period, but the tendency to present with longer-lasting or recurrent complaints increases in the following weeks (17). Our study suggests that the reasons for readmission, which were mostly based on subacute respiratory or general symptoms (dyspnoea, cough, headache, dry eyes) rather than cardiovascular symptoms, indicate that physiological frailty and health-seeking behaviour, which increase with age, contribute to this clinical picture. In our study, the increased likelihood of readmission to the hospital in individuals with low initial pH levels suggests that systemic metabolic disturbances are more prominent in these patients after exposure to fire smoke. In the literature, it has been reported that fire-related PM2.5 and CO exposure disrupts mitochondrial functions and increases reactive oxygen species (ROS), resulting in tissue hypoxia and metabolic acidosis (2,6,7,13,16,18,19). This acidosis may contribute to cellular dysfunction and long-term clinical symptoms, especially in vulnerable individuals. Therefore, assessment of acid-base status at initial presentation after fire exposure may be important in predicting both short- and medium-term health outcomes.

In a study conducted in patients with heart failure in North Carolina, it was reported that moderate-severe or intense smoke exposure increased 7- and 30-day hospital readmission rates, but no significant individual factor associated with readmission time was found (20). This finding is in parallel with the fact that no significant relationship was found between the duration of readmission and parameters such as age, carboxyhemoglobin, troponin and bicarbonate levels in our study. This suggests that post-fire health effects may develop as a result of a multifactorial and complex interaction rather than individual factors.

In our study, headache was one of the most prominent symptoms in both the first admissions and re-admissions, and ocular complaints such as conjunctival hyperemia and dry eye were also significantly observed.

Elser et al. reported that short-term exposure to fire smoke caused a significant increase in tension-type and other primary headaches (9). Headache is thought to develop as a result of hypoxia due to carbon monoxide exposure and central nervous system inflammation triggered by particles in fire smoke (11). In the literature, it has been shown that emergency admissions with eye irritation, dryness, and conjunctivitis-like symptoms increase during wildfire periods (4). Schwarz et al. emphasized that wildfire-induced particulate matter may not only have physical but also neurotoxic effects and cause long-term effects on the eye and nervous system (21). In light of this information, it is thought that the headache and ocular complaints found in our study may be both direct effects of acute exposure and clinical reflections of the ongoing inflammatory process after the fire.

In the literature, some studies have reported increased cardiac effects due to fire (7,22,23), while others have not shown this relationship (2,3,15,24). Cardiovascular effects of fire smoke are not as consistent and predictable as respiratory effects. In our study, no significant elevation in troponin levels was found, and one of the possible reasons for this is that our patients presented to the emergency department with more acute symptoms and in the early post-exposure period. It is thought that cardiac biochemical changes were not yet clinically evident during this early presentation and sufficient time may not have elapsed for biomarkers such as troponin to be elevated. Moreover, the presence of fire-induced cardiovascular effects is influenced by many factors such as patient profile, exposure duration, individual physiological differences and follow-up period. In this context, in order to evaluate the cardiovascular effects after fire more accurately, repeated measurements should be performed by considering the dynamic change of biomarkers and longer duration of follow-up.

Finally, the fact that the Izmir fire also affected residential areas classified this event as a “wildland-urban interface” (WUI) fire. It has been emphasized that such fires may contain more toxic components, have higher particulate matter density, and therefore their effects on public health may be more pronounced (13). The high rate of ED admissions, multisystem symptoms, and a significant rate of re-admissions in the 6-month follow-up found in our study show that WUI fires may cause not only short-term but also medium-term health consequences, and these effects cannot be ignored in the population living in urban areas.

This study has some limitations. Its generalizability is limited due to its single-center and retrospective design. Another important limitation is that the level and duration of exposure to fire smoke at the individual level could not be measured. Exposure levels may differ between patients and this makes it difficult to evaluate the dose-response relationship. Factors such as proximity to the fire zone, duration of time indoors/outdoors, personal protective measures and ventilation conditions may affect the individual exposure level.

In future studies, it is recommended that more sensitive exposure assessments be made using data from air quality monitoring stations, personal exposure measurement devices and detailed questionnaires. Nevertheless, the 6-month follow-up period and detailed examination of the reasons for readmission make an important contribution to the literature.

Conclusion

Our study demonstrates the importance of both acute and medium-term health effects in individuals exposed to forest fires. It has been observed that biomarkers such as low pH at the time of admission may be helpful in predicting the risk of re-admission. Advanced age has been identified as a significant risk factor for fire smoke-related health problems. These findings may contribute to the development of strategies for early identification of individuals at risk after fires, close monitoring, and appropriate protective measures. In addition, considering the increasing frequency of WUI fires, early warning systems should be strengthened to protect the population living in urban areas. Special protection protocols for vulnerable populations (elderly, children, those with chronic diseases) should be developed, expansion of air quality monitoring networks should be implemented, capacity building of emergency health services should be prioritized, and public health policies such as community education should be developed. In addition, regular training of healthcare workers on triage, diagnosis and treatment protocols specific to fire situations and the establishment of equipment and preparedness plans for effective response in field conditions are also critical.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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Can Alexithymia and Metacognitions be Predictors of Treatment Approaches in Panic Disorder Patients?

Panik Bozukluğu Hastalarında Aleksitimi ve Üstbilişler Tedavi Yaklaşımlarının Yordayıcıları Olabilir mi?

Nazan DOLAPOĞLU *0000-0003-1400-7580
Tülay Satı KIRKAN ** 0000-0003-1102-0560

*Department of Psychiatry, Balikesir University Faculty of Medicine, Balikesir, Turkey.
** Department of Psychiatry, Bandırma Onyedi Eylül Faculty of Medicine, Balikesir, Turkey.

Corresponding Author: Nazan DOLAPOĞLU
Department of Psychiatry, Balikesir University Faculty of Medicine, Balikesir, Turkey.
Email: nazandolapoglu@yahoo.com

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Abstract

Objectives: Alexithymia is characterized by difficulties in identifying and expressing emotions. Within the context of panic disorder, research suggests that individuals with alexithymia may be more susceptible to heightened anxiety and impaired emotional regulation. Metacognition, defined as the capacity to monitor and control one's own cognitive processes, plays a crucial role in emotional and psychological functioning. The present study aims to examine the differences in metacognitive beliefs between panic disorder patients with and without alexithymia and to investigate the predictive role of these beliefs in individuals with alexithymia.

Materials and Methods: This cross-sectional study included 61 individuals aged between 18 and 65 who were diagnosed with panic disorder. Participants were assessed using the Toronto Alexithymia Scale (TAS-20), the Metacognitions Questionnaire (MCQ-30), and the Panic and Agoraphobia Scale (PAS). A TAS-20 score of 61 or above was used as the cut-off point to identify the presence of alexithymia.

Results: A total of 61 patients were included in the study, comprising 14 men (23%) and 47 women (77%). Participants ranged in age from 18 to 65, with a median age of 40 years. Among the participants, 47.5% (n=29) of those with panic disorder were identified as having alexithymia. Statistical analyses revealed that, with the exception of the Panic Attack (PA), Cognitive Self-Consciousness (CS), and Externally Oriented Thinking (EOT) subscale scores, all other scale scores were significantly higher in panic disorder patients with alexithymia ($p < 0.05$).

Conclusion: These findings indicate that a more comprehensive understanding of metacognitive theory, along with the implementation of metacognitive therapy, may provide significant therapeutic benefits for patients with panic disorder who also exhibit alexithymia.

Keywords: Panic disorder; alexithymia; metacognition

Öz

Amaç: Aleksitimi, duyguları tanımlama ve ifade etmede yaşanan zorluklarla karakterizedir. Panik bozukluk bağlamında, araştırmalar aleksitimik bireylerin artan kaygıya ve bozulmuş duygusal düzenlemeye daha yatkın olabileceğini düşündürmektedir. Kişinin kendi bilişsel süreçlerini izleme ve kontrol etme kapasitesi olarak tanımlanan üstbiliş, duygusal ve psikolojik işleyişte önemli bir rol oynamaktadır. Bu çalışmanın amacı, aleksitimisi olan ve olmayan panik bozukluk hastaları arasındaki üstbilişsel inanç farklılıklarını incelemek ve aleksitimisi olan bireylerde bu inançların yordayıcı rolünü araştırmaktır.

Gereç ve Yöntemler: Bu kesitsel çalışmaya yaşları 18 ile 65 arasında değişen ve panik bozukluğu tanısı almış 61 hasta katılmıştır. Katılımcılar Toronto Aleksitimi Ölçeği (TAS-20), Üstbilişler Anketi (MCQ-30) ve Panik ve Agorafobi Ölçeği (PAS) kullanılarak değerlendirilmiştir. TAS-20 skorunun 61 veya üzerinde olması aleksitimi varlığını belirlemek için kesme noktası olarak kullanılmıştır.

Bulgular: Çalışmaya 14 erkek (%23) ve 47 kadın (%77) olmak üzere toplam 61 hasta dahil edilmiştir. Katılımcıların yaşları 18 ile 65 arasında değişmekte olup ortanca yaş 40'tır. Katılımcılar arasında panik bozukluğu olanların %47,5'inde (n=29) aleksitimi olduğu tespit edilmiştir. İstatistiksel analizler, Panik Atak (PA), Bilişsel Özbilinç (CS) ve Dışa Yönelik Düşünme (EOT) alt ölçek puanları hariç, diğer tüm ölçek puanlarının aleksitimisi olan panik bozukluğu hastalarında anlamlı derecede yüksek olduğunu ortaya koymuştur ($p < 0.05$).

Sonuç: Bu bulgular, üstbiliş kuramının daha derinlemesine anlaşılmasının ve üstbilişsel terapinin uygulanmasının, aleksitimisi olan panik bozukluğu hastalarının tedavisinde önemli terapötik faydalar sağlayabileceğini göstermektedir.

Anahtar Kelimeler: Panik bozukluk; aleksitimi; üstbiliş

Introduction

Panic disorder (PD) is characterized by recurrent and unexpected panic attacks, accompanied by persistent concern about future attacks and their potential consequences (1). Panic disorder (PD) is associated with considerable personal distress, occupational impairment, and excessive utilization of medical services (2). Various theoretical models propose that PD arises from an interplay of biological, psychological, and environmental vulnerabilities, with particular emphasis on cognitive factors (3). However, current treatment approaches are not universally effective; relapse and the persistence of symptoms remain common challenges. Cognitive models, in particular, highlight the central role of maladaptive thought patterns and beliefs in the development and maintenance of PD (4).

It has been observed that cognitive factors alone are not sufficient to distinguish PD from other anxiety disorders (5). As a result, it is crucial for clinicians to consider additional therapeutic frameworks, such as Metacognitive Therapy (MCT) alongside Cognitive Behavioral Therapy (CBT), in the conceptualization and treatment of PD. Research indicates that both CBT and MCT yield long-term benefits for individuals with anxiety disorders. Notably, MCT may demonstrate greater effectiveness over time, potentially resulting in more stable and enduring improvements. Nonetheless, further research involving larger sample sizes is necessary to validate these findings (6).

The construct of alexithymia encompasses a cluster of symptoms, including difficulties in identifying and articulating subjective emotional experiences, a restricted imaginative capacity, and a marked focus on external events at the expense of internal mental processes (7).

Initially identified in psychosomatic patients, the concept of alexithymia has since evolved and extended beyond the psychosomatic context (8). Over the past five decades, researchers and clinicians have actively debated its conceptual nature—questioning whether alexithymia is unique to certain patient populations, whether it serves as a precursor to symptom development or constitutes a symptom itself, and whether it should be understood as primary or secondary, innate or acquired, a transient state or enduring trait, a defense mechanism, or a structural deficit (9). Alexithymia, as a distinct personality trait, is now understood to involve disruptions in cognitive-emotional processing and affect regulation (10). While the precise definition of alexithymia aligns more closely with a form of anomia than agnosia, for many clinicians and researchers, particularly those influenced by the work of Sifneos and Nemiah, it represents a multifaceted construct that goes beyond mere difficulty in verbalizing emotional states. Rather, it refers to the use of words that lack emotional significance. Alexithymia is also viewed as a significant defense mechanism against uncomfortable emotions, as well as a limitation in the capacity for emotional mental representation (11). Although alexithymia is not formally recognized as a clinical diagnosis in the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD), it is estimated to affect approximately 10% of the general population (12).

Metacognition encompasses a broad array of cognitive functions, including the ability to reflect on one's own thinking, recognize emotions, thoughts, and goals, and integrate these elements into coherent representations. As a result, individuals with well-developed metacognitive skills are able to address psychological and social challenges with greater efficiency and accuracy (13). An expanding body of literature suggests that metacognitive models play a significant role in understanding psychological vulnerability (14).

One of the most influential metacognitive models is the Self-Regulatory Executive Function (S-REF) model (15). This model was developed to address generalized anxiety disorder (GAD), panic disorder (PD), obsessive-compulsive disorder (OCD), and social anxiety disorder (SAD) (16). The S-REF model outlines the concept of cognitive-attentional syndrome (CAS), which includes the activation of dysfunctional beliefs, increased self-focused attention, threat monitoring, and ruminative processing (15).

To date, five key areas of metacognitive beliefs have been extensively explored in studies of mental disorders: (1) positive metacognitive views about worry; (2) negative beliefs about uncontrollability and risk; (3) positive beliefs about anxiety; (4) beliefs regarding the necessity of exerting control over one's thoughts; and (5) cognitive self-assurance and self-consciousness (17). According to the S-REF model, negative metacognitive beliefs play a crucial role in maintaining the cognitive-attentional syndrome (CAS). This connection, which involves the loss of mental control due to the misinterpretation of threatening mental events, has a significantly detrimental impact on mental well-being (18).

Grounded in the perspective that cognitive factors alone are insufficient to distinguish PD from other anxiety disorders, the present study aimed to examine differences in metacognitive beliefs between individuals with PD with and without alexithymia and to explore the extent to which these beliefs predict alexithymic traits among those who exhibit such characteristics.

Materials and Methods

Subjects and Study Design

Our target population consisted of outpatients diagnosed with PD. A sequential sampling method was employed by enrolling patients in the order they arrived for mental evaluation. Inclusion criteria were: ages 18 to 65, both genders, and the ability to complete the surveys independently. Exclusion criteria included the presence of additional somatic or mental health conditions. As a result, the study sample comprised 61 patients diagnosed with PD. A qualified psychiatrist, during a clinical interview, diagnosed the patients according to the ICD-10 criteria, which was further validated using the Panic Disorder Severity Scale (PDSS) for PD patients. The same psychiatrist administered the PDSS. Both the clinical interview and a self-report questionnaire developed specifically for this study were used to screen participants for exclusion criteria, including comorbidities. Prior to enrollment, a power analysis was conducted. Expected TAS-20 values were drawn from the study by Cucchi et al. (19), with the significance level set at $p < 0.05$, the required power at 80%, and the minimal detectable difference set to match the findings of the referenced study. The TAS-20 scale required the largest sample size, n = 60.

The participants were assessed using the Toronto Alexithymia Scale (TAS-20), the Metacognition Questionnaire (MCQ-30), and the Panic and Agoraphobia Scale (PAS). This cross-sectional study was conducted at the Faculty of Medicine, Bandırma Onyedi Eylül University. Ethical approval for this study was obtained from the Bandırma Onyedi Eylül University Health Sciences Non-Interventional Research Ethics Committee on 14.03.2023 under decision number 2023/45. Written informed consent was obtained from each participant, and their identities were kept confidential through the use of a coding system. Completed questionnaires and signed informed consent forms were stored separately. The study's goals and purpose were explained to participants in the informed consent form. The research adhered to the principles set forth in the 2013 Declaration of Helsinki by the World Medical Association (20).

Measures

Panic and Agoraphobia Scale (PAS)

The Panic and Agoraphobia Scale (PAS) is used to assess the severity of panic disorder in patients, considering factors such as panic attacks, disability, anticipatory anxiety, agoraphobic avoidance, and health concerns.

The scale evaluates the characteristics of panic attacks (PA), agoraphobic avoidance (AA), anticipatory anxiety (AA^2), disability (D), and health concerns (HC). The scale was originally developed by Bandelow (1999) (21). Turkish adaptation of the scale was conducted by Tural et al. (2000) and the Cronbach's alpha coefficients for the Turkish version were reported to range between 0.86 and 0.88. (22).

Metacognition Questionnaire (MCQ-30)

The Metacognition Questionnaire (MCQ), developed by Cartwright-Hatton and Wells, consists of five conceptually distinct but interrelated factors. These factors are: Positive Beliefs about Worry (PBAW), Cognitive Confidence (CC), Negative Beliefs about Uncontrollability and the Danger of Worry (NBAU), Cognitive Self-Consciousness (CS), and the Need to Control Thoughts (NCT) (23). The reliability of the Metacognition Questionnaire (MCQ) was supported by a Cronbach's alpha coefficient of 0.86, as reported in the Turkish adaptation by Tosun and Irak (2008) (24).

Toronto Alexithymia Scale (TAS-20)

The Toronto Alexithymia Scale (TAS-20) is a Likert-type self-report scale consisting of twenty items, scored on a range from 1 to 5, used to assess alexithymia, defined as the inability to identify one's own emotions. A score of 61 or higher on the TAS- 20 are considered to be within the alexithymia range (25). The scale includes three subscales: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally oriented thinking (EOT). Higher scores on the scale indicate higher levels of alexithymia (26). The Turkish adaptation, validity, and reliability of the TAS-20 were established by Güleç et al. (2009) and the Cronbach's alpha coefficient for the total TAS-20 scale was reported as 0.78. For the three subscales—Difficulty Identifying Feelings (DIF), Difficulty Describing Feelings (DDF), and Externally Oriented Thinking (EOT)—the coefficients were 0.80, 0.57, and 0.63, respectively (27).

Statistical Analyses

The data collected for the study were analyzed using the Statistical Package for the Social Sciences (SPSS) version 29.0 for macOS, developed by IBM Corp, Armonk, NY. Frequencies and percentages were reported for categorical data, while descriptive statistics such as median, minimum, and maximum values were provided for continuous data. The "Chi-Square or Fisher's Exact Test" was used to compare categorical variables, while the "Mann-Whitney U-Test" was employed for group comparisons. To assess the relationship between continuous variables, "Spearman's Correlation Analysis" was performed. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 61 patients, consisting of 14 men (23%) and 47 women (77%), were included in the study. The participants' ages ranged from 18 to 65, with a median age of 40. Of the panic disorder patients, 29 (47.5%) were diagnosed with alexithymia.

Table 1 presents the distribution of clinical and demographic characteristics based on the presence of alexithymia. Upon reviewing the table, it was found that there were no statistically significant differences between the groups in terms of demographic and clinical variables.

Table 1: Distribution of Demographic and Clinical Characteristics According to Toronto Alexithymia Scores

Variables	**Total (N=61)**	**Non-Alexithymic Patients (n=32)**	**Alexithymic Patients (n=29)**	**p-value**
	n (%) Median (Min-Max)	**n (%) Median (Min-Max)**	**n (%) Median (Min-Max)**	
Age (years)	40 (18-65)	40 (20-65)	38 (18-65)	0.925
Gender				0.481
Woman	47 (77)	23 (71.9)	24 (82.8)	
Male	14 (23)	9 (28.1)	5 (17.2)	
Marital Status				0.818
Single	23 (37.7)	13 (40.6)	10 (34.5)	
Married	38 (62.3)	19 (59.4)	19 (65.5)	
Educational Background				0.276
Primary Education	24 (39.3)	10 (31.3)	14 (48.3)	
High School	19 (31.1)	10 (31.3)	9 (31)	
University and Above	18 (29.5)	12 (37.5)	6 (20.7)	
Working Status				0.161
Not Working	42 (68.9)	19 (59.4)	23 (79.3)	
Working	19 (31.1)	13 (40.6)	6 (20.7)	
People Living with				0.118
With family	54 (88.5)	26 (81.3)	28 (96.6)	
With friend(s)	3 (4.9)	2 (6.3)	1 (3.4)	
Alone	4 (6.6)	4 (12.5)	0 (0)	
Physical Illness				1.000
Yes	24 (39.3)	13 (40.6)	11 (37.9)	
No	37 (60.7)	19 (59.4)	18 (62.1)	
Known Physical Illness	24 (39.3)	13 (40.6)	11 (37.9)	1.000
Cardiac	6 (25)	4 (30.8)	2 (18.2)	
Respiratory	4 (16.7)	2 (15.4)	2 (18.2)	
Others	14 (58.3)	7 (53.8)	7 (63.6)	
Diagnosis of Panic Disorder in a First-Degree Relative	18 (29.5)	10 (31.3)	8 (27.6)	0.974

Table 2 presents the distribution of scale scores based on the presence of alexithymia in patients. Upon reviewing the table, a statistically significant difference was observed between the groups in all scale scores, except for the Panic Attack (PA), Cognitive Self-Consciousness (CS), and Externally Oriented Thinking (EOT) scores ($p<0.05$). Patients with alexithymia exhibited higher scale scores compared to those without alexithymia.

Table 2: Distribution of Metacognition Questionnaire (MCQ-30), Panic and Agoraphobia Scale (PAS) Total and Subscale Scores According to Toronto Alexithymia Scores (TAS-20)

Total and Subscale Scores	**Total (N=61)**	**Non-Alexithymic Patients (n=32)**	**Alexithymic Patients (n=29)**	**p-value**
	n (%) Median (Min-Max)	**n (%) Median (Min-Max)**	**n (%) Median (Min-Max)**	
PA	7 (1-13)	7 (1-11)	8 (5-13)	0.055
AA	6 (0-11)	**3 (0-11)**	**7 (0-10)**	**0.036**
AA²	5 (0-8)	**5 (0-8)**	**6 (4-8)**	**0.005**
D	6 (0-11)	**5.5 (0-11)**	**7 (0-11)**	**0.002**
HC	4 (0-8)	**3 (0-8)**	**5 (0-8)**	**0.014**
PAS (Total)	30 (1-48)	**22 (1-48)**	**33 (18-47)**	**<0.001**
PBAW	11 (5-23)	**9.5 (6-19)**	**13 (5-23)**	**0.021**
NBAU	18 (9-24)	**15.5 (9-24)**	**20 (11-24)**	**<0.001**
CC	14 (7-24)	**13 (7-24)**	**16 (7-24)**	**<0.001**
NCT	14 (7-24)	**12.5 (7-22)**	**16 (10-24)**	**0.003**
CS	17 (8-23)	15 (10-23)	19 (8-23)	0.090
MCQ-30 (Total)	76 (50-112)	**69 (50-94)**	**85 (57-112)**	**<0.001**
DIF	23 (8-35)	**16.5 (8-29)**	**27 (21-35)**	**<0.001**
DDF	15 (6-25)	**14 (6-20)**	**18 (9-25)**	**<0.001**
EOT	23 (13-31)	22 (13-27)	23 (14-31)	0.067
TAS-20 (Total)	60 (35-83)	**49.5 (35-60)**	**69 (61-83)**	**<0.001**

PA: Panic Attacks, **AA:** Agoraphobic Avoidance, **AA²:** Anticipatory Anxiety, **D:** Disability, **HC:** Health Concerns, **PAS:** Panic and Agoraphobia Scale, **PBAW:** Positive Beliefs About Worry, **NBAU:** Negative Beliefs About Uncontrollability and Danger of Worry**, CC:** Cognitive Confidence, **NCT:** Need to Control Thoughts, **CS:** Cognitive Self-Consciousness. **MCQ-30:** Metacognition Questionnaire, **DIF:** Difficulty Identifying Feelings, **DDF:** Difficulty Describing Feelings, **EOT:** Externally Oriented Thinking, **TAS-20:**Toronto Alexithymia Scale

When examining the correlation between the scale scores of alexithymic panic disorder patients, a significant correlation was found between the total score of the Metacognition Questionnaire (MCQ-30) and the anticipatory anxiety (AA^2) subscale of the Panic and Agoraphobia Scale (PAS) (p = 0.003 and p = 0.028, respectively). Additionally, a significant correlation was observed between the total score of the Toronto Alexithymia Scale (TAS-20) and the negative beliefs about uncontrollability and the danger of worry (NBAU) subscale of the Metacognition Questionnaire (MCQ-30) (p = 0.001).

The total score of the Metacognition Questionnaire (MCQ-30) was found to have a significant correlation with difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and the total score of the Toronto Alexithymia Scale (TAS-20) (p = 0.001, p = 0.002, and p = 0.001, respectively). The relationship between the scale scores of alexithymic patients is presented in Table 3.

Table 3. Examination of the Relationship Between Scale Scores of Alexithymic Patients

		PA	AA	AA^2	D	HC	PAS (Total)	PBAW	NBAU	CC	NCT	CS	MCQ-30 (Total)	DIF	DDF	EOT	TAS-20 (Total)
PA	r	1.000	0.012	0.105	**0.368**	0.164	**0.488**	-0.045	0.289	0.106	0.136	0.225	0.153	0.310	0.141	-0.185	0.155
	p		0.953	0.589	**0.050**	0.395	**0.007**	0.818	0.129	0.585	0.483	0.240	0.428	0.102	0.467	0.336	0.422
AA	r		1.000	0.259	**0.410**	0.201	**0.569**	0.150	-0.117	0.296	0.098	0.053	0.169	0.145	0.213	-0.062	0.172
	p			0.174	**0.027**	0.295	**0.001**	0.437	0.547	0.119	0.614	0.784	0.380	0.454	0.267	0.748	0.372
AA^2	r			1.000	**0.509**	0.298	**0.627**	0.195	0.266	**0.444**	0.350	0.121	**0.527**	0.312	0.289	-0.142	0.319
	p				**0.005**	0.116	**0.000**	0.311	0.163	**0.016**	0.063	0.530	**0.003**	0.100	0.128	0.464	0.091
D	r				1.000	**0.530**	**0.860**	0.059	0.270	0.331	0.035	0.141	0.188	0.279	0.018	-0.003	0.160
	p					**0.003**	**0.000**	0.760	0.156	0.080	0.859	0.466	0.328	0.143	0.928	0.990	0.408
HC	r					1.000	**0.657**	0.136	0.149	0.231	0.252	0.002	0.228	0.302	0.193	-0.015	0.324
	p						**0.000**	0.483	0.441	0.228	0.188	0.993	0.235	0.111	0.316	0.937	0.086
PAS (Total)	r						1.000	0.144	0.285	**0.391**	0.311	0.175	**0.409**	**0.464**	0.235	-0.124	0.359
	p							0.457	0.134	**0.036**	0.101	0.363	**0.028**	**0.011**	0.219	0.520	0.056
PBAW	r							1.000	-0.335	-0.325	0.165	0.351	0.310	-0.186	-0.036	0.035	-0.226
	p								0.075	0.085	0.391	0.062	0.102	0.334	0.853	0.856	0.238
NBAU	r								1.000	0.336	**0.595**	0.068	**0.518**	**0.685**	0.277	-0.096	**0.567**
	p									0.075	**0.001**	0.727	**0.004**	**<0.001**	0.146	0.620	**0.001**
CC	r									1.000	0.148	-0.023	**0.428**	0.295	**0.447**	-0.172	**0.497**
	p										0.445	0.905	**0.021**	0.121	**0.015**	0.371	**0.006**
NCT	r										1.000	0.010	**0.709**	**0.492**	**0.641**	-0.132	**0.631**
	p											0.961	**<0.001**	**0.007**	**<0.001**	0.495	**<0.001**
CS	r											1.000	**0.523**	**0.477**	-0.085	-0.295	0.081
	p												**0.004**	**0.009**	0.662	0.121	0.678
MCQ-30 (Total)	r												1.000	**0.597**	**0.544**	-0.245	**0.588**
	p													**0.001**	**0.002**	0.201	**0.001**
DIF	r													1.000	0.249	-0.263	**0.670**
	p														0.193	0.169	**<0.001**
DDF	r														1.000	-0.075	**0.767**
	p															0.699	**<0.001**
EOT	r															1.000	0.146
	p																0.450
TAS-20 (Total)	r																1.000
	p																

Discussion

A total of 61 patients were included in the study, comprising 14 men (23%) and 47 women (77%). The patients' ages ranged from 18 to 65, with a median age of 40. Among the patients with panic disorder, 29 (47.5%) were found to have alexithymia. It was observed that patients with both panic disorder and alexithymia had significantly higher scores on all scales, except for the Panic Attack (PA), Cognitive Self-Consciousness (CS), and Externally Oriented Thinking (EOT) scales ($p<0.05$).

Studies have shown that patients with panic disorder exhibit higher levels of alexithymia compared to non-clinical participants, particularly in their ability to identify and describe emotions (28). In this study, 29 (47.5%) of patients with panic disorder were found to have alexithymia. A review of the literature reveals a strong association between alexithymia and panic disorder, with the estimated prevalence of alexithymia in PD patients ranging from 29% to 58% (29). This finding supports the hypothesis of a higher rate of alexithymia in patients with panic disorder.

Furthermore, the focus has primarily been on the relationship between PD and generalized anxiety disorder (GAD), with clinical studies indicating that the metacognitive beliefs associated with these disorders are often dysfunctional (30). The "need to control thoughts" and "negative beliefs about uncontrollability and danger" are examples of dysfunctional metacognitive beliefs that are believed to be more prevalent in patients with PD compared to healthy individuals (31). According to the proposed underlying mechanism, these negative metacognitive views can lead to increased self-focused attention, which in turn may exacerbate pathological anxiety. These cognitive processes may contribute to the worsening of symptoms in both PD and generalized anxiety disorder (GAD) (32). Consistent with previous studies, our research found that all scale scores, except for those related to Panic Attack (PA), Cognitive Self-Consciousness (CS), and Externally Oriented Thinking (EOT), were statistically significantly higher in panic disorder patients with alexithymia ($p<0.05$). Furthermore, the current study demonstrated a significant correlation between the total score of the Toronto Alexithymia Scale (TAS-20) and the negative beliefs about uncontrollability and danger of worry (NBAU) subscale of the Metacognition Questionnaire (MCQ-30). These findings align with earlier studies (33,34).

The findings of this study underscore the limitations of exclusively focusing on cognitive factors in the conceptualization and treatment of panic disorders. They further emphasize the potential benefits of integrating alternative therapeutic frameworks—such as Metacognitive Therapy (MCT)—which target a wider spectrum of self-regulatory and metacognitive processes.

Our study has several limitations that should be considered when interpreting the findings. The relatively small sample size may have reduced the statistical power and the ability to detect more subtle associations.

The use of self-report instruments to assess alexithymia, somatic symptoms, and attitudes toward seeking psychological support introduces the possibility of response biases, such as social desirability bias. Additionally, the cross-sectional design of the study, which only allows for the examination of the current state, complicates the identification of causal relationships between the variables, and only correlations between the variables can be observed. This limitation hinders the understanding of how the variables interact over time and how one variable may influence another. Therefore, to make definitive inferences about causality, studies employing longitudinal or experimental designs are required.

Conclusion

This study demonstrates that metacognitive beliefs are heightened in panic disorder patients with alexithymia, and that different characteristics of alexithymia are associated with distinct metacognitive beliefs. Furthermore, various metacognitive beliefs have the potential to predict the presence of alexithymia. These findings suggest that a deeper understanding of metacognitive theory and the application of metacognitive therapy may benefit patients with alexithymia. However, further research is needed to elucidate the complex relationship between metacognitive beliefs and alexithymia, as well as to explore the effectiveness of metacognitive therapy for this population.

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Cases Of AV Complete Block: A Retrospective Review

AV Tam Blok Vakaları: Retrospektif Bir İnceleme

Ramazan KIYAK* 0000-0002-8866-8595
Özgen ŞAFAK 0000-0001-8245-0117**

* Balıkesir Üniversitesi Tıp Fakültesi Acil Tıp Anabilim Dalı
** Balıkesir Üniversitesi Tıp Fakültesi Kardiyoloji Anabilim Dalı

Yazışma Adresi: Ramazan KIYAK
Balıkesir Üniversitesi Tıp Fakültesi
Acil Tıp Anabilim Dalı Balıkesir, Türkiye
E-mail: kiyak1903@hotmail.com

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Abstract

Objective: This study aimed to examine the clinical and demographic characteristics of patients diagnosed with atrioventricular (AV) complete block in the Emergency Department of Balıkesir University and to evaluate the interventions applied.

Materials and Methods: The study population consisted of all bradycardia cases presenting to the emergency department between January 1, 2020, and January 1, 2025. The sample included patients aged ≥18 years with AV complete block on ECG, no missing data, and accessible medical records. A total of 147 bradycardia cases were evaluated, of which 34 were diagnosed as AV complete block.

Results:A total of 34 patients with complete AV block were evaluated. 52.9% of the patients were in the age group of 75 years and older, and the gender distribution was equal. The most common presenting complaints were syncope and dizziness (26.5%). Hypertension (82.4%) and previous myocardial infarction (41.2%) were the most common comorbid conditions. 55.9% of the patients were not taking regular medication; antihypertensives and antiarrhythmics were the most common drugs used. In clinical outcome, 91.2% of the patients were hospitalised in the intensive care unit and 5.9% of the patients died. The rate of interventional procedures was 52.9% and the most common procedures were permanent pacemaker implantation (23.5%) and temporary pacemaker implantation.

Conclusion: This study demonstrates that AV complete block predominantly affects elderly patients with a high cardiovascular risk profile. The results support the contribution of myocardial fibrosis and hypertension to its pathogenesis. A considerable proportion of patients required emergency interventions, Intensive Care Unit admission, and permanent pacemaker implantation. Prompt emergency diagnosis and timely management are critical for reducing mortality and improving outcomes; therefore, AV complete block should be considered in every elderly patient presenting with syncope or unexplained bradycardia.

Keywords: AV complete block, Bradycardia, Emergency department,

Öz

Amaç: Atriyoventriküler (AV) tam blok, atriyum ve ventrikül arasındaki elektriksel iletişimin tamamen kesildiği, ciddi bradikardi ve ani kardiyak ölüm riski taşıyan bir iletim bozukluğudur. AV tam blok genellikle ileri yaş, iskemik kalp hastalıkları ve elektrolit bozuklukları gibi altta yatan nedenlere bağlı olarak gelişir. Bu çalışmada, Balıkesir Üniversitesi Acil Servisi'ne başvuran AV tam blok tanılı hastaların klinik ve demografik özelliklerinin incelenmesi ve müdahale süreçlerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmanın evrenini, 01.01.2020 ile 01.01.2025 tarihleri arasında acil servise başvuran tüm bradikardi vakaları oluşturmuştur. Örnekleme, EKG'lerinde AV tam blok saptanan, ≥18 yaşında olan, eksik verisi bulunmayan ve arşiv kayıtlarına ulaşılabilen hastalar dahil edilmiştir. Toplamda 147 bradikardi vakası değerlendirilmiş, bunlardan 34'ü AV tam blok olarak tanımlanmıştır.

Bulgular: Toplam 34 AV tam blok hastası değerlendirildi. Olguların %52.9'u 75 yaş ve üzeri grupta yer almakta olup, cinsiyet dağılımı eşitti. Başvuru şikayetleri arasında en sık senkop ve baş dönmesi (%26.5) görüldü. Komorbid hastalıklar arasında hipertansiyon (%82.4) ve geçirilmiş miyokard enfarktüsü (%41.2) ön plandaydı. Hastaların %55.9'u düzenli ilaç kullanmıyordu; kullanılan ilaçlar arasında en sık antihipertansifler ve antiaritmikler saptandı. Klinik sonlanımda hastaların %91.2'si yoğun bakım ünitesine yatırıldı, %5.9'u exitus oldu. Girişimsel işlem oranı %52.9 olup, en sık uygulamalar kalıcı kalp pili implantasyonu (%23.5) ve geçici kalp pili yerleştirilmesi olarak belirlendi.

Tartışma ve Sonuç: Bu çalışma, AV tam blok olgularının ileri yaş ve yüksek kardiyovasküler risk profiliyle ilişkili olduğunu ortaya koymuştur. Bulgularımız, miyokardiyal fibrozis ve hipertansiyonun AV blok gelişimindeki rolünü desteklemektedir. Hastaların önemli bir kısmında acil müdahale, yoğun bakım yatışı ve kalıcı pacemaker gereksinimi doğmuştur. Erken ve doğru acil tanı, mortaliteyi azaltmanın ve prognozu iyileştirmenin anahtarıdır; bu nedenle senkop veya açıklanamayan bradikardi ile başvuran her yaşlı hastada AV tam blok olasılığı mutlaka akılda tutulmalıdır.

Anahtar Kelimeler: AV tam blok, Acil servis, Bradikardi

Introduction

Complete atrioventricular (AV) block is a serious, potentially life-threatening cardiac conduction disorder that occurs when impulses from the sinoatrial node cannot be transmitted to the ventricles. In this condition, the electrical connection between the atria and ventricles is completely interrupted and the ventricles work slowly with their own intrinsic rhythm. Clinically, it may progress with serious complications such as syncope, hypotension due to bradycardia, congestive heart failure and sudden cardiac death (1).

The most common causes of AV complete block include acute or chronic ischaemic heart diseases, congenital conduction system disorders, myocarditis, cardiac surgeries, systemic diseases, some drugs (especially antiarrhythmics and beta-blockers) and electrolyte imbalances (2).Although AV blocks are more common in elderly patients, they may also occur in young individuals with congenital causes or toxic effects (3).

Emergency departments are a critical step in the diagnosis and management of rhythm disorders such as complete AV block. A detailed anamnesis should be taken and a good physical examination should be performed.

In line with the patient's presenting complaints, further investigations other than ECHO and coronary angiography should be performed to investigate the etiology of AV complete block. Early diagnosis, rapidly initiated supportive treatment (e.g. transcutaneous pacemaker applications) and appropriate follow-up directly affect the prognosis of these patients. Early differentiation of high-grade AV block from benign bradycardias is of vital importance. Indeed, since patients may rapidly decompensate haemodynamically in the presence of underlying high-grade AV block, early diagnosis and emergency interventions such as temporary/permanent pacemaker application decrease mortality (4). However, data on the demographic and clinical characteristics of patients presenting with complete AV block are limited in our country.

The aim of this study was to retrospectively examine the patients admitted to the Emergency Department of Balıkesir University Faculty of Medicine Hospital between 01.01.2020 and 01.01.2025 and diagnosed with AV complete block, to analyse the clinical, laboratory and outcome data, and to provide recommendations for the diagnosis and treatment process based on these data.

Material And Method

This study is a descriptive, observational study in which the files of patients admitted to the Emergency Department of Balıkesir University Faculty of Medicine Hospital and diagnosed with complete AV block were retrospectively analysed. Ethics committee approval was obtained from Balıkesir University Health Sciences Non-Interventional Research Ethics Committee.(decision no:2025/94 ,date:18.2.2025)

The study population consisted of all bradycardia cases admitted to the emergency department between 01.01.2020 and 01.01.2025. Patients who had complete AV block on ECG, were ≥18 years old, had no missing data, and whose archive records could be accessed were included in the sample. A total of 147 bradycardia cases were evaluated and 34 of them were defined as AV complete block.

The data were obtained through the hospital information management system (MIA-MED) by scanning the digital archive records of the patients. The variables collected are as follows:

Demographic information (age, gender)

Presenting complaints (syncope, dizziness, weakness, etc.)

Vital signs (blood pressure, pulse)

ECG findings

Laboratory parameters (creatinine, potassium, calcium levels)

Comorbid diseases

Medicines used

Clinical outcome (intensive care admission, discharge, exitus)

Data analysis was performed using SPSS version 26.0. Since the study involved a limited number of cases and no intergroup comparisons were conducted, only descriptive statistics were used. These included mean, standard deviation, median, minimum-maximum values, and frequency distributions.

Results

When the demographic characteristics of the 34 patients who presented with complete AV block were analysed, the ratio of males and females was the same (50%, n=17). When the age distribution of the 34 individuals included in this study was examined, it was seen that 26.5% of the participants were 65 years of age or younger, 20.6% were 66-74 years of age and 52.9% were 75 years of age or older. The age range was between 45-93 years (Table I.).

Table I. Demographic data of patients with AV complete block

Variable	Category	n	%
Gender	Male	17	50
	Female	17	50
Age Group (years)	≤ 65 years	9	26.5
	66-74 years	7	20.6
	≥ 75 years	18	52.9
Mean Age (years)	-	72.76 ± 13.73	-
Age Range (years)	-	45-93	-

When the symptoms reported by the 34 patients at the time of presentation to the emergency department were analysed, the most frequently reported complaints were dizziness (n=9; 26.5%) and syncope (n=9; 26.5%). In addition, more non-specific symptoms, such as general disturbance (n=5; 14.7%) and malaise (n=5; 14.7%) were also observed at a considerable level. To a lesser extent, symptoms such as confusion, nausea and vomiting, shortness of breath, fatigue, hypertension and cardiac arrest were observed in one patient (2.9%) each (Figure I.).

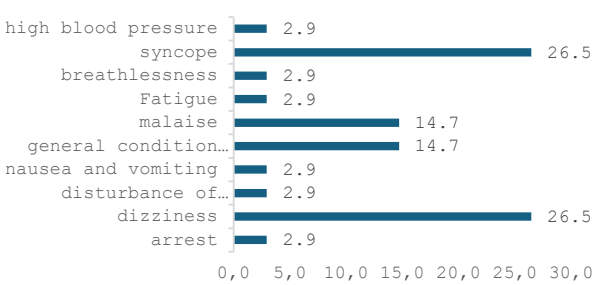

Figure I. Presenting complaints of patients with AV complete block

When the comorbidities and risk factors of the 34 patients included in the study were evaluated, the most common comorbidity was hypertension, which was found to be present in 82.4% (n=28) of the patients. The rate of patients with a history of previous myocardial infarction was 41.2% (n=14), and diabetes mellitus and hyperlipidaemia were found in 20.6% (n=7) of the patients. When regular medication use was questioned, 47.1% (n=16) of the patients were found to be taking medication (Table II.).

Table II. Distribution of patients with comorbidities and drug use

Variable	No	Yes	Total	%
Diabetes	27	7	34	20.6
Hypertension	6	28	34	82.4
Hyperlipidaemia	27	7	34	20.6
Previous heart attack	20	14	34	41.2
Rhythm disturbance	29	5	34	14.7
Drug use	18	16	34	47.1

When the blood pressures of the patients at admission were analysed, systolic blood pressure was 130 mmHg or less in 50% (n=17), 131-139 mmHg in 17.6% (n=6) and 140 mmHg or more in 32.4% (n=11) of 34 patients. When diastolic blood pressure values were analysed, it was found that 76.5% (n=26) of the patients had a diastolic blood pressure of 85 mmHg and below, and 23.5% (n=8) had a diastolic blood pressure of 86-89 mmHg (Table III.).

Table III. Blood pressure values

Category	n	%
Systolic 130 mmHg and below	17	50
Systolic 131-139 mmHg	6	17.6
Systolic 140 mmHg and above	11	32.4
Diastolic 85 mmHg and below	26	76.5
Diastolic 86-89 mmHg	8	23.5

When potassium levels, one of the biochemical parameters measured at the time of admission, were evaluated, potassium levels were within normal limits (3.5-5.1 mmol/L) in 88.2% (n=30) of the patients, while hypokalemia was found in 11.8% (n=4). When calcium levels were analysed, 76.5% (n=26) of the patients had levels within normal limits (8.8-10.6 mg/dL) and 23.5% (n=8) had hypocalcaemia. When creatinine levels were analysed, half of the patients (50%; n=17) had creatinine levels within the reference range (0.67-1.17 mg/dL), while the other half (50%; n=17) had low creatinine levels (Table IV.).

Table IV. Blood values

Parameter	Category	n	%
Potassium	Normal	30	88.2
Potassium	Low	4	11.8
Calcium	Normal	26	76.5
Calcium	Low	8	23.5
Creatinine	Normal	17	50
Creatinine	Low	17	50

Regarding the outcome of patients with complete AV block, 91.2% (n:31) were admitted to the ICU,and 5.2% (n:2) patients were exited (Table V.).

Table V. Finalisation of patients

		Frequency	%
	Exitus	2	5.9
	Hospitalisation	1	2.9
	ICU admission	31	91.2
	Total	34	100

When the drug use status of a total of 34 patients included in the study was evaluated, it was found that 55.9% (n=19) of the patients did not use any regular medication. The rate of single drug use was 23.5% (n=8), dual drug use was 14.7% (n=5) and triple drug use was 5.9% (n=2). When the drug types were analysed, it was observed that the most commonly used drugs were antihypertensives (20.6%; n=7) and antiarrhythmic agents (20.6%; n=7). This was followed by antiplatelet drugs (17.6%; n=6), anticoagulants (5.9%; n=2) and statins (5.9%; n=2), respectively (Figure II.).

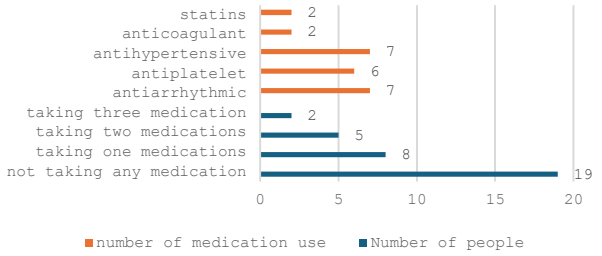

Figure II. Medication uses

The rates of use of drugs known to slow down atrioventricular conduction in our patients with AV complete block are presented in Table 6. According to our findings, the most common bradycardia-inducing drug groups were beta-blockers and digitalis glycoside. Approximately 14.7% of the patients were using beta-blockers (e.g. metoprolol or bisoprolol) and 11.8% were using digoxin. The use of non-dihydropyridine calcium channel blockers (verapamil) and class III antiarrhythmic drugs (amiodarone) was observed at lower rates (5.9% and 8.8%) (Table VI.).

Table VI. Distribution of drugs causing bradycardia.

Drug Class	Molecule	Number of Patients	%
Beta-blocker	Metoprolol	3	8,8
Beta-blocker	Bisoprolol	2	5,9
Calcium channel blocker (non-DHP)	Verapamil	2	5,9
Cardiac glycoside	Digoxin	4	11,8
Antiarrhythmic (Class III)	Amiodarone	3	8,8

Cardiac intervention processes of 34 patients diagnosed with AV complete block after the emergency department were evaluated. It was determined that 47.1% (n=16) of the patients did not undergo any interventional procedure, while 52.9% (n=18) underwent various interventions. 8.8% (n=3) patients underwent only temporary pacemaker application, 2.9% (n=1) patients underwent only coronary angiography (CAG), 5.9% (n=2) patients underwent temporary pacemaker implantation after CAG, 23.5% (n=8) patients underwent permanent pacemaker implantation after CAG, and 11.8% (n=4) patients underwent direct permanent pacemaker implantation (Figure III.).

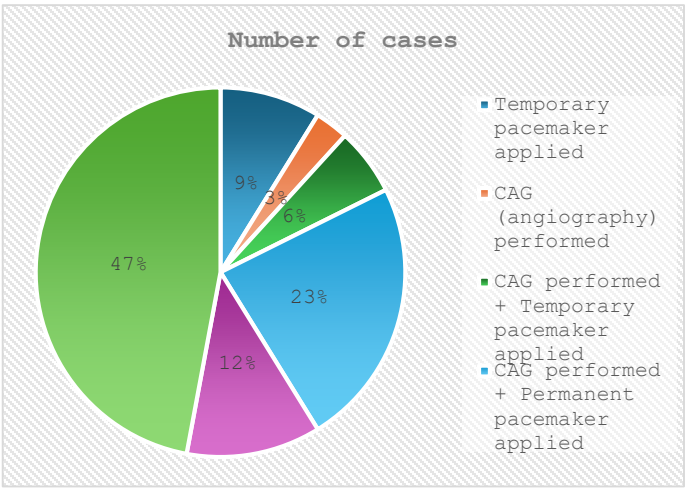

Figure III. Number of cases

Discussion

Complete Atrioventricular (AV) block is a life-threatening conduction disorder in which impulses originating in the atria fail to reach the ventricles, resulting in profound bradycardia and a risk of syncope, heart failure and sudden death (5). The resulting severe bradycardia may lead to complications including syncope, hypotension due to bradycardia, congestive heart failure or sudden cardiac death if left untreated.

The demographic characteristics of the 34 patients with AV complete block analysed in this study revealed the prominent role of advanced age, in accordance with the literature. The mean age of our patients was 72.7 ± 13.7 years, 52.9% were 75 years or older, and the gender distribution was equal. Similarly, in a larger-scale study (n=191), the mean age of patients with AV complete block was 62.7 ± 14 years (range 21-90) and a slight female predominance was reported (6). These data support that AV blocks are mostly seen in the elderly population. Degenerative fibrosis occurring in the conduction system with age is thought to play an important role in the pathogenesis of AV block. Indeed, the fact that no obvious acute triggering cause was found in most of our patients suggests that primary conduction system degeneration plays a role.

When the complaints of our patients admitted to the emergency department were analysed, the most common symptoms were syncope and dizziness. In addition, symptoms such as weakness, general condition disorder, confusion, nausea-vomiting and dyspnoea were also observed, but each of them remained at lower rates. These symptoms reflect cerebral hypoperfusion due to severe bradycardia and are quite typical in the presence of complete AV block. One study reported that syncope was the presenting symptom in approximately 40% of patients with atrioventricular complete block. This rate shows that syncope is a common symptom in patients with AV complete block (7). In a study by Alyan et al., more than half of 191 patients presented with a history of syncope (6). Therefore, high-grade AV conduction disorders should definitely be kept in mind and electrocardiographic evaluation should be performed urgently, especially in elderly patients presenting to the emergency department with unexplained syncope or marked dizziness.

Hypertension was the most prevalent comorbidity (82.4 %), followed by previous myocardial infarction (41.2 %). Both conditions promote myocardial fibrosis and damage to the conduction system, a link confirmed in multicentre studies (8). Diabetes and hyperlipidaemia each affected one-fifth of the cohort, emphasising the clustered cardiovascular risk typical of this population. Nearly half of the patients were receiving negative chronotropic drugs, most commonly β-blockers, non-dihydropyridine calcium-channel blockers or digoxin. Drug-induced AV block can be reversible, but recurrence is common after withdrawal (9-10,11). Therefore, drug history should definitely be evaluated in patients with complete AV block and patients should be kept under close follow-up even if agents that may be the culprit are discontinued. Even if a significant drug-related blocks are reversible, the block may reappear in approximately two thirds of patients over time.

Again, 41% of our patients had a history of previous MI, suggesting that ischaemic aetiology may be an important contributor. Ischaemic heart disease is considered to be one of the leading causes of complete AV block (6). The prognostic burden of ischaemia persists even in the era of primary PCI; complete block complicating anterior infarction remains an independent predictor of mortality (12,13).

Severe bradycardia in patients with complete AV block led to notable haemodynamic compromise. Half of the patients had a systolic blood pressure ≤130 mmHg at presentation, and 76.5 % had diastolic pressures <85 mmHg, reflecting reduced cardiac output. Even among those with systolic pressures >140 mmHg (32.4 %), perfusion may have remained inadequate due to slow ventricular rates. Critically low pulse rates (<40 bpm) were documented in 14.3 % of cases, reinforcing the urgency of pacing support.

In line with international guidelines, temporary transcutaneous or transvenous pacing should be promptly initiated in third-degree AV block when bradycardia compromises perfusion (14). Permanent pacemaker implantation remains the cornerstone of therapy; without it, long-term survival is markedly reduced, whereas pacing significantly improves prognosis and quality of life patients (15).

Electrolyte disturbances were uncommon but clinically relevant: hypokalaemia (11.8 %) and hypocalcaemia (23.5 %) can aggravate conduction abnormalities, while hyperkalaemia absent in our patients – has been shown to necessitate pacemaker support when severe (16,17). Rapid correction of such derangements remains a key component of acute management.

Across the broader cohort of 147 bradycardia cases seen during the study period, only 23.1 % were due to complete AV block, yet this subgroup accounted for the vast majority of ICU admissions (91.2 %) and all observed in-hospital deaths, highlighting the critical importance of early identification and intervention (4).

Although AV complete block is usually seen in individuals with a history of cardiovascular disease, a significant proportion of patients (55.9%) in our study were not on regular medication. This finding may indicate the presence of subclinical cardiac conduction disorders that have not yet been detected in the general population. The high rates of antiarrhythmic and antihypertensive drug use are compatible with the literature findings supporting that these agents may be related with the development of AV complete block (18).

Therefore, patients receiving antiarrhythmic or antihypertensive therapy should be closely monitored for conduction system complications. Moreover, the risk of AV complete block is not limited to those with known cardiovascular risk factors; even asymptomatic individuals may be affected.

In our study, nearly half of the patients with complete AV block were on regular medications, including agents known to cause bradycardia such as beta-blockers, calcium channel blockers, and digoxin. This highlights the importance of considering drug-induced AV block, which may be reversible and not always require permanent pacemaker implantation. However, recurrence can occur even after discontinuation. Therefore, a thorough review of medication history is essential, and any potentially causative agents should be stopped. In our study, beta-blockers and digoxin were the most frequently used drugs. Similarly, Damirbek et al. reported beta-blockers as the leading culprit, followed by digoxin (10), while Zeltser et al. found that 54% of patients had used beta-blockers and/or verapamil or diltiazem (19).

Even when the AV block appears drug-related, recurrence is observed in up to two-thirds of cases (19), underscoring the need for careful medication evaluation, discontinuation of risky agents, and close follow-up to monitor for recurrence and facilitate potential recovery.

Permanent pacemaker implantation is the cornerstone of treatment in patients with complete AV block. Without it, long-term survival is significantly reduced, while pacing markedly improves outcomes (18). In our study, a considerable number of patients required urgent cardiac interventions. The high proportion of patients who underwent permanent pacemaker implantation following coronary angiography (CAG) suggests that underlying coronary artery disease often coexists with AV block. Conversely, the presence of patients managed with only temporary pacing indicates that, in some cases, the block may be transient and reversible. These findings align with previous studies, which highlight permanent pacing as especially important in elderly patients with AV block and concomitant coronary disease (18). Meanwhile, the notable proportion of patients who required no intervention further supports that AV block may occasionally result from reversible causes.

Therefore, individualised evaluation and appropriate risk stratification are essential in the management of complete AV block. Treatment decisions should consider the underlying cause and clinical stability of the patient. In a previous study, two-thirds of patients diagnosed with complete AV block eventually required pacemaker implantation, with many initially managed with temporary pacing before receiving a permanent device (7).

Conclusion

Complete AV block is a high-risk conduction disorder, most frequently affecting the elderly and commonly encountered in emergency settings. The majority of patients require intensive care and have underlying cardiac conditions such as hypertension or a prior myocardial infarction. In patients presenting with syncope, dizziness, or unexplained weakness, high-grade AV block should be considered, and immediate ECG evaluation is warranted. Syncope and bradycardia in older adults must not be overlooked, as the incidence of AV conduction disorders increases with age. This study contributes to the clinical understanding of AV complete block by analysing the demographic and clinical features of affected patients in the emergency department. Further large-scale, multicentre studies are needed to validate these findings and guide optimal management strategies.

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Anesthetic Management And Clinical Experience İn Pediatric Patients Undergoing Rigid Bronchoscopy

Pediatrik Rijid Bronkoskopi Hastalarında Anestezi Deneyimlerimiz

Fatih ŞAHİN* 0000-0002-8501-0675
Melike KAR ÜNLÜ 0009-0004-3506-858X**
Aybars ÖZKAN* 0000-0003-0214-4203**
Havva KOCAYİĞİT 0000-0002-8719-7031**
Fikret BAYAR* 0000-0001-9953-4018

* Sakarya Üniversitesi, Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, Sakarya
**Sakarya Üniversitesi, Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Sakarya
*** Sakarya Üniversitesi, Eğitim ve Araştırma Hastanesi, Çocuk Cerrahisi Kliniği, Sakarya

Yazışma Adresi: Fatih ŞAHİN
Sakarya Üniversitesi, Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, Sakarya
E-mail adresi: tyflfatih16@hotmail.com

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Abstract

Objective: Foreign body aspiration (FBA) is a potentially life-threatening emergency, particularly in the pediatric population, requiring prompt diagnosis and intervention. This study aims to present our anesthetic management experience in pediatric FBA cases.

Methods: This retrospective study, pediatric patients who underwent rigid bronchoscopy for FBA between 2021 and 2024 were included. Data regarding surgical indications, anesthetic agents used for induction and maintenance, orotracheal intubation status, type and location of the foreign body (FB), timing of the operation, and perioperative complications were evaluated.

Results: A total of 170 pediatric patients were included. Of these, 25.9% were under 3 years of age, while 74.1% were older than 3 years. The most frequently encountered FBs were organic substances, primarily nuts (54.7%). Inorganic FBs included coins, pins, toys, and batteries, respectively. In 17.6% of patients, no FB was detected. The most common FB locations were the left main bronchus, esophagus, and right main bronchus. The most frequently used anesthetic agent was propofol (90%), and the most common neuromuscular blocker was rocuronium bromide (87.1%). Controlled positive pressure ventilation was used in all cases. Intraoperative desaturation occurred in 19.4% of patients, often associated with FBs lodged at the bronchial level. One patient experienced cardiopulmonary arrest; however, there was no mortality.

Conclusion: Intraoperative desaturation was more common in cases with FBs located in the main bronchi. Effective communication and coordination between surgical and anesthetic teams are essential for the successful management of these shared airway procedures, emphasizing the importance of experienced personnel.

Keywords: Bronchoscopy, Foreign body aspiration, Pediatric patient, Ventilation, Anesthesia

Öz

Amaç: Yabancı cisim aspirasyonu (YCA), özellikle pediatrik yaş grubunda hızlı tanı ve müdahale gerektiren, potansiyel olarak hayatı tehdit eden bir acil durumdur. Bu çalışmada amacımız pediatrik YCA vakalarında anestezi yönetimimizi sunmaktır.

Yöntem: Bu retrospektif çalışmada, 2021–2024 yılları arasında YCA nedeniyle rijid bronkoskopi uygulanan pediatrik hastalar çalışmaya dahil edilmiştir. Hastaların opereasyon endikasyonu, anestezi indüksiyonu ve idamesinde kullanılan anestezik ilaçlar, orotrakeal entübasyon durumu, yabancı cisim (YC) türü, YC lokalizasyonu, operasyon zamanlaması ve komplikasyonlar değerlendirilmiştir.

Bulgular: Toplam 170 pediatrik hasta çalışmaya dahil edildi. Hastaların % 25,9'u 3 yaş altı, % 74,1 ise 3 yaş üzeri hastalardı. En sık karşılaşılan YC organik ürün olan kuruyemişti (% 54,7). İnorganik maddeler ise sırasıyla para, iğne, oyuncak ve pildi. Hastaların % 17,6'sında ise YC bulunamadı. En yaygın YC yerleşimi sırasıyla sol ana bronş, özofagus ve sağ ana bronştu. En sık kullanılan anestezik ilaç propofol (%90), kas gevşetici ise roküronyum bromür (%87,1) idi. Tüm vakalarda kontrollü pozitif basınçlı ventilasyon uygulanmıştır. İntraoperatif desatürasyon %19,4 hastada gelişmiş olup, bu durum sıklıkla bronş düzeyinde yerleşmiş YC'lerle ilişkili bulunmuştur. Bir hastada kardiyopulmoner arrest gelişirken, exitus olan hasta yoktur.

Sonuç: Özellikle sol ve sağ ana bronş lokalizasyonlu YC'lerde intraoperatif desatürasyon riskinin daha yüksek olduğu görülmüştür. Cerrah ve anestezi uzmanın havayolunu ortak bir kullandığı hastalarda bu durumun başarılı yönetiminde cerrahi ve anestezi ekipleri arasında etkin iletişim ile deneyimli ekiplerin varlığının hayati önem taşıdığını düşünmekteyiz.

Anahtar Kelimeler: Bronkoskopi, Yabancı cisim aspirasyonu, Pediatrik hasta, Ventilasyon, Anestezi

Introductıon

Foreign body aspiration (FBA) is a potentially life-threatening condition, particularly in the pediatric population, if not promptly diagnosed and treated (1,2). In cases of FBA, rigid bronchoscopy under general anesthesia is generally the preferred method for foreign body (FB) removal (3).

Airway bronchoscopy is a critical interventional procedure that allows direct visualization of the trachea and bronchi and is widely used in the diagnosis and treatment of various airway disorders in pediatric patients. Recent advancements in anesthetic techniques have led to significant improvements in bronchoscopy procedures (4). However, potential complications during bronchoscopy include laryngospasm, bronchospasm, airway trauma, cardiac dysrhythmias due to increased vagal tone, cardiac events related to structural heart disease, and aspiration of pulmonary contents. These adverse airway events are particularly more common when anesthesia is superficial and airway management is not meticulously maintained (5).

There remains ongoing debate regarding optimal airway management during such procedures under anesthesia. Some clinicians prefer positive pressure mechanical ventilation, citing its advantages: securing the airway, enabling administration of 100% oxygen, and facilitating neuromuscular blockade to minimize patient movement. However, concerns have been raised that this technique may lead to distal displacement of the FB or create a ball-valve effect, potentially resulting in airway obstruction (6). Successful execution of these procedures requires a skilled surgeon, an experienced anesthesiologist, a vigilant support team, and effective communication and coordination among all team members (4).

The aim of this study is to present our institutional experience in the anesthetic management of pediatric FBA cases over an extended period.

Materials and Methods

This retrospective study was conducted in accordance with the Helsinki Declaration and received approval from the Local Ethics Committee of Sakarya University Faculty of Medicine (Approval number: E-43012747-050.04-450733-55). Data of pediatric patients who underwent surgery due to FBA between January 2021 and December 2024 were retrieved from the hospital electronic medical records system at a university-affiliated teaching and research hospital operating room.

Patients under 18 years of age who underwent rigid bronchoscopy for FB removal performed by the pediatric surgery department were included in the study. Patients were categorized into four age groups: ≤6 months, 6–12 months, 12–36 months, and >36 months. Diagnoses were established by the pediatric surgery team based on patient history, radiological imaging, and physical examination findings.

Data collected included surgical indications, anesthetic agents used during induction and maintenance, neuromuscular blockers, and narcotics. Orotracheal intubation status during bronchoscopy was recorded. Medications used to reverse neuromuscular blockade at the end of the procedure were noted. FB type (nuts, coins, needles, toys, batteries), FB location (esophagus, trachea, left main bronchus, right main bronchus), and operative duration were documented. Operation timing was classified into three shifts: 08:00–16:00, 16:00–24:00, and 24:00–08:00. Any complications arising during the procedures were also recorded.

Statistical Analysis

Statistical analyses were performed using SPSS version 20. Qualitative data were presented as counts and percentages, while quantitative data were expressed as mean ± standard deviation.

Results

A total of 170 patients were included in the study. Of these, 25.9% were under 3 years of age, while 74.1% were older than 3 years. The majority of patients were male (62.9%), and 37.1% were female. The most common FB was an organic material, specifically nuts, accounting for 54.7% of cases. Inorganic FB included coins, needles, toys, and batteries, in descending order of frequency. In 17.6% of the patients, no FB was detected. At presentation, 70% of the patients exhibited respiratory distress. A history of the FB being placed in the mouth by family members was reported in 30% of cases (Table 1).

Table 1. Demographic Characteristics

	Total patient, n=170
Age	
Under 3 years of age	44 (25.9 %)
0-6 months	2 (1.2 %)
6-12 months	14 (8.2 %)
12-36 months	28 (16.5 %)
3 years of age or older	126 (74.1 %)
Gender	
Female	63 (37.1 %)
Male	107 (62.9 %)
Foreign body type	
Nut	93 (54.7 %)
Coin	34 (20 %)
Pin	7 (4.1 %)
Toy	6 (3.5 %)
Battery	2 (1.2 %)
Non	30 (17.6 %)
Respiratory Distress	119 (70 %)
Family-reported history of foreign body ingestion	51 (30 %)

Propofol was the most commonly used induction agent, administered in 90% of cases. During anesthesia maintenance, sevoflurane was used in 18.2% of patients, while desflurane was used in 1.2%. The remaining patients received intermittent intravenous anesthetic agents for anesthesia maintenance. Neuromuscular relaxation was achieved with rocuronium bromide in 87.1% of patients. Orotracheal intubation was performed intraoperatively in 25.9% of cases. Steroids were administered to 52.4% of patients. The mean operative time was 25.8 minutes, while the mean anesthesia duration was 37.6 minutes. Intraoperative desaturation occurred in 33 patients, with 17 foreign bodies located in the right main bronchus and 16 in the left main bronchus. Postoperative intensive care unit (ICU) admission was required in 5 patients. One patient developed postoperative pulmonary atelectasis, and one experienced intraoperative cardiac arrest (Table 2).

Table 2. Intraoperative and postoperative characteristics

		Total patient, n=170
Administered Medications	Propofol	153 (90 %)
	Midazolam	74 (43.5 %)
	Ketamine	3 (1.8 %)
	Fentanyl	32 (18.8 %)
	Remifentanil	1 (0.6 %)
	Rocuronium	148 (87.1 %)
	Sugammadex	148 (87.1 %)
	Sevoflurane	31 (18.2 %)
	Desflurane	2 (1.2 %)
	Steroid	89 (52.4 %)
Peroperative intubation		44 (25.9 %)
Operation Time		
08.00-16.00		92 (54.1 %)
16.00-24.00		64 (37.6 %)
24.00-08.00		14 (8.2 %)
Operation duration (min)		25,8 ± 12,3
Anesthesia duration (min)		37,6 ± 13,4
Intraoperative desaturation		33 (19.4 %)
Foreign body in the left main bronchus		14 (8.2 %)
Foreign body in the right main bronchus		13(7.6 %)
Postoperative pulmonary atelectasis		1 (0.6 %)
Postoperative intensive care unit admission		5 (2.9 %)
İntraoperative cardiac arrest		1 (0.6 %)

The most frequent FB location was the left main bronchus (28.8%), followed by the esophagus (24.1%) and the right main bronchus (23.5%). No FB was detected in 18.2% of the patients (Figure 1).

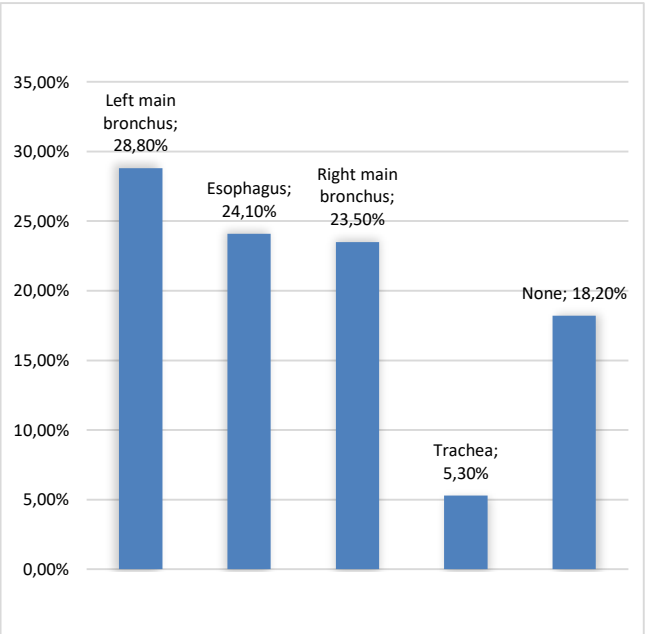

Figure 1. Foreign Body Locations

Discussion

Rigid bronchoscopy plays a critical role in the diagnosis and treatment of FBA in pediatric patients. One of the major challenges during this procedure is ensuring safe and effective airway management. Complications such as laryngospasm, bronchospasm, airway trauma, cardiac arrhythmias, and pulmonary aspiration may arise, particularly when anesthesia is superficial. To maintain airway security and adequate oxygenation, anesthetic approaches including neuromuscular blockade and controlled ventilation offer significant advantages. Furthermore, due to the shared airway between the anesthesiologist and surgeon, continuous communication and coordination throughout the procedure are essential to prevent complications. Ensuring adequate ventilation and maintaining airway control during rigid bronchoscopy are of paramount importance. While spontaneous ventilation reduces the risk of distal displacement of the FB compared to positive pressure ventilation, it allows uninterrupted ventilation. However, spontaneous ventilation may provoke airway reflexes such as coughing, straining, laryngospasm, and bronchospasm, complicating FB removal. These complications can be controlled with intravenous anesthetics, deepened anesthesia, and neuromuscular blockade during controlled ventilation. Additionally, controlled ventilation helps reduce the risks of atelectasis and hypercapnia, thereby improving oxygenation (4). Although positive pressure ventilation has been suggested to cause distal air trapping due to a ball-valve effect, current literature does not provide clear clinical evidence supporting this as a significant concern (7,8). In our cases, controlled positive pressure ventilation was applied considering the potential risks of spontaneous ventilation.Sevoflurane is frequently preferred for anesthesia maintenance in pediatric patients (9). While inhaled anesthetics can be used, intravenous agents such as propofol, dexmedetomidine, ketamine, and remifentanil are increasingly popular for providing predictable and stable anesthesia levels (4). The sole use of volatile anesthetics may lead to leaks around the rigid bronchoscope, resulting in superficial anesthesia. Combination intravenous anesthesia with sevoflurane, propofol, and remifentanil has been shown to reduce side effects (10). Littman et al. recommend intravenous anesthetics as the first choice for maintenance, although sevoflurane may be used as an inhaled agent (6). In our study, most patients received intravenous anesthetics for maintenance, with 18.2% receiving sevoflurane and 1.2% desflurane. Pediatric patients have a lower functional residual capacity and higher oxygen consumption compared to older children and adults, which predisposes them to rapid oxygen desaturation during apnea under anesthesia. Hypoxemia is the most common complication encountered during difficult pediatric airway management (11). We connect the anesthesia circuit to the rigid bronchoscope and ventilate the patient with low volume, frequent positive pressure after passing the vocal cords to minimize apnea duration. Despite adequate oxygenation and absence of desaturation in some cases, elevated end-tidal carbon dioxide (CO_2) levels are observed. Therefore, patients with end-tidal CO_2 values exceeding 55 mmHg at the end of the procedure may be intubated to effectively reduce CO_2, with extubation performed once levels normalize.

The intubation rate in our patients was 25.9%, with no significant difference in anesthesia duration compared to non-intubated patients. Mindru et al. reported that foreign bodies are most commonly located in the right main bronchus (51.2%) and left main bronchus (33.4%), regardless of age or gender (12). Xu et al. similarly found FB localization to be 45.8% in the left main bronchus and 44.8% in the right main bronchus, with no correlation between localization and age, gender, operation timing, or granulomatous formation (13). Our findings also show the highest frequency of foreign bodies in the main bronchi and esophagus. Localization is particularly important for anesthesia management and ventilation during rigid bronchoscopy. Among the 33 patients who experienced desaturation, 81.1% had foreign bodies in the left or right main bronchus. In routine practice, when desaturation occurs, the surgical team is informed, and the rigid bronchoscope is withdrawn above the carina to facilitate ventilation; the procedure resumes once oxygen saturation normalizes. Mindru et al. indicated that aspirated foreign bodies are mostly organic materials (12). Similarly, Acar et al. reported organic food products as the most frequently aspirated materials (14). In our study, organic materials, particularly nuts, were the most common aspirated foreign bodies. Nuts pose a clinical challenge due to volatile oils causing rapid bronchial injury and volume increase from fluid absorption leading to complete airway obstruction.Bronchoscopy remains the optimal method for FBremoval in pediatric patients, despite the potential for life-threatening complications during the procedure. While removal is generally safe, complications occur in 6-8% of cases and can lead to severe outcomes (15). Liang et al. reported no anesthesia-related complications in 2000 tracheobronchial FB cases, with 15 postoperative mortalities (16). In our cohort, one patient experienced cardiopulmonary arrest but no mortalities occurred. The patient with cardiac arrest had a hazelnut shell causing complete subglottic obstruction after neuromuscular blockade, emphasizing the need for caution with rigid, subglottically lodged foreign bodies. This patient was intubated postoperatively in the ICU. Overall, 5 patients (2.9%) required postoperative ICU admission. Since the clinical status of initially stable FBA cases can deteriorate rapidly, prompt and accurate diagnosis and treatment are crucial (17). Consequently, bronchoscopy is performed emergently without delay by the pediatric surgery team, with about half of the operations conducted outside regular working hours. This study retrospectively evaluated anesthesia management and related complications in 170 pediatric patients undergoing rigid bronchoscopy for FBA. Our results indicate a higher risk of intraoperative desaturation in foreign bodies located in the left and right main bronchi. Successful management depends critically on effective communication and the presence of experienced surgical and anesthesia teams. Anesthetic drug protocols and ventilation strategies were individualized based on patient clinical status, enabling safe completion in most cases. Although severe complications occurred in a minority, these were successfully managed through multidisciplinary collaboration. Our findings suggest that early diagnosis, appropriate anesthesia techniques, and coordinated team efforts are key determinants in reducing complications in pediatric FBA.

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Predictive Utility of the ALBI Score for Contrast-Induced Acute Kidney Injury Following PCI in Acute Coronary Syndrome Patients

Perkütan Koroner Girişim Uygulanan Akut Koroner Sendrom Hastalarında Kontrast Kaynaklı Akut Böbrek Hasarı İçin ALBI Skorunun Öngörücü Değeri

Özkan BEKLER*0000-0002-0031-6457
Alparslan KURTUL0000-0003-0817-8906**

* İstanbul Medipol Üniversitesi, Kardiyoloji Anabilim Dalı, İstanbul
** Hatay Mustafa Kemal Üniversitesi, Kardiyoloji Anabilim Dalı, Hatay

Yazışma Adresi: Özkan BEKLER
Istanbul Medipol University, Faculty of Medicine, Medipol Mega University Hospital, Department of Cardiology, TEM Avrupa
E-mail: ozkanbekler111@gmail.com

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Abstract

Objective: This study aimed to evaluate the predictive value of the preprocedural albumin-bilirubin (ALBI) score for contrast-induced acute kidney injury (CI-AKI) in patients undergoing percutaneous coronary intervention (PCI) for acute coronary syndrome (ACS).

Methods: This retrospective single-center study was conducted between January 2022 and March 2024, and 552 consecutive patients with ACS who underwent PCI were enrolled. The ALBI score was calculated using the serum albumin and total bilirubin levels prior to the procedure. CI-AKI was defined as an increase in serum creatinine ≥0.5 mg/dL or ≥25% within 48–72 hours after contrast exposure.

Results: CI-AKI occurred in 70 (12.7 %) patients. These patients were significantly older, had a higher prevalence of diabetes, and elevated ALBI scores. Lower eGFR, hemoglobin, and albumin levels and higher CRP and glucose levels were observed in the CI-AKI group. Multivariate logistic regression identified the ALBI score as an independent predictor of CI-AKI (odds ratio [OR]: 7.32; p=0.001), along with age, glucose level, and eGFR. ROC analysis revealed that the ALBI score had an acceptable discriminative ability for predicting CI-AKI, with an AUC of 0.733.

Conclusion: The ALBI score is a simple, objective, and laboratory-based tool that may allow early risk stratification of CI-AKI in patients with ACS undergoing PCI. Given its ease of use and reliance on routinely measured biomarkers, it may serve as a complementary prognostic index to traditional scoring systems. Further prospective multicenter validation studies are needed.

Keywords: ALBI score, Contrast-induced acute kidney injury, Percutaneous coronary intervention

Öz

Amaç: Bu çalışmanın amacı, perkütan koroner girişim (PKG) uygulanan akut koroner sendrom (AKS) hastalarında kontrast kaynaklı akut böbrek hasarının (CI-AKI) öngörülmesinde pre-prosedürel ALBI skorunun prediktif değerini araştırmaktır.

Yöntem: Ocak 2022–Mart 2024 tarihleri arasında tek merkezde gerçekleştirilen retrospektif çalışmaya, AKS nedeniyle PKG uygulanan 552 ardışık hasta dahil edildi. ALBI skoru, girişim öncesi ölçülen serum albümin ve total bilirubin düzeyleri kullanılarak hesaplandı. CI-AKI, prosedür sonrası 48–72 saat içinde serum kreatininde ≥0.5 mg/dL veya ≥%25 artış olarak tanımlandı.

Bulgular:CI-AKI, hastaların %12.7'sinde (n=70) gelişti. CI-AKI grubunda yaş, diyabet sıklığı ve ALBI skoru anlamlı olarak daha yüksekti. eGFR, serum albümin ve hemoglobin düzeyleri daha düşüktü.

CRP ve glukoz gibi inflamasyon ve metabolik parametreler CI-AKI ile ilişkili bulundu. ALBI skoru, çok değişkenli lojistik regresyon analizinde CI-AKI için bağımsız bir prediktör olarak belirlendi (OR: 7.32; p=0.001). ROC eğrisi analizi sonucunda ALBI skorunun CI-AKI öngörüsündeki ayırt edici gücü AUC = 0.733 ile kabul edilebilir düzeyde bulunmuştur.

Sonuç:ALBI skoru, CI-AKI riskinin erken değerlendirilmesinde kolay uygulanabilir, objektif ve rutin biyokimyasal parametrelere dayalı bir araç olarak öne çıkmaktadır. ALBI, mevcut risk skorlama sistemlerine tamamlayıcı bir biyobelirteç olarak entegre edilebilir. Bulguların geçerliliği için çok merkezli ileriye dönük çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: ALBI skoru, Kontrast kaynaklı akut böbrek hasarı, Perkütan koroner girişim

Introduction

Acute coronary syndrome (ACS) remains one of the leading causes of morbidity and mortality worldwide. Percutaneous coronary intervention (PCI) is the most commonly utilized treatment modality aimed at achieving early reperfusion in these patients. However, the use of iodinated contrast agents during PCI procedures can lead to the development of contrast-induced acute kidney injury (CI-AKI), particularly in individuals with impaired renal reserve(1,2). CI-AKI is associated with prolonged hospitalization, increased healthcare costs, and a significant rise in both short- and long-term mortality (3,4).

Although several risk factors such as advanced age, diabetes mellitus, baseline renal function, and the volume of contrast media have been identified, existing risk stratification tools have limited predictive accuracy. Therefore, there is a pressing need for objective, simple, and effective predictors of CI-AKI (5).

The Albumin-Bilirubin (ALBI) score, initially developed to assess prognosis in hepatocellular carcinoma, is a straightforward and objective scoring system calculated solely using serum albumin and total bilirubin levels (6). Recent studies suggest that the ALBI score may also be associated with heart failure, myocardial infarction, and overall mortality (7,8). Additionally, as liver function parameters can reflect systemic inflammation, hypoperfusion, and multiorgan dysfunction, they may indirectly correlate with the development of renal injury (9).

To date, very few studies have explored the relationship between the ALBI score and the incidence of CI-AKI following PCI. Given its reliance on routinely available laboratory values and ease of calculation, the ALBI score may serve as a novel and practical risk indicator in this clinical context.

The aim of this study is to investigate the predictive value of the preprocedural ALBI score for the development of CI-AKI in patients undergoing PCI for acute coronary syndrome, and to evaluate whether it can serve as an alternative or complementary biomarker to existing risk prediction models.

Methods

Study Design and Population

This retrospective, single-center observational study was carried out at a tertiary cardiovascular center between January 2022 and March 2024. The study population comprised 552 consecutive patients who were hospitalized with ACS and subsequently underwent PCI. This study was approved by the Non-Invasive Clinical Research Ethics Committee of Istanbul Medipol University (Decision No: 777, Date: 03.07.2025). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Eligible participants were adults (≥18 years) who underwent either urgent or elective PCI for ACS. Patients were excluded if they had end-stage renal disease (ESRD), chronic hepatic failure, active malignancy, systemic infection, or if their laboratory data were incomplete. Additional exclusion criteria included receiving nephrotoxic medications or undergoing dialysis at baseline(Figure 1).

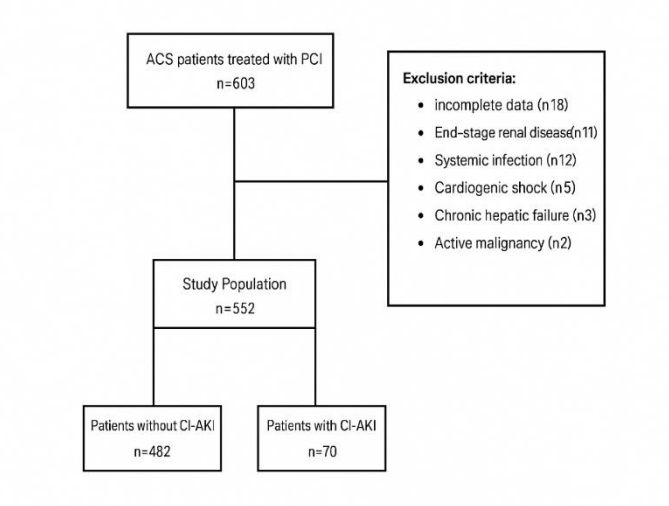


Figure 1. Flowchart illustrating the selection of the study population.

CI-AKI: Contrast-induced acute kidney injury ACS: acute coronary syndrome PCI: percutaneous coronary intervention

Definition of CI-AKI

CI-AKI was defined as an increase in serum creatinine by ≥0.5 mg/dL or a ≥25% rise from baseline within 48 to 72 hours following contrast exposure, in the absence of alternative etiologies. This definition aligns with widely accepted criteria in the literature.

Laboratory Assessment and ALBI Score Calculation

Baseline laboratory values, including serum albumin, total bilirubin, and creatinine, were obtained from blood samples collected prior to the PCI procedure. The ALBI score is determined using baseline serum albumin and total bilirubin levels, according to the following formula: log10(bilirubin in mmol/L) X 0.66 -0.085 X albumin in g/L(10). Patients were categorized into tertiles based on the ALBI score distribution within the study cohort.

Statistical Analysis

Statistical analyses were performed using the SPSS version 21.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation or median with interquartile range (IQR), and categorical variables as frequencies and percentages. Group comparisons were performed using the independent samples t-test, Mann–Whitney U test, chi-square test, or Fisher's exact test, as appropriate.

Receiver operating characteristic (ROC) curve analysis was utilized to assess the discriminative ability of the ALBI score for predicting CI-AKI. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of CI-AKI. A two-tailed p-value <0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 552 patients with ACS who underwent PCI were included. Among them, 70 patients (12.7%) developed CI-AKI, whereas 482 patients (87.3%) did not. Patients who developed CI-AKI were significantly older (64 [IQR: 40–104] vs. 60 [27–96] years, $p = 0.001$). The prevalence of diabetes mellitus was significantly higher in the CI-AKI group (62.9% vs. 41.9%, $p = 0.001$). A significantly lower left ventricular ejection fraction (LVEF) was observed in patients with CI-AKI (45% vs. 50%, $p = 0.012$). Additionally, a prior history of myocardial infarction ($p = 0.048$) and absence of family history of coronary artery disease ($p = 0.010$) were significantly associated with CI-AKI (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Non-CI-AKI (n=482)	CI-AKI (n=70)	p-value
Age (years)	60 (27–96)	64 (40–104)	**0.001***
Male sex, (%)	77.6	68.6	0.068
BMI (kg/m²)	27.11 (19,60-48,90)	27.10 (22,31-40,56)	0.480
Systolic BP(mmHg)	123 (115–135)	127 (116–137)	0.177
Diastolic BP(mmHg)	78 (68–85)	80 (70–88)	0.122
Heart rate (bpm)	80 (72–91)	83 (73–95)	0.066
Diabetes mellitus, n (%)	202 (41,9)	44 (62,9)	**0.001***
Hypertension, n (%)	266 (55,2)	43 (61,4)	0.197
Hyperlipidemia, n (%)	110 (22,8)	13 (18,6)	0.264
Smoking, n (%)	166 (34,1)	25 (35,7)	0.466
Family history of CAD, n (%)	58 (12,0)	2 (2,9)	**0.010***
Previous CABG, n (%)	29 (6,0)	5 (7,1)	0.437
Previous MI, n (%)	31 (6,4)	9 (13,0)	**0.048***
History of stroke, n (%)	11 (2,3)	3 (2,9)	0.507
Prior ASA use (%)	52 (12,0)	7 (10,0)	0.399
Prior ACEi/ARB use (%)	28 (8,8)	4 (9,1)	0.869
Prior β-blocker use (%)	33 (9,0)	8 (14,3)	0.160
Prior CCB use (%)	17 (4,7)	5 (8,9)	0.156
Prior ADP-antagonist use (%)	12 (3,3)	4 (7,1)	0.153
Prior statin use (%)	17 (4,7)	3 (5,5)	0.502
Ejection fraction (%)	50 (20–65)	45 (20–55)	**0.012***

*A p-value of ,0.05 was considered statistically significant, and it has been written in bold.

Abbreviations: BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CABG, coronary artery bypass grafting; MI, myocardial infarction; ASA, acetylsalicylic acid; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; ADP-antagonist, adenosine diphosphate receptor antagonist.

Laboratory Findings

Patients with CI-AKI demonstrated significantly worse baseline renal function as reflected by lower estimated glomerular filtration rate (eGFR) values (64.4 vs. 87.8 mL/min/1.73 m², p = 0.001), and higher serum creatinine (1.12 vs. 0.92 mg/dL, p = 0.001) and blood urea nitrogen (BUN) levels (22.4 vs. 17.5 mg/dL, p = 0.003). Notably, ALBI scores were significantly higher (less negative) in the CI-AKI group (−2.48 vs. −2.78, p = 0.001), indicating reduced hepatic reserve.

Serum albumin levels were lower (3.57 vs. 4.01 g/dL, p = 0.001), and C-reactive protein (CRP) levels were markedly elevated (49.34 vs. 22.67 mg/L, p = 0.001) in the CI-AKI group, suggesting a heightened inflammatory state. Glucose levels were also significantly increased (181.1 vs. 141.3 mg/dL, p = 0.001), while hemoglobin levels were reduced (13.6 vs. 14.4 g/dL, p = 0.006) (Table 2).

Table 2. Laboratory Parameters and Liver Function Scores

Variable	Non-CI-AKI (n=482)	CI-AKI (n=70)	p-value
WBC (×10³/μL)	10.61 (2,70-27,90)	11.02 (6,30-26,57)	**0.032***
Hemoglobin (g/dL)	14.40 (7,40-18,20)	13.60 (8,70-16,60)	**0.006***
Platelet count (×10³/μL)	261.94 (198,84-323,95)	273.01 (185,25-368,62)	0.356
Glucose (mg/dL)	141.29 (91,20-193,40)	181.10 (91,70-271,70)	**0.001***
HbA1c (%)	7.54 (3,55-11,56)	11.50 (0,22-24,52)	0.080
eGFR (mL/min/1.73 m²)	87.77 (65,61-109,88)	64.43 (42,32-86,54)	**0.001***
Total cholesterol (mg/dL)	178.88 (133,66-224,02)	168.50 (124,44-212,65)	0.075
LDL (mg/dL)	110.62 (71,95-149,35)	99.49 (65,88-133,11)	**0.026***
HDL (mg/dL)	39.42 (28,84-49,11)	39.70 (29,51-49,89)	0.841
Triglycerides (mg/dL)	174.01 (166,86-272,21)	167.38 (76,96-258,23)	0.615
AST (U/L)	87.94 (82-89)	131.02 (110-52)	0.064
ALT (U/L)	34.29 (32-36)	38.60 (35-43)	0.298
Albumin (g/dL)	4.01 (3,71-4,32)	3.57 (3,27-3,87)	**0.001***
CRP (mg/L)	22.67 (19-25)	49.34 (42-57)	**0.001***
BUN (mg/dL)	17.54 (11-26)	22.37 (12-33)	**0.003***
Creatinine (mg/dL)	0.92 (0,62-1,12)	1.12 (0,71-1,42)	**0.001***
Total bilirubin (mg/dL)	0.57 (0,10-0,97)	0.45 (0,31-0,60)	**0.014***
Direct bilirubin (mg/dL)	0.24 (0,12-0,36)	0.15 (0,25-0,36)	**0.001***
Indirect bilirubin (mg/dL)	0.44 (0,21-0,66)	0.37 (0,17-0,57)	0.434
ALBI score	-2.78 (-2,98--2,58)	-2.48 (-2,58--2,38)	**0.001***

*A p-value of ,0.05 was considered statistically significant, and it has been written in bold.
Abbreviations: WBC, white blood cell count; HbA1c, glycated hemoglobin; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; BUN, blood urea nitrogen; ALBI, albumin-bilirubin score.

Angiographic and Procedural Features

The incidence of STEMI was higher in the CI-AKI group (67.2% vs. 60.5%), though not statistically significant (p = 0.187). There was a trend toward longer procedural duration (42.0 vs. 39.3 minutes, p = 0.254) and higher contrast volume usage (201.5 vs. 177.1 mL, p = 0.075) in the CI-AKI group, though these differences did not reach statistical significance. Multivessel disease (56.9% vs. 48.1%, p = 0.437) and anterior STEMI localization were also more common among those with CI-AKI(Table 3).

Table 3. Angiographic and Procedural Characteristics

Variable	Non-CI-AKI (n=482)	CI-AKI (n=70)	p-value
ACS type (STEMI) (%)	257 (60,5)	43 (67,2)	0.187
Anterior MI (%)	105 (41,0)	20 (50,0)	0.560
Multivessel disease (%)	181 (48,1)	33 (56,9)	0.437
Stent diameter (mm)	2,95 (2,51-3,32)	2,87 (2,32-3,56)	0.187
Stent length (mm)	29,76 (15-45)	30,16 (18-42)	0.847
Number of stents	1,35 (1-2)	1,29 (1-2)	0.495
Contrast volume (mL)	177.11 (94-267)	201.50 (98-304)	0.075
Procedure time (min)	39.29 (25-55)	42.02 (22-62)	0.254

Abbreviations: ACS, Acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction

Predictive Value of ALBI Score

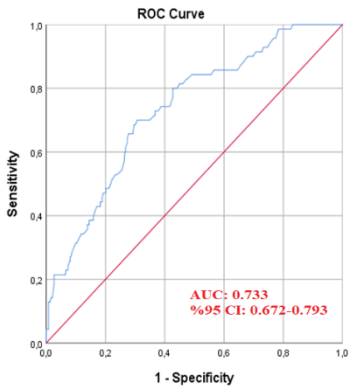
When patients were stratified into tertiles based on ALBI score, a progressive increase in CI-AKI incidence was observed from the lowest to highest tertile (p for trend < 0.001). Multivariate logistic regression analysis identified the ALBI score as an independent predictor of CI-AKI (OR: 7.32; 95% CI: 2.69–19.96; p = 0.001), along with age (p = 0.023), glucose (p = 0.001), and eGFR (p = 0.005). Other variables, such as diabetes mellitus and BUN, were not independently associated with CI-AKI in the adjusted model(Table 4). ROC curve analysis demonstrated an acceptable discriminative ability of the ALBI score in predicting CI-AKI, with an area under the curve (AUC) of 0.733, indicating that the score performs better than chance and possesses good diagnostic utility (Figure 2).

Tablo 4: Multivariable logistic regression model revealing the association with CI-AKI.

		95% C.I.for OR		
	OR	Lower	Upper	P value
Age	1.034	1.005	1.063	**0.023**
Diabetes Mellitus	1.040	0.492	2.196	0.918
Hemoglobin	1.132	0.969	1.322	0.118
Glucose	1.010	1.005	1.015	**0.001**
eGFR	0.970	0.949	0.991	**0.005**
BUN	0.975	0.934	1.017	0.243
ALBI score	7.324	2.687	19.964	**0.001**

Abbreviations: BUN: blood urea nitrogen; eGFR, estimated glomerular filtration rate; ALBI score: albumin-bilirubin score OR: odds ratio; CI: confidence interval

Figure 2. Receiver operating characteristic (ROC) curve for the prediction of contrast-induced acute kidney injury (CI-AKI) using the ALBI score.



Discussion

In this study, we investigated the predictive value of preprocedural ALBI score for CI-AKI in patients undergoing PCI for ACS. We found a significant and independent association between higher ALBI scores and incidence of CI-AKI. This finding highlights the potential utility of ALBI, an objective and easily calculated score for evaluating renal risk in high-risk cardiovascular populations.

The biological plausibility of this association is supported by the pathophysiological roles of albumin and bilirubin. Serum albumin acts as a carrier protein and exerts anti-inflammatory and antioxidant effects. Hypoalbuminemia compromises endothelial function, reduces oncotic pressure, exacerbates renal hypoperfusion, and enhances tubular vulnerability to contrast-induced oxidative damage(11). Conversely, bilirubin, particularly in its unconjugated form, has antioxidant activity that may buffer free-radical injury(10,12). Neužil and Stocker showed that bilirubin can protect serum albumin and other proteins from oxidative modification(13). Thus, a lower bilirubin level, combined with low albumin level, as captured by the ALBI score, may reflect a systemic state of reduced antioxidative capacity, which predisposes patients to renal tubular injury upon contrast exposure.

Several clinical studies have explored the association between liver function parameters and adverse outcomes in the cardiovascular setting. For instance, Han et al. demonstrated that ALBI score independently predicted mortality in patients with decompensated heart failure. Similarly, Huseynov et al. reported a link between cholestatic and liver parameters and the risk of in-hospital MACE in patients with acute coronary events(7,8). Our findings extend this association to contrast-related renal outcomes, suggesting that ALBI may serve as a universal biomarker of systemic stress and organ crosstalk in cardiovascular disease.

Unlike other risk stratification tools, such as the Mehran or Bartholomew scores, which incorporate procedural and hemodynamic variables, such as hypotension, intra-aortic balloon pump use, and contrast volume, the ALBI score is derived solely from two routine biochemical markers(3,15). This simplicity allows rapid and objective assessment without relying on invasive or time-sensitive data. Our findings show that even in patients without overt hepatic disease, variations in ALBI score meaningfully stratify CI-AKI risk aligning with studies by Huang et al. and Luo et al. who both demonstrated prognostic value for ALBI in broader cardiovascular settings(6,12)

Compared to Guler et al., who examined STEMI patients, our cohort included a broader ACS population and emphasized the predictive capacity of ALBI across both elective and emergency PCI cases. While Guler et al. also found a stepwise increase in CI-AKI with higher ALBI tertiles, our study adds to this by showing its relevance in a more heterogenous real-world setting, supporting generalizability(16).

Another notable observation was the significantly lower albumin and higher CRP levels among the patients with CI-AKI. This supports the inflammatory basis of CI-AKI, consistent with the concept that inflammation-related endothelial dysfunction drives renal injury. Furthermore, patients in the CI-AKI group had a higher prevalence of diabetes, multivessel coronary disease, and anterior infarctions, all of which are established risk factors for renal injury post-PCI. Interestingly, although the contrast volume did not reach statistical significance, it showed a numerical trend toward higher amounts in the CI-AKI group. This observation aligns with the existing literature but also highlights the need for risk models that go beyond contrast dose alone. The ALBI score, which is not influenced by contrast volume, may thus serve as a complementary tool, adding the baseline vulnerability context to procedural risk.

The main strength of our study is the use of a novel hepatic index in the context of renal outcome in patients with ACS. However, our results must be interpreted with caution owing to some limitations. The retrospective nature of the study and its single-center design may limit the generalizability of the results. In addition, data on hydration protocols and nephrotoxic drug use post-PCI, which might confound the incidence of CI-AKI, are not detailed. Lastly, while ALBI score cut-off values showed statistical significance, ROC analyses are still pending to determine the optimal predictive thresholds.

Conclusion

Preprocedural ALBI score was independently associated with CI-AKI after PCI in patients with ACS. The ease of use, objectivity, and reliance on commonly available laboratory parameters make it a promising tool for early renal risk stratification. Future prospective multicenter studies are warranted to validate these findings and to evaluate the integration of ALBI into existing CI-AKI risk algorithms.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
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Holmium Laser Enucleation of the Prostate and Urethral Stricture: A Bibliometric Analysis

Prostat ve Üretral Darlıkta Holmium Lazer Enükleasyonu: Bibliyometrik Analiz

Hakan TEKİNASLAN* 0000-0001-9106-0495
Serkan ÖZCAN0000-0002-2459-139X**
Osman KÖSE0000-0003-4912-2597**
Enis Mert YORULMAZ0000-0003-2109-2015**
Sacit Nuri GÖRGEL0000-0001-7628-1249**
Yiğit AKIN0000-0001-7627-3476**

* T.C. Sağlık Bakanlığı Menderes Devlet Hastanesi, Üroloji Kliniği, İzmir, Türkiye
** İzmir Kâtip Çelebi Üniversitesi Tıp Fakültesi, Üroloji Ana Bilim Dalı, İzmir, Türkiye

Yazışma Adresi: Serkan ÖZCAN
Department of Urology, Izmir Kâtip Celebi University School of Medicine, 35640, Izmir, Turkey
E-posta: drserkanozcan@hotmail.com

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Abstract

Objective: Holmium laser enucleation of the prostate(HoLEP) has emerged as a widely accepted surgical treatment for benign prostatic hyperplasia(BPH). Although its efficacy and safety have been well established, urethral stricture remains a rare but clinically significant complication. This bibliometric analysis aims to assess the scope and trends of the current literature on HoLEP and urethral stricture, identify leading contributors, and highlight research gaps.

Materials and Methods: A systematic search was conducted using the Web of Science Core Collection database to identify relevant articles published between 2001 and 2025. Studies focusing on HoLEP and urethral stricture were included. Data were analyzed using Microsoft Excel and VOSviewer to assess publication metrics, co-authorship patterns, country-level productivity, and keyword co-occurrence.

Results: A total of 92 articles met the inclusion criteria. A significant increase in publication volume was observed after 2010, with most articles originating from the United States, China, Germany and Turkey. Collaboration networks showed regional clustering, while keyword analysis identified three main thematic areas: clinical efficacy, perioperative techniques, and postoperative complications. Although urethral stricture was frequently referenced, it rarely served as the primary research focus.

Conclusion: This bibliometric analysis demonstrates increasing academic interest in HoLEP, particularly over the past decade. However, studies specifically focusing on urethral stricture remain limited. Future research should prioritize multicenter collaboration and focus on preventing and managing this complication to improve surgical outcomes and patient quality of life.

Keywords: Bibliometric analysis, HoLEP, urethral stricture

Öz

Amaç: Prostatın Holmium lazerle enükleasyonu (HoLEP), iyi huylu prostat hiperplazisi (BPH) için yaygın olarak kabul gören bir cerrahi tedavi olarak ortaya çıkmıştır. Etkinliği ve güvenliği iyi belirlenmiş olsa da üretra darlığı nadir görülen ancak klinik olarak önemli bir komplikasyon olmaya devam etmektedir. Bu bibliyometrik analiz, HoLEP ve üretra darlığı hakkındaki literatürün kapsamını ve eğilimlerini değerlendirmeyi, önde gelen katkıda bulunanları belirlemeyi ve araştırma boşluklarını vurgulamayı amaçlamaktadır.

Gereçler ve Yöntemler: 2001 ile 2025 yılları arasında yayınlanmış ilgili makaleleri belirlemek için Web of Science Core Collection veritabanı kullanılarak sistematik bir arama yapıldı. HoLEP ve üretra darlığına odaklanan çalışmalar dahil edildi.

Veriler; yayın metriklerini, ortak yazarlık modellerini, ülke düzeyinde üretkenliği ve anahtar kelime birlikteliğini değerlendirmek için Microsoft Excel ve VOSviewer kullanılarak analiz edildi.

Bulgular: Toplam 92 makale dahil etme kriterlerini karşıladı. 2010'dan sonra yayın hacminde belirgin bir artış gözlemlendi ve makalelerin çoğu Amerika Birleşik Devletleri, Çin, Almanya ve Türkiye'den geldi. İş birliği ağları bölgesel kümelenme gösterirken, anahtar kelime analizi üç ana tematik alanı ortaya koydu: klinik etkinlik, perioperatif teknik ve postoperatif komplikasyonlar. Üretra darlığı sıklıkla referans alınmasına rağmen, nadiren birincil araştırma odağı oluşturdu.

Sonuç: Bu bibliyometrik analiz, özellikle son on yılda HoLEP'e yönelik artan bir akademik ilgiyi göstermektedir. Ancak, üretra darlığı üzerine özel çalışmalar sınırlı kalmaktadır. Gelecekteki araştırmalar, çok merkezli iş birliğine öncelik vermeli ve cerrahi sonuçları ve hastanın yaşam kalitesini iyileştirmek için bu komplikasyonun önlenmesi ve yönetimine odaklanmalıdır.

Anahtar Kelimeler: Bibliometrik analiz, HoLEP, üretra darlığı

Introduction

Benign prostatic hyperplasia(BPH) has historically been addressed through transurethral resection of the prostate(TURP), a procedure that has been widely regarded as the surgical gold standard(1). However, holmium laser enucleation of the prostate(HoLEP) has emerged as a minimally invasive alternative, offering complete adenoma removal with durable outcomes across all prostate sizes(2). Considering its proven superiority in terms of efficacy and safety, HoLEP is increasingly regarded as the new gold standard in the field of BPH surgery(3).

Although numerous studies have demonstrated the superiority of HoLEP to TURP, particularly in terms of long-term symptom relief and reduced complication rates, it is important to note that both procedures carry inherent risks. Urethral stricture, although reported in only 1–2% of cases, remains a notable complication due to its impact on patient quality of life(4,5). 2015 meta-analysis by Cornu et al. noted a 1.7% stricture rate for enucleation procedures versus 3.8% after monopolar TURP(6). Similarly, large single-center HoLEP series have observed stricture occurrences under 2%(7). Understanding the body of research focused on HoLEP and its relationship to urethral stricture is important for identifying best practices to minimize this complication.

Despite the proliferation of literature on HoLEP, there is a paucity of focused analysis on urethral stricture as a complication(8,9). Bibliometric analysis is a valuable tool for the evaluation of research productivity, trends, and thematic focus. Previous bibliometric studies in the urology field have examined laser-based BPH treatments in general(10) and even the most-cited HoLEP papers(11). The present study addresses a lacuna in the extant literature by means of a comprehensive bibliometric assessment of publications related to HoLEP and urethral stricture, with a view to identifying leading contributors, key publications, and current research priorities.

The objective of the present findings is twofold: firstly, to inform future studies, and secondly, to support strategies that have the potential to minimise complications and optimise surgical outcomes.

Methods

2.1 Data Source and Search Strategy

A bibliometric search was performed in the Web of Science(WoS) Core Collection to identify publications focusing on both holmium laser enucleation of the prostate(HoLEP) and urethral stricture. The topic search(TS) included terms such as “HoLEP”, “Holmium laser enucleation”, “urethral stricture”, and “urethral stenosis.” The search query used was: *TS=("HoLEP" OR "Holmium laser enucleation") AND TS=("urethral stricture" OR "urethral stenosis").*The search, conducted on March 1, 2025, was limited to full-text journal articles published between 2001 and 2025, excluding conference abstracts. No language restrictions were applied. After duplicate removal and relevance screening, a final set of *92 articles* was included for analysis.

2.2 Data Extraction and Bibliometric Analysis

From each included study, bibliographic information such as title, authors, journal, year, document type, citation count, affiliations, and keywords was extracted. Bibliometric mapping was conducted using *VOSviewer v1.6.20 (Leiden University, Netherlands)* and Microsoft Excel. Keyword co-occurrence analysis was based on terms appearing in at least three publications to identify thematic clusters. Author collaboration networks were visualized for contributors with two or more publications. International affiliations were analyzed to explore global collaboration trends. Citation counts and publication trends over time were also assessed to highlight influential articles, authors, and evolving research directions.

2.3 Network Visualization Parameters

In the network maps, node size represents keyword frequency or author productivity, while line thickness indicates the strength of associations such as co-authorship or keyword co-occurrence. Spatial proximity of terms in keyword maps reflects semantic closeness. Author clusters often aligned with institutional or regional collaborations.

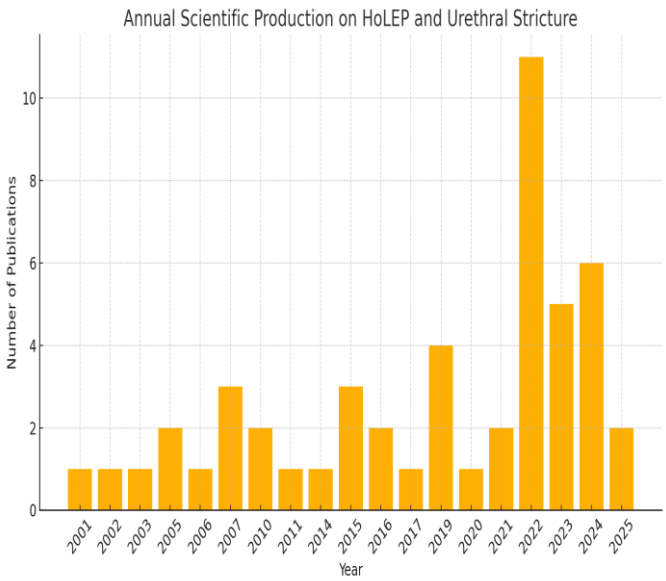
2.4 Ethical Considerations

This study was based entirely on publicly accessible bibliographic records and did not involve human participants or patient data. Therefore, ethical approval was not required, and the study conforms to established standards for the ethical use of published literature.

Results

A comprehensive review of the extant literature revealed a total of 108 publications addressing HoLEP and urethral stricture that were published between 2001 and 2025. Following the satisfaction of the inclusion criteria, a total of 92 publications were subjected to analysis.

Figure 1. Annual Number of Publications on HoLEP and Urethral Stricture Between 2001 and 2025



3.1 Journals and Publication Venues

A survey of the extant literature reveals that approximately 52% of studies related to HoLEP have been published in six major urology journals.

The Journal of Endourology has the highest publication volume, which is indicative of the endoscopic nature of HoLEP. Key randomised trials and long-term outcome studies have been featured in high-impact journals such as European Urology and Journal of Urology. The five most frequently cited articles on HoLEP and urethral stricture, according to Web of Science(2025), are listed in Table 1.

In recent times, open-access platforms such as World Journal of Urology and Frontiers in Urology have gained prominence, thereby enhancing the visibility and citation potential of HoLEP research.

Table 1. Top Five Most-Cited Articles on HoLEP and Urethral Stricture(Web of Science, 2025)

Rank	First Author (Year)	Journal	Title / Focus	Citation Count	Key Contributions
1	**Gilling et al. (2012)**	BJU International	7-year follow-up of HoLEP vs TURP(RCT)	410	Demonstrated long-term durability and low reoperation rates; benchmark for HoLEP efficacy
2	**Kuntz et al. (2008)**	European Urology	HoLEP vs open prostatectomy for large prostates(>100 mL)	320	Supported HoLEP use in very large glands with fewer complications than open surgery
3	**Krambeck et al. (2010)**	Journal of Urology	Outcomes of the first 1,000 HoLEP cases at Indiana University	300	Provided real-world data with low complication rates, including ~1% urethral stricture
4	**Cornu et al. (2015)**	European Urology	Meta-analysis of surgical treatments for BPH	270	Showed HoLEP's advantages in durability and safety; widely cited in international guidelines
5	**Ahyai et al. (2010)**	Journal of Urology	Meta-analysis comparing HoLEP and TURP	250	Confirmed comparable efficacy with fewer transfusions; pivotal for early consensus on HoLEP advantages

3.2 Leading Authors and Collaboration Network

A total of 285 authors contributed to the analysed publications. It is noteworthy that the top 10 authors were responsible for approximately 43% of all studies, indicative of a concentrated authorship structure.

James E. Lingeman(USA) led with 251 publications, primarily from Indiana University, reflecting his pioneering role and institutional impact.

Amy E. Krambeck(USA) has contributed to the field through 312 publications, including the widely cited 1,000-case series, which focuses on outcomes and surgical training.

Thomas R.W. Herrmann(Germany) has published extensively, with 455 publications to his name. He has played a central role in advancing endoscopic enucleation techniques, including thulium laser applications.

Sascha A. Ahyai(Germany) has authored 302 studies, notably randomised trials and systematic reviews that have provided substantial support for HoLEP's clinical validation.

Other significant contributors include Mark Fraundorfer(New Zealand), Mostafa Elhilali(Canada), and Alexander Bachmann(Switzerland). The presence of prominent researchers from China(e.g., Haitao Liu) and South Korea(e.g., Jae Heon Kim) further demonstrates the internationalisation of HoLEP research.

3.3 Collaboration Network

Co-authorship analysis revealed eight main clusters shaped by institutional and regional affiliations. The most prominent group is centred on Lingeman and Krambeck(USA), with extensive high-volume and technique-based contributions. Gilling's network(New Zealand–Europe) demonstrated notable international collaborations, particularly with Bachmann and de la Rosette. Herrmann is the leader of a European cluster that is engaged in multicentre laser trials.

The Asia-Pacific and Middle East/Turkey clusters are oriented towards regional studies and bibliometric work, although global integration remains limited. The expansion of multicentre initiatives has the potential to enhance data quality and comprehension of rare complications, such as urethral strictures.

3.4 Country Productivity and International Collaboration

This bibliometric analysis identified contributions from 18 countries. The United States led with 35 publications(36.5%), largely driven by high-volume HoLEP centres such as Indiana University and the Mayo Clinic, and key authors like Lingeman and Krambeck. The People's Republic of China followed with 20 publications(20.8%), reflecting its rapid uptake of HoLEP and increasing academic output. Germany(10 publications, 10.4%) and Turkey(9 publications, 9.4%) also made significant contributions, with Germany contributing through laser surgery trials led by Herrmann and Turkey through comparative and bibliometric studies.

Other contributors included New Zealand(the origin of HoLEP), Canada(notably McGill University under Elhilali), and the UK, with early involvement in clinical implementation and training.

Despite global interest, most studies originated from single-country institutions. Notable collaborations include USA–Canada(laser safety), USA–New Zealand(via Gilling), and a European network (Germany, France, UK, Netherlands), primarily producing reviews and guidelines. Examples like the 2015 Cornu et al. meta-analysis, with authors from seven countries, demonstrate the value of international efforts. However, original multinational clinical trials remain limited.

In conclusion, although international engagement in HoLEP research is growing, output remains concentrated in a few countries, primarily the USA, China, Germany, and Turkey. The enhancement of multicentre and cross-border collaborations has the potential to improve data quality and facilitate more effective evaluation of rare complications, such as urethral stricture. (See Figure 2.)

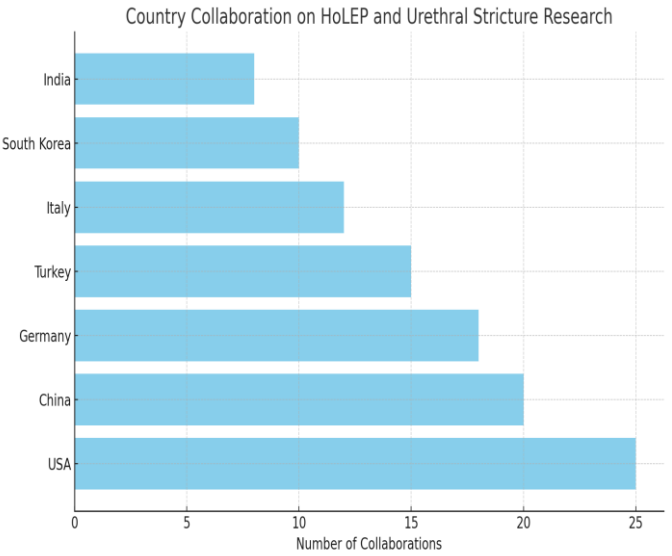


Figure 2. International Collaboration by Country Based on Co-authorship in HoLEP and Urethral Stricture Research

3.5 Keyword Co-occurrence Analysis: Thematic Clustering and Focus Areas of the Literature

The keyword co-occurrence analysis identified key research themes in the HoLEP and urethral stricture literature, revealing three main thematic clusters. As shown in Figure 3, terms such as ‘urethral stricture,’ ‘HoLEP,’ and ‘complication’ were among the most frequently used, highlighting the central focus areas.

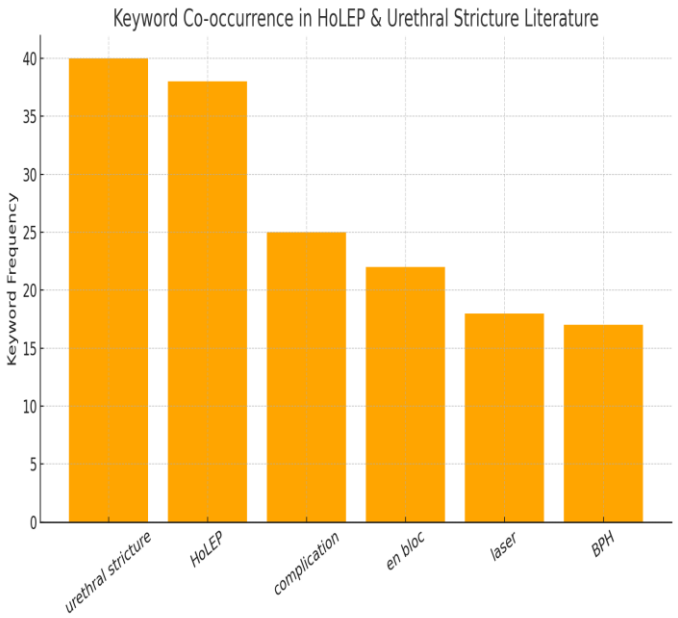


Figure 3. Frequency of top co-occurring keywords in HoLEP and urethral stricture publications

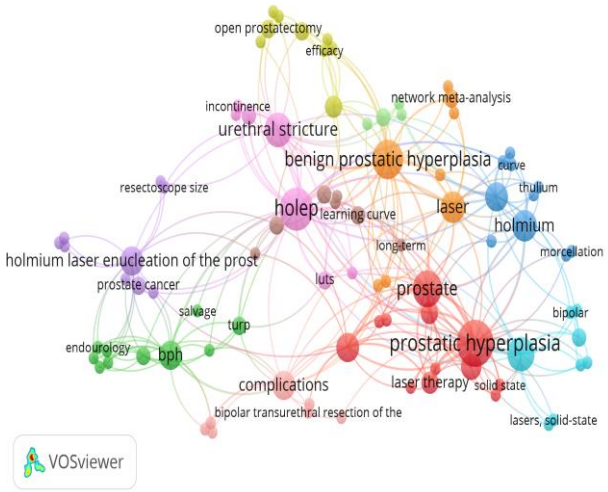


Figure 4. Thematic Clusters in HoLEP and Stricture Literature(VOSviewer)

3.6 Thematic Clustering of the Literature

The extant literature on HoLEP and urethral stricture is primarily grouped into three clusters:

Clinical Effectiveness:

Key words such as BPH, HoLEP, TURP, prostate volume, and laser enucleation highlight comparative studies, particularly in the context of large prostates, and underscore a focus on long-term outcomes and efficacy validation.

Perioperative Management and Technique:

The utilisation of terminology such as 'morcellation', 'catheterization time', 'hematuria', and 'learning curve' signifies endeavours to enhance surgical workflow, ensure safety, and address procedural training.

Postoperative Complications and Quality of Life:

The presence of urethral stricture, incontinence, IPSS, and sexual dysfunction all serve to emphasise the significance of patient-reported outcomes in this context.

It is noteworthy that there is an absence of dedicated research focusing on stricture management, thereby underscoring the necessity for targeted interventional studies in this area.

In summary, the research in HoLEP is structured around three pillars: efficacy, technical refinement, and postoperative outcomes. The underrepresentation of stricture management signifies a pivotal domain for future investigation. (see Figure 4)

Discussion

This bibliometric analysis provides a thorough overview of the evolving research landscape surrounding HoLEP and urethral stricture(7,12). The significant increase in publications, particularly since 2010, reflects the global adoption of HoLEP as the preferred surgical approach for benign prostatic hyperplasia (BPH), as endorsed by clinical guidelines such as the 2021 American Urological Association(AUA) guidelines(13).

The highly cited works of Gilling, Krambeck and Lingeman have played a key role in shaping the field(3,5,14). Their impact lies not only in their contribution to clinical outcomes, but also in their role in setting benchmarks for surgical safety. The low incidence of strictures reported has been attributed to superior endoscopic visibility, precise laser dissection and the absence of electrocautery.

An analysis of authorship networks showed that early research efforts were concentrated among a small number of high-volume centres, with collaborations largely national or institutional in nature. The limited global integration in the initial phases may be attributed to the technical demands of HoLEP and the need for specialised equipment(15). However, the recent increase in multicentre studies, particularly in Europe and Asia, signals a growing trend towards international cooperation(16–18). The development of global registries could improve the tracking of complications and standardise outcomes, particularly for rare events such as urethral stricture.

The application of keyword clustering analysis yielded the identification of three primary research domains, namely procedural efficacy, perioperative technique, and postoperative complications.

Urethral stricture was a prominent feature in the latter, but rarely constituted the primary focus. The extant literature on the subject remains limited in terms of targeted investigations into the aetiology, risk factors and preventive strategies. For instance, a 2024 study by Chen et al. identified smaller prostate size and urinary tract infections as potential predictors; however, these findings require validation in larger cohorts(19). The role of surgeon experience in stricture formation remains ambiguous and requires further study. Long-term data, extending beyond a period of 15 years, and outcomes in high-risk populations, including patients with a history of urethral disease, are limited. Addressing these gaps would facilitate the optimisation of patient selection and follow-up strategies. Nevertheless, the present study is not without its limitations, including the potential for author duplications and the underrepresentation of newer studies with fewer citations. In summary, while urethral stricture is a known complication of HoLEP, dedicated research remains limited.

It is recommended that future efforts place a priority on multicentre studies and international collaboration, with a view to generating high-quality evidence for prevention and management strategies. This, in turn, should result in an improvement in patient outcomes.

Conclusion

HoLEP has now become a widely accepted standard treatment for benign prostatic hyperplasia, with robust evidence supporting its long-term efficacy and safety. This study demonstrates a marked increase in publications related to HoLEP after 2010, indicative of both an escalation in clinical utilisation and a concomitant rise in academic interest. Although rare, urethral stricture remains a significant complication with the potential to impact quality of life. It is recommended that future research endeavours concentrate on the following three key areas: the implementation of preventative measures; the enhancement of patient-reported outcomes; and the cultivation of international multicentre collaboration. HoLEP is regarded as a successful model of surgical innovation, with results that are both durable and favourable in terms of safety.

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KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (2): 117- 121

Evaluation Of Infections Developing In Chronic Lmphocytic Leukemia Patients Receiving Ibrutinib Treatment

İbrutinib Tedavisi Alan Kronik Lenfositer Lösemi Hastalarında Gelişen Enfeksiyonların Değerlendirilmesi

Şebnem ÇALIK* 0000-0003-3798-4819
Zehra NARLI ÖZDEMİR 0000-0003-3237-320X**
Oktay BİLGİR 0000-0001-9579-0583**
Hale BÜLBÜL* 0009-0001-0759-0686**
Fatma KEKLİK KARADAĞ* 0000-0001- 6078-5944**
Seda KÖSE* 0000-0003-1418-5360**

*Sağlık Bilimleri Üniversitesi İzmir Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, İzmir
** Sağlık Bilimleri Üniversitesi İzmir Tıp Fakültesi, Hematoloji Anabilim Dalı, İzmir
*** İzmir Şehir Hastanesi, Hematoloji Kliniği İzmir

Yazışma Adresi: Şebnem ÇALIK
Sağlık Bilimleri Üniversitesi İzmir Tıp Fakültesi,
Enfeksiyon Hastalıkları ve Klinik
Mikrobiyoloji Anabilim Dalı, İzmir
E- posta: sebnemozkoren@yahoo.com

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Abstract

Aim: In this study, the frequency of serious infections and developing infections in chronic lymphocytic leukemia (CLL) patients receiving ibrutinib treatment in the Hematology Unit of a tertiary healthcare institution were evaluated retrospectively.

Method: The study was conducted retrospectively in a training and research hospital. Patients diagnosed with CLL and receiving ibrutinib treatment between November 2023 and January 2025 were included. Demographic data of the patients, concomitant diseases, treatment duration, antimicrobial prophylaxis use, exposure to hepatitis viruses and HIV, development status and location of infection, and microbiological findings were evaluated in electronic patient files. Statistical analyses were performed with SPSS 26 software. Continuous variables are presented as mean, standard deviation, and median. Categorical variables are presented as numbers and proportions.

Findings: The study included 50 patients and the median follow-up period was 17 months (range 2-66). The mean age of the patients was 70 (49-86) years and 33 (66%) were male. Thirty-four (68%) patients were receiving ibrutinib as their first treatment. At least one infectious disease developed in 18 (36%) of the patients. A total of 30 infectious diseases were detected. The most common infections were pneumonia (n: 18, 60%) ve urinary tract infection (n: 5, 16.7. The causative agent was isolated in 15 (50%) of the infections. Two (4%) patients developed urinary tract infection and died. Twelve patients were exposed to HBV. One patient was HBsAg positive. Four patients developed HBV reactivation. Three patients were exposed to HCV. No patient had latent tuberculosis or *P. jirovecii* infection.

Conclusion: CLL patients receiving ibrutinib treatment should be closely monitored for the development of bacterial infection and hepatitis B reactivation.

Keywords: Chronic lymphocytic leukemia, ibrutinib, infection, hepatitis B

Öz

Amaç: Bu çalışmada bir şehir hastanesinin Hematoloji Ünitesinde ibrutinib tedavisi alan kronik lenfositer lösemi (KLL) hastalarında ciddi enfeksiyon gelişme sıklığı ve gelişen enfeksiyonlar geriye yönelik olarak değerlendirilmiştir.

Yöntem: Bu çalışma Sağlık Bilimleri Üniversitesi İzmir Şehir Sağlık Uygulama ve Araştırma Hastanesi Hematoloji bölümünde Kasım 2023-Ocak 2025 tarihleri arasında KLL tanısı ile ibrutinib tedavisi alan hastalar dahil edilmiştir.

Elektronik hasta dosyalarında, hastaların demografik verileri, eşlik eden hastalıkları, tedavi süresi, antimikrobiyal profilaksi kullanımı, hepatit virüsleri ve HIV ile karşılaşma durumu, enfeksiyonun gelişme durumu ve yeri, mikrobiyolojik bulgular değerlendirilmiştir. İstatistiksel analizler, SPSS 26 yazılımı ile yapılmıştır. Sürekli değişkenler, ortalama, standart sapma ve medyan olarak sunulmuştur. Kategorik değişkenler sayılar ve oranlar olarak sunulmuştur.

Bulgular: Çalışmaya 50 hasta dahil edilmiş olup medyan takip süresi 17 aydır (aralığı 2-66). Hastaların yaş ortalaması 70(49-86)'tir ve 33'ü (%66) erkektir. Otuz dört (%68) hasta ilk tedavi olarak ibrutinib almaktadır. Hastaların 18'inde (%36) en az bir enfeksiyon hastalığı gelişmiştir. Toplam 30 enfeksiyon hastalığı saptanmıştır. En sık enfeksiyonlar sırasıyla pnömoni (n:14, %60) ve üriner sistem enfeksiyonudur (n:5, %16,7). Gelişen enfeksiyonların 15 (%50)'inde etken izole edilmiştir. İki hastada (%4) üriner sistem enfeksiyonu gelişmiş ve kaybedilmiştir. On iki hasta HBV ile karşılaşmıştır. Bir hasta HBsAg pozitiftir. Dört hastada HBV reaktivasyonu gelişmiştir. Üç hasta HCV ile karşılaşmıştır. Hiçbir hastada latent tüberküloz ve *P.jirovecii* enfeksiyonu görülmemiştir.

Sonuç: İbrutinib tedavisi alan KLL hastaları, bakteriyel enfeksiyon gelişmesi ve hepatit B reaktivasyonu açısından yakın izlenmelidir.

Anahtar Kelimeler: Kronik lenfositer lösemi, ibrutinib, enfeksiyon, hepatit B

Introduction

Ibrutinib, a Bruton Tyrosine Kinase (BTK) inhibitor, has established itself as a well-tolerated, effective non-chemotherapy treatment for chronic lymphocytic leukemia (CLL). Infections are a major cause of morbidity and mortality in CLL patients. Patient-specific risk factors that increase the risk of infection include age, comorbidities, patient functional status, number and type of previous treatments, disease stage, and refractory status to treatment (1).

Ibrutinib affects critical components of the immune system, as evidenced by the increased burden of infection reported in patients with inherited mutations in both Bruton tyrosine kinase and PIK3-delta. For these reasons, the risk of infection in patients treated with ibrutinib is higher than the general risk reported in the CLL population (1). In clinical studies in which ibrutinib was used alone or in combination with monoclonal antibodies, the rate of serious infection ranged from 12.8% to 45% (2). There are also case reports that ibrutinib treatment increases the risk of latent tuberculosis and hepatitis B exacerbation (1). Despite its increasing use in clinical practice, experience with the spectrum of infection remains limited. In this study, the frequency of serious infections and the infections that developed in CLL patients treated with ibrutinib in the Hematology Unit of a city hospital were evaluated retrospectively.

Material and Methods

The study was conducted retrospectively. After the approval of the Izmir City Hospital Non-Interventional Ethics Committee, patients diagnosed with CLL and treated with ibrutinib between November 2023 and January 2025 were included. Demographic data, concomitant diseases, duration of treatment, use of antimicrobial prophylaxis, exposure to hepatitis viruses and HIV, microbiological findings were evaluated in electronic patient files.

The primary outcome of the analysis was the rate of severe infection defined as grade 3 or higher according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.24 (3). According to these criteria, the severity of the infection describes situations requiring intravenous broad-spectrum antibiotic, antifungal, or antiviral treatments, and invasive interventions requiring hospitalization. Patients hospitalized for infectious disease by a hematologist were evaluated for survival up to 30 days later.

Study population

Adult patients (>18 years) who received ibrutinib for CLL treatment for one or more months were included in the study. Exclusion criteria were discontinuation of treatment within 1 month of initiation of treatment and follow-up at other institutions.

Statistical analysis

Statistical analyses were performed using IBM® SPSS® 26 (SPSS, United States) software. Continuous variables are presented as mean, standard deviation, and median. Categorical variables are presented as numbers and proportions.

Results

Ibrutinib treatment was administered to 52 patients who were followed up with a diagnosis of chronic lymphocytic leukemia during the study period. Two patients were excluded due to missing data during follow-up. Fifty patients were included in the study and the median follow-up was 17 months (range 2-66). The mean age of the patients was 70 (49-86) years and 33 (66%) were male. Thirty-four (68%) patients received ibrutinib as their first treatment. Twenty-five (50%) patients had a concomitant disease. The most common concomitant disease was diabetes mellitus (n:15, 60%). Demographic characteristics of the patients are shown in Table 1.

Table 1. Demographic and clinical characteristics of patients

Variable	Number (%)	
Disease status	New diagnosed	34
	Relapsed/refractory	16
Concomitant diseases	Diabetes mellitus	15
	COPD*	5
	CAH**	4
	Connective tissue disease	3
	Malignancy	3
	Chronic renal failure	3
	Cirrhosis	2

* Chronic obstructive pulmonary disease
** Coronary artery disease

Four (8%) patients received levofloxacin, three (6%) patients received trimethoprim-sulfamethoxazole, five (10%) patients received valacyclovir, and three (6%) patients received entecavir prophylaxis.

Of the 50 patients receiving ibrutinib treatment, 18 (36%) developed at least one infectious disease. A total of 30 infectious diseases developed. These infections were pneumonia (n: 14, 46.7%), urinary tract infection (n: 5, 16.7%), and chronic obstructive pulmonary disease exacerbation (n: 4, 13.3%), respectively. Infections observed in patients receiving ibrutinib treatment are shown in Table 2.

Table 2. Infections observed in patients receiving ibrutinib treatment

Infection	Number (%)	
Pneumonia	Bacterial	12 (%40)
	Viral	5 (%16.7)
	Fungal	1 (%3.3)
Soft tissue infection	2 (%6.7)	
Urinary tract infection	5 (%16.7)	
Peritonitis	2 (%6.7)	
Zona zoster	1 (%3.3)	
Otitis media	2 (%6.7)	

The agent was isolated in 4 (%50) of 8 patients who developed bacterial pneumonia.Two of these agents were *Pneumococcus*, 1 was *H. influenzae*, and 1 was *Acinetobacter baumannii*. In 3 of the patients who developed viral pneumonia, the causative agent was COVID-19, and in 2, it was Influenza type A. In fifteen (50%) of the infections, the causative agent was isolated in the cultures. The agents grown in the culture materials taken from the patients are shown in Table 3.

Table 3. Bacteria isolated in culture materials

Etken	Sayı (%)
Escherichia coli	4 (%26.8)
Klebsiella pneumoniae	2 (%13.3)
Hemophilus influenzae	2 (%13.3)
Moraxella catarrhalis	2 (%13.3)
Pnömokok	3(%20)
Enterococcus faecalis	2 (%13.3)

Two patients (4%) died due to urinary tract infection and sepsis. A 69-year-old female patient had chronic hepatitis C and liver cirrhosis. The causative agent was *Klebsiella pneumoniae*. The other patient was a 79-year-old female. The causative agent *was E. faecalis*. The patient had no accompanying disease other than chronic HBV carriage.

A 69-year-old male patient with liver cirrhosis due to HBV had herpes zoster, followed by bacterial pneumonia and HBV exacerbation. The patient recovered.

Nine (18%) patients were not investigated for exposure to HBV, HCV and HIV before ibrutinib treatment. Seventeen (34%) patients were susceptible to HBV and all patients were vaccinated after the test results were obtained. Twelve patients had exposure to HBV. One patient was HBsAg positive. Three patients had exposure to HCV. No patient was found to be infected with HIV. The patients' exposure status to HBV, HCV and HIV is shown in Table 4.

Table 4. Patients' exposure to HBV, HCV, HIV

	Number(%)	Prophylaxis	Reactivation
HBV serology not investigatd	9	0	0
HBV naive	1	0	0
Isolated antiHBc total(+)	4	1	1
HBsAg(-),AntiHBc total(+),AntiHbs (+)	8	0	3
HbsAg (+), AntiHBctotal (+), AntiHbs(-)	1	1	0
Incomplet HBV test	1	0	0
HBV vaccinated	10	-	-
antiHCV(+), HCVRNA(+)	2	-	-
HCV treated	1	-	-
antiHIV	0	-	-

HBV prophylaxis (entecavir) was used in 3 patients. An isolated anti-HBc total positive patient used entecavir prophylaxis irregularly. Hepatitis B reactivation developed in this patient. HBsAg became negative in the 48th month of entecavir prophylaxis in a HBsAg positive patient. HBV reactivation developed in 4/12 (33.3%) patients who had encountered hepatitis B and were not recommended for prophylaxis. None of them died due to HBV activation.

Three (6%) patients had encountered hepatitis C. One patient had received antiviral treatment five years ago, was HCV RNA negative, and had no cirrhosis. Two patients had chronic HCV infection. One patient was detected as genetic type 3. HCV RNA was 723,000 IU/mL, and had liver cirrhosis. The patient could not complete the sofosbuvir-ledipasvir treatment due to nausea and vomiting. The patient died due to urinary tract infection due to *K. pneumonai*e during follow-up. HCV RNA: 2810000 IU/mL, genotype 1b was detected in the other chronic HCV patient. The patient, who has been diagnosed with HCV for ten years, has not accepted antiviral treatment. His follow-up is ongoing.

No patient had latent tuberculosis or *Pneumocystis jirovecii* pneumonia. Solid organ tumors developed in two (4%) patients. Ibrutinib treatment was started as the first treatment in a 77-year-old patient, and malignant melanoma (rectum) developed in the 64th week of treatment. The other patient developed lung cancer.

Discussion

Of the 50 patients with CLL who received ibrutinib treatment, 18 (36%) developed at least one infectious disease. The most common infectious diseases were pneumonia (60%), and urinary tract infection (16.6%) respectively. In a phase 2, open-label, multicenter study, the most common grade ≥ 3 infections in 144 patients with relapsed or refractory CLL who received ibrutinib (RESONATE-17) were pneumonia (14.5%) and urinary tract infection (5%) (3). In the extended follow-up of the RESONATE study, the long-term safety profile of ibrutinib was consistent with the 3-year follow-up in the phase 2 study (4). The most common infections (> 10%) included upper respiratory tract infections, sinusitis, pneumonia, and urinary tract infections. It has been reported that the frequency of infection development in patients receiving regular ibrutinib treatment decreases over time, and this is thought to be related to the improvement of immunity

One patient developed a probable fungal infection in the study. In a multicenter study of invasive fungal infections in CLL patients treated with ibrutinib in France, 27 of 33 IFDs were proven, probable, or possible invasive aspergillosis [5]. Forty percent of cases were intracranial. Other infections included cryptococcosis (n: 4), mucormycosis (n: 1), and *Pneumocystis jirovecii* pneumonia (PJP) (n: 1). Eighty-five percent of fungal infections occurred within the first six months after starting ibrutinib. Most cases were associated with other conditions that may contribute to a decreased antifungal response, such as corticosteroids, neutropenia, or combined immune-chemotherapy. In a small study of central nervous system lymphoma, 39% of patients treated with ibrutinib and corticosteroids developed aspergillosis (6). Early-onset fungal infection appears typical after initiation of ibrutinib therapy, with the lungs and central nervous system being the most common sites of infection (7). Although antifungal prophylaxis is not necessary for the general ibrutinib-treated patient population, special attention and close monitoring may be beneficial for patients with high-risk features, especially during the first months of treatment.

According to the results of our study, HBV reactivation developed in 33.3% of patients who had encountered hepatitis B. Three patients had used ibrutinib for 36 weeks or more. In a single center experience in the literature, seven CLL patients with hepatitis B positive serology (HBsAg neg/HBcAb positive) who were treated with ibrutinib did not receive any antiviral prophylaxis and were closely monitored for HBsAg and HBV DNA. After a mean follow-up of 25 months, none of the patients showed HBV reactivation (8).

Chronic hepatitis B reactivation occurs in approximately 20-50% of HBsAg positive patients and 1-10% of HBsAg negative/antiHBc positive patients in hematological patients receiving immunosuppressive therapy. HBV screening is recommended for planning antiviral prophylaxis in all patients who will receive immunosuppressive therapy (9). In our study, HBV, HCV and HIV exposure before ibrutinib treatment was not investigated in 9 (18%) patients. It is important to obtain a detailed history of past infections from patients who will start ibrutinib treatment and to test for hepatitis B, hepatitis C and HIV serology. Physicians can be informed about hepatitis serology screening for all patients receiving immunosuppressive therapy. Hepatitis B, hepatitis C and HIV screening alert can be added to the hospital automation program for hematology and oncology outpatient clinics.

Limitation

The limitations of our study are; the inclusion of a relatively small number of patients, and the collection of data according to electronic medical records since it is retrospective. Another limitation is that we evaluated ibrutinib patients used in primary care and relapse together.

Conclusison

As a result; in this study where infections developed in 50 patients receiving ibrutinib treatment were evaluated retrospectively, the most common infections were pneumonia and urinary tract infection, respectively. HBV reactivation developed in 33.3% of patients exposed to HBV. Two patients (4%) died due to bacterial infection. It was thought that future well-designed prospective studies with longer follow-up periods are needed to truly evaluate the relationship between ibrutinib and the risk of infection in CLL patients.

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OLGU SUNUMU /CASE REPORT
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Incidental Diagnosis of Zinner Syndrome in a Male Presenting with Right Upper Quadrant Pain: A Case Report

Sağ Üst Kadran Ağrısıyla Başvuran Bir Erkekte Rastlantısal Zinner Sendromu Tanısı: Olgu Sunumu

Ali SALBAS* 0000-0002-6157-6367

* İzmir Kâtip Çelebi Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, Radyoloji Anabilim Dalı, İzmir, Türkiye

Yazışma Adresi: Ali SALBAS
İzmir Kâtip Çelebi Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, Radyoloji Anabilim Dalı, İzmir, Türkiye
E-Mail: dralisalbas@gmail.com

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Abstract

Zinner syndrome is an uncommon congenital condition caused by developmental anomalies of the mesonephric (Wolffian) duct during embryogenesis. It is characterized by unilateral renal agenesis, ipsilateral seminal vesicle cyst, and ejaculatory duct obstruction. While frequently asymptomatic, some individuals may experience symptoms such as pelvic discomfort, painful urination, blood in semen, or reproductive difficulties. In this report, we present a 48-year-old male who was admitted with right upper quadrant pain and was found to have radiologic findings consistent with Zinner syndrome. Computed tomography revealed renal agenesis, a cystic lesion in the seminal vesicle, and dilation of the ipsilateral vas deferens. Although the patient's presenting complaint was not directly related to the syndrome, the accompanying radiologic findings supported the diagnosis. This rare condition should be considered, especially in male patients with unilateral renal agenesis, and radiologic imaging methods should be utilized in the diagnostic process.

Keywords: Zinner syndrome, Renal agenesis, Seminal vesicle, Computed tomography, Cyst

Öz

Zinner sendromu, embriyogenez sırasında mezonefrik (Wolffian) kanalın gelişimsel anomalilerine bağlı olarak ortaya çıkan nadir bir konjenital durumdur. Unilateral renal agenezi, ipsilateral seminal vezikül kisti ve ejakülatör kanal obstrüksiyonu ile karakterizedir. Genellikle asemptomatik seyretmesine rağmen bazı bireylerde pelvik rahatsızlık, ağrılı işeme, menide kan veya üreme ile ilgili sorunlar gibi belirtiler görülebilir. Bu olgu sunumunda, sağ üst kadran ağrısı ile başvuran ve yapılan radyolojik değerlendirmede Zinner sendromu ile uyumlu bulgular saptanan 48 yaşındaki erkek bir hasta sunulmuştur. Bilgisayarlı tomografide renal agenezi, seminal vezikülde kistik lezyon ve ipsilateral duktus deferens dilatasyonu saptanmıştır. Hastanın başvuru şikâyeti sendromla doğrudan ilişkili olmamakla birlikte eşlik eden radyolojik bulgular tanıyı desteklemiştir. Bu nadir durum, özellikle unilateral renal agenezi saptanan erkek hastalarda akılda bulundurulmalı ve tanı sürecinde radyolojik görüntüleme yöntemlerinden yararlanılmalıdır.

Anahtar Kelimeler: Zinner sendromu, Renal agenezi, Seminal vezikül, Bilgisayarlı tomografi, Kist

Introduction

Zinner syndrome is an uncommon developmental disorder of the male urogenital tract that arises due to anomalies in the embryological formation of the mesonephric (Wolffian) duct. Originally described in 1914, Zinner syndrome typically presents with three key features: unilateral absence of a kidney, a cystic lesion in the seminal vesicle on the same side, and obstruction or maldevelopment of the ejaculatory duct (1).

The condition results from failure of the ureteric bud, which arises from the mesonephric duct during embryogenesis, to fuse with the metanephric blastema, leading to renal agenesis, ejaculatory duct malformation, and seminal vesicle cyst formation (2,3). Although ultrasound is frequently preferred as the first-line imaging method, magnetic resonance imaging (MRI) provides superior anatomical detail and is the most reliable modality for evaluating seminal vesicle cysts and detecting ejaculatory duct obstruction (5). To date, approximately 200 cases have been reported in the literature (4,6), with an estimated prevalence of 0.002–0.004% (7). Due to its rarity and nonspecific presentation, diagnosis may be delayed. This report presents a 48-year-old male diagnosed incidentally with Zinner syndrome based on radiologic findings during evaluation for unrelated abdominal pain. Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Case Report

A 48-year-old male presented to the emergency department with right upper quadrant abdominal pain.

His medical history was unremarkable, except for a previously known congenital solitary kidney, which had not been previously investigated in detail. Physical examination showed no abnormal findings. Laboratory tests revealed leukocytosis (WBC: 13.76 $\times 10^9$/L; reference: 4.00–10.00 $\times 10^9$/L) and neutrophilia (NEU: 10.15 $\times 10^9$/L; reference: 1.80–7.00 $\times 10^9$/L), with other hematologic and biochemical parameters within normal limits. Serum amylase was mildly elevated (150 U/L). Urinalysis showed 2+ leukocytes without evidence of infection. Cardiac markers, coagulation tests, and C-reactive protein (CRP) were normal.

Contrast-enhanced abdominal computed tomography (CT) revealed absence of the left kidney and no ectopic renal tissue, consistent with left renal agenesis. A well-defined 54 × 44 mm cystic lesion was observed at the location of the left seminal vesicle, along with a 12 mm cyst anterior to the prostate gland. The left vas deferens appeared markedly dilated compared to the contralateral side (Figure 1). These imaging features collectively supported the diagnosis of Zinner syndrome.

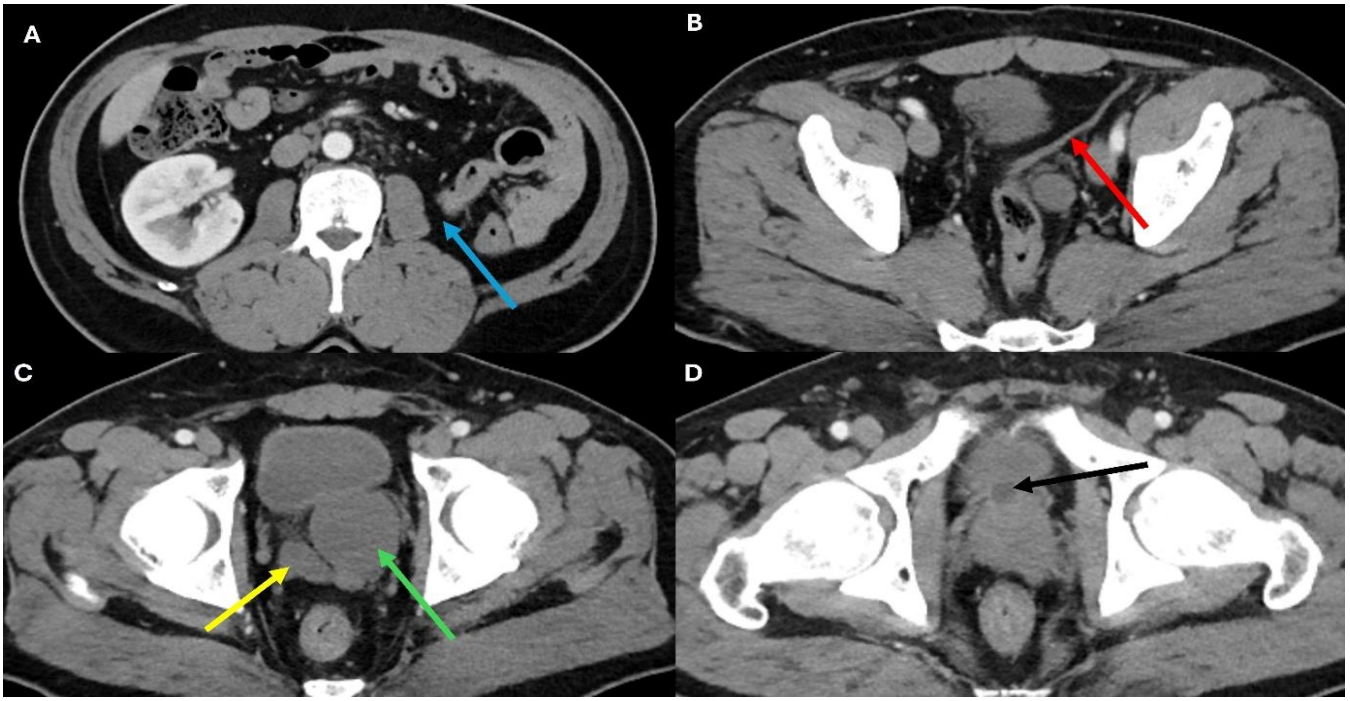

Figure 1. Contrast-enhanced axial abdominal CT images of the patient. In the first image (A), the left kidney is not visualized in its normal anatomical location (blue arrow). In the second image (B), dilation of the left vas deferens is observed (red arrow). In the third image (C), the right seminal vesicle appears normal (yellow arrow), whereas a cystic lesion originating from the left seminal vesicle is noted (green arrow). In the final image (D), a well-defined cystic lesion is seen anterior to the prostate gland (black arrow).

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Discussion

Since its original identification in 1914, the total number of Zinner syndrome cases reported has remained limited. A systematic review identified 214 cases published between 1999 and 2020 (6). Diagnosis is often incidental, discovered through imaging performed for unrelated symptoms (3,6).

In this case, although the patient presented with abdominal pain, the complaints were not directly attributable to Zinner syndrome. However, the co-occurrence of unilateral renal agenesis, seminal vesicle cyst, and ipsilateral vas deferens dilation on imaging supported the diagnosis. The literature emphasizes that the combination of renal agenesis and pelvic cystic lesions—especially at the level of the seminal vesicle—should prompt consideration of this syndrome (5,7).

Magnetic resonance imaging (MRI) is particularly effective in characterizing seminal vesicle cysts and evaluating ejaculatory duct anatomy. T2-weighted images typically show these cysts as hyperintense, while T1-weighted signals vary depending on the cyst contents (5). In our case, CT was sufficient to establish the diagnosis based on these typical findings. Clinical manifestations of Zinner syndrome can vary and may include nonspecific symptoms such as discomfort in the pelvis, urinary symptoms, or reproductive complaints (4).

Although the presenting complaint in this case was unrelated, the combination of radiologic findings justified the diagnosis.

Management depends on the presence or absence of symptoms. Asymptomatic patients are often managed conservatively, while those with symptoms may require surgical or minimally invasive interventions (2,6). In this case, due to the absence of urogenital symptoms, surgical treatment was not indicated, and the patient's initial complaint resolved with supportive care. According to current literature, conservative management with periodic clinical and imaging surveillance is recommended for asymptomatic individuals, whereas surgical intervention is reserved for symptomatic or complicated cases (4,6).

Conclusion

Zinner syndrome should be considered in male patients presenting with unilateral renal agenesis and pelvic cystic lesions. Radiologic imaging plays an important role in identifying hallmark features. Even in cases where presenting symptoms are unrelated, accurate recognition of this anomaly ensures proper diagnosis and enables appropriate clinical follow-up.

Conflict of interest: The author declares no conflicts of interest.

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