EGE KLİNİKLERİ TIP DERGİSİ
MEDICAL JOURNAL OF AEGEAN CLINICS

Cilt /No: 63 **Sayı**/No: 1 **Nisan** /April 2025

İÇİNDEKİLER/CONTENTS

KLİNİK ÇALIŞMALAR/ CLINICAL TRIALS

1. Predictors Of Long Procedure Time in Patients With ST-Segment Elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention
Serdar SÖNER ve Ark.

2. Evaluation of Congenital Diaphragmatic Hernia Cases Diagnosed Prenatally Between 2016 and 2023
Raziye TORUN ve Ark.

3. ***Evaluation of Shock Appropriateness in Patients Admitted to the Emergency Department After ICD Shocking***
Efe KANTER ve Ark.

4. ***Evaluation Of Bifurcation Lesion Procedures Performed In A Tertiary Centre***
Dogac Caglar GURBUZ ve Ark.

5. Analysis of Early Term Results of Elective Ascending Aortic Aneurysm Surgery
Ahmet DOLAPOĞLU ve Ark.

6. Human Equivalent Phantom Computed Tomography Study for Foreign Body Detection in the Body
Halil İbrahim ÖZDEMİR ve Ark.

7. Relationship Between Serum Uric Acid Level And Frequency Of Gastrointestinal Bleeding in Patients Using New Oral Anticoagulants
Eyyüp ERKİZ ve Ark.

OLGU SUNUMU/ CASE REPORT

1. Delayed-Onset Morbilliform Drug Eruption Induced by Hydroxychloroquine: A Clinical Observation in a Patient with Systemic Sclerosis
Gülşah ÇELİK

EGE KLİNİKLERİ TIP DERGİSİ
THE MEDICAL JOURNAL OF AEGEAN CLINICS

«EGE KLİNİKLERİ TIP DERGİMİZ HAKEMLİ BİR DERGİDİR»

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

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

Uz. Dr. Hikmet Mücahit ATALAY
Dernek Başkanı
Chairman of the society

Sorumlu Müdür / Director in charge
Doç. Dr. Tuncay KIRIŞ

Yönetim Adresi/ Administration address

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

Dökümantasyon ve Tasarım
Documentation and Design
Aslı GİRİT

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

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

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

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

DERGİMİZİN YAZIM DİLİ 2025 YILI İTİBARİYLE İNGİLİZCE'DİR.

DANIŞMA KURULU/ADVISORY BOARD

***Prof. Dr. Murat AKSUN**-İ.K.Ç.Ünv.A.E.A.Hast., Anesteziyoloji Reanimasyon Kliniği*
***Prof. Dr. Galip AKHAN**-İ.K.Ç.Ünv. A.E.A.Hast., Nöroloji Kliniği*
***Op. Dr. İsmail AKKOL** Atatürk Eğitim Ve Araştırma Hastanesi Beyin Cerrahi Kliniği*
***Prof. Dr. Ahmet ALACACIOĞLU** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Tıbbi Onkoloji*
***Uzm. Dr. H. Mücahit ATALAY-** A.E.A.Hast., Nükleer Tıp*
***Prof. Dr. Mehmet Serdar BAYATA-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Kardiyoloji Kliniği*
***Uz. Dr. Emine Ebru BAYAR-** Atatürk Eğitim Ve Araştırma Hastanesi Nükleer Tıp*
***Doç. Dr. Çetin AYDIN -**E.A.Hast. Kadın Doğum Kliniği*
***Prof. Dr. Cengiz AYDIN-** İzmir Şehir Hastanesi,Genel Cerrahi A.B.D.*
***Uz. Dr. Ayhan AYDIN** SBÜ Dr. Suat Seren Göğüs Hastalıkları ve Cerrahisi Eğitim Araştırma Hastanesi Radyasyon Onkolojisi Kliniği*
***Prof. Dr. Serpil AYDOĞMUŞ-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Kadın Hastalıkları Ve Doğum Kliniği*
***Doç. Dr. Kaan BAL -** A.E.A.Hast. Üroloji Kliniği*
***Doç. Dr. Uğur BALCI -** A.E.A.Hast. Üroloji Kliniği*
***Doç. Dr. Korhan Barış BAYRAM-** İ.K.Ç.Ünv. A.E.A.Hast. Fizik Tedavi ve Reh. Kliniği*
***Uzm. Dr. İlgül BİLGİN-** A.E.A.Hast ., Dermatoloji Kliniği*
***Prof. Dr. Yeşim BECKMANN-** İ.K.Ç.Ünv. A.E.A.Hast., Nöroloji Kliniği*
***Prof. Dr. Şahin BOZOK-** Bakırçay Üniversitesi Hast., . Kalp Damar Cer. A.B.D.*
***Prof. Dr. Tuğrul BULUT –**İ.K.Ç.Ü. Atatürk Eğitim ve Araştırma Hastanesi Ortopedi ve Travmatoloji Kliniği*
***Prof. Dr. Erdem CANDA**-Koç Üniversitesi Üroloji A.B.D*
***Prof. Dr. Fulya ÇAKALAĞAOĞLU-** A.E.A.Hast., Patoloji Labaratuvarı*
***Prof. Dr. Mehmet ÇELEBİSOY-** A.E.A.Hast., Nöroloji Kliniği*
***Prof. Dr. Giuseppe DODİ**-Padua University Hospital, First General Surgery Unit*
***Uz. Dr. Neşe EKİNCİ-** Atatürk Eğitim Ve Araştırma Hastanesi Patoloji Laboratuvarı*
***Prof. Dr. Atilla ÇÖKMEZ-** Atatürk Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniği*
***Prof. Dr. Demet ETİT**-Acıbadem Sağlık Grubu Patoloji*
***Prof. Dr. Hamza DUYGU** -Yakın Doğu Üniversitesi Hastanesi Kardiyoloji A.B.D.*
***Prof. Dr. Mustafa Fazıl GELAL-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Radyoloji Kliniği*
***Prof. Dr. Sacit Nuri GÖRGEL-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Üroloji Kliniği*
***Prof. Dr. Orhan GÖKALP-** İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Kalp Damar Cer. A.B.D.*
***Doç. Dr. Şeref GÜLSEREN-** Atatürk Eğitim Ve Araştırma Hastanesi Psikiyatri Kliniği*
***Prof. Dr. Ali GÜRBÜZ-** Atatürk Eğitim Ve Araştırma Hastanesi Kalp Damar Kliniği*
***Prof. Dr. Abdülkadir İMRE** İ.K.Ç.Ünv. A.E.A.Hast.,Kulak Burun Boğaz Kliniği*
***Prof. Dr. Mehmet HACIYANLI-** İ.K.Ç.Ünv. A.E.A.Hast.,Genel Cerrahi Kliniği*
***Doç. Dr. Haldun KAR** A.E.A.Hast.,Genel Cerrahi Kliniği*
***Prof. Dr. Erdinç KAMER**-Tepecik.E.A.Hast.,Genel Cerrahi Kliniği*
***Prof. Dr. Mustafa KARACA-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Kardiyoloji Kliniği*
***Doç. Dr. Volkan KARAÇAM-** Dokuz Eylül Ünv. Hastanesi, Göğüs Cer. ABD.*
***Prof. Dr. Ali KARAKUZU-** İ.K.Ç.Ünv. A.E.A.Hast., Dermatoloji Kliniği*
***Prof. Dr. Kaan KATIRCIOĞLU-** İzmir Tınaztepe Üniversitesi Özel GalenHastanesi Anesteziyoloji Reanimasyon Kliniği*
***Doç. Dr. Esin EVREN KILIÇASLAN-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Psikiyatri Kliniği*
***Uz. Dr. Doğu Barış KILIÇÇIOĞLU-** Atatürk Eğitim Ve Araştırma Hastanesi Adli Tıp Kliniği*
***Prof. Dr. Mehmet Hicri KÖSEOĞLU-** Bakırçay Üniversitesi Hast., Tıbbi Biyokimya ABD.*
***Prof. Dr. Yüksel KÜÇÜKZEYBEK** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Tıbbi Onkoloji*
***Prof. Dr. Ahmet Levent METE-** Medical Point, Psikiyatri Kliniği*
***Prof. Dr. Okay NAZLI-** Muğla Sıtkı Koçman Ünv., Genel Cerrahi ABD.*
***Prof. Dr. Cem NAZLI-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Kardiyoloji Kliniği*
***Doç. Dr. Meltem AYHAN ORAL-** Atatürk Eğitim Ve Araştırma Hastanesi Plastik Rekonstrüktif ve Estetik Cerrahi Kliniği*
***Prof. Dr. Orhan OYAR-** İ.K.Ç.Ünv. A.E.A.Hast., Radyoloji*
***Doç. Dr. Güzide Gonca ÖRÜK** Atatürk Eğitim Ve Araştırma Hastanesi Endokrinoloji Polikliniği*
***Prof. Dr. Haydar Kazım ÖNAL** Atatürk Eğitim Ve Araştırma Hastanesi Kulak Burun Boğaz Kliniği*
***Prof. Dr. F. Esra ÖZER -**Muğla Sıtkı Koçman Ünv, Neonataloji Kliniği*
***Prof. Dr. Peter PETROS-** UNSW Academic Dept. Of Surgery St Vincent's Clinical School, University of Western Australia*
***Prof. Dr. Ercan PINAR-** A.E.A.Hast., KBB Kliniği*
***Prof. Dr. Taylan Özgür SEZER** -Ege Ünv. Tıp Fakültesi Genel Cerrahi A.B.D.*
***Prof. Dr. Dilek SOLMAZ** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Romatoloji*
***Uz. Dr. Mehmet SONBAHAR-** Atatürk Eğitim Ve Araştırma Hastanesi Dâhiliye Kliniği*
***Uzm. Dr. Atilla ŞENCAN-** A.E.A.Hast.,Anesteziyoloji ve Reanimasyon Kliniği*
***Op. Dr. Bekir TATAR-** A.E.A.Hast., KBB Kliniği*
***Doç. Dr. Fatma TATAR-** A.E.A.Hast., Genel Cerrahi Kliniği*
***Doç. Dr. Cengiz TAVUSBAY-** A.E.A.Hast., Genel Cerrahi Kliniği*
***Prof. Dr. Tuba TUNCEL-** İ.K.Ç.Ü. İzmir Şehir Hastanesi Çocuk Alerji ve İmmünoloji Bilim Dalı*
***Prof. Dr. Muzaffer Onur TURAN-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Göğüs Hastalıkları Kliniği*
***Doç. Dr. Nesrin TÜRKER-** İ.K.Ç.Ünv. A.E.A.Hast., İntaniye Kliniği*
***Uz. Dr. Muhsin Engin ULUÇ** Atatürk Eğitim Ve Araştırma Hastanesi Radyoloji Kliniği*
***Prof. Dr. Şeyda UĞURLU-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Göz Hastalıkları Kliniği*
***Doç. Dr. Dilek UYSAL-**A.E.A.Hast., Kadın Doğum Kliniği*
***Prof. Dr. Erden Erol ÜNLÜER-** Uşak Ünv. A.E.A.Hast., Acil Tıp ABD.*
***Prof. Dr. Nurettin ÜNAL-** Medical Point Çocuk Kardiyolojisi*
***Prof. Dr. Bülent ÜNAL -**Osman Gazi Üniversitesi, Genel Cerrahi A.B.D.*
***Doç. Dr. Sezgin VATANSEVER-** Atatürk Eğitim Ve Araştırma Hastanesi Gastroenteroloji Kliniği*
***Doç. Dr. Aşkın YILDIZ-** A.E.A.Hast., Kadın Doğum Kliniği*
***Prof. Dr. Levent YILIK-** İ.K.Ç.Ü. Atatürk Eğitim Ve Araştırma Hastanesi Kalp Damar Kliniği*
***Prof. Dr. Seyran YİĞİT-** İzmir Tınaztepe Buca Tıp Merkezi, Patoloji Labaratuvarı*
***Prof. Dr. Süreyya GÜL YURTSEVER-** İ.K.Ç.Ünv. A.E.A.Hast., Mikrobiyoloji Labaratuvarı*
***Uz. Dr. Samim YURTSEVER-** Atatürk Eğitim Ve Araştırma Hastanesi Radyasyon Onkolojisi*
***Prof. Dr. Derya ARSLAN YURTLU-** İzmir Şehir Hastanesi Anestezi ve Reanimasyon A.B.D.*
***Uz. Dr. Kamil YÜCEL-** Atatürk Eğitim Ve Araştırma Hastanesi Radyoloji Kliniği*

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)

YAZI GÖNDERİMİ

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

MAKALE GÖNDERİM KURALLARIMIZ

• Telif Hakkı Devir Formu tüm yazarlar tarafından imzalanılmalıdır.

• Makalenin tüm yazarları ORCID numaralarını göndermelidir. (Http://orcid.org adresinden ücretsiz olarak ORCID ID edinebilir ve kayıt olabilirsiniz. Dergimizin sayfa düzenine uygun olarak ; Yazının ilk sayfası.)

• Etik Kurul Onayı'nın kendisi (Etik Kurul Onay Belgesi) çalışma ile birlikte gönderilmelidir. Ayrıca çalışmanın başlığı Etik Kurul Belgesi'ndeki ile birebir aynı olmalıdır.

• 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

**

***

Yazışma Adresi: Ali BİGE

Zonguldak Bülent Ecevit Üniversitesi,

Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, ZONGULDAK

Gsm: 0532,,,,,,,

e-mail adresi: alibige@gmail.com

GENERAL INFORMATION

The Medical Journal of Aegean Clinics is a periodical of the Society of Aid to Hospitals of İzmir and Fosterage of Scientific Investigations. The journal is published three times in a year. The printing months are April, August and December. The articles which could be prospective or retrospective on investigational studies, case reports, letter to the editor and reviews of every aspect of medicine are published. The studies should have paramount ethical and scientific standards as well as no commercial concerns. Articles are accepted for publication on the condition that they are original, are not under consideration by another journal, or have not been previously published.

The studies that are sent to the journal provided that the study is appropriate for formal principles are evaluated by the head editor and two peer reviewers.

The study is published once the approval of the reviewers have been taken. Hence, the authors should make the necessary changes in accordance with the reviewers comments.

SCIENTIFIC RESPONSIBILITY

All authors should have contributed to the article directly either academically or scientifically. All persons designated as authors should plan or perform the study, write the paper or review the versions, approve the final version. It is the authors' responsibility to prepare a manuscript that meets scientific criterias.

ETHICAL RESPONSIBILITY

Manuscripts concerned with human studies must contain statements indicating that informed, written consent has been obtained, that studies have been performed according to the World Medical Association Declaration of Helsinkihttp://www.wma.net/en/30/publications/10policies/b3/index.html) and that the procedures have been approved by a local ethics committee. The approval form of the ethics committee should be sent along with the manuscript. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.All Authors are responsible for the quality, accuracy, and ethics of the work. *The Medical Journal of Aegean Clinics* takes no responsibility for the Authors' statements. The manuscripts, once accepted, become property of the journal and cannot be published elsewhere without the written permission of the Journal.

STATISTICALLY EVALUATION

All retrospective, prospective and experimental research articles must be evaluated in terms of biostatics and it must be stated together with appropriate plan, analysis and report. p values must be given clearly in the manuscripts (e.g. p=0.014).

LANGUAGE

The official language of the Journal is English.

COPYRIGHT STATEMENT

A copyright transfer statement indicating that the ' *The copyright to this article is transferred to The Medical Journal of Aegean Clinics and will be effective if and when the article is accepted for publication'* should be sent in the content of cover letter. No payment is done to authors for their articles.

ARTICLE TYPES

Reviews: The reviews highlight or update new and/or controversial areas. The editor of the Journal invites author/authors for reviews.

Original articles: Original articles describe the results of basic or clinical studies or clinical trials. Original articles should not exceed 2500 words and 25 references.

Case Reports: The Journal publishes significant case reports related to the every aspect of medicine. The number of authors should not exceed 6 in the case reports.

Letter to the Editor: Text should not exceed 400 words, and include no more than 3 references (one of them should be the commenting article). Letters are selected for their importance, relevance, and originality; not all letters submitted can be published.

MANUSCRIPT SUBMISSION

All manuscripts must be submitted electronically to the idhdergi @yahoo.com

Cover letter: Cover letter should include statements about manuscript category designation, single-journal submission affirmation, conflict of interest statement, copyright transfer statement, sources of outside funding, equipments (if so).

Title Page: On the title page provide the complete title and a running title (not to exceed 55 characters and spaces). List each contributor's name and institutional affiliation. Corresponding Author is the contributor responsible for the manuscript and proofs. This is the person to whom all correspondence and reprints will be sent. The corresponding author is responsible for keeping the Editorial office updated with any change in details until the paper is published. All authors are also asked to submit their ORCID number, if they do not have it, it is kindly asked to be enrolled for the number form the webpage of http://orcid.org.

Abstract and Key Words: The abstract must not exceed 250 words. It should summarize the aim of the study and describe the work undertaken, results and conclusions. In addition, you should list up to three key words in alphabetical order.

Introduction: The Introduction should briefly discuss the objectives of the study and provide the background information to explain why the study was undertaken, and what hypotheses were tested.

Materials and methods: Clearly explain the methods and the materials in detail to allow the reader to reproduce the results. Equipment and apparatus should cite the make and model number and the company name and address (town, county, country) at first mention. Give all measurements in metric units. Use generic names of drugs.

Results: Results must be presented in a logic sequence with text, tables and illustrations. Underline or summarize only the most important observation. Tables and text should not duplicate each other.

Discussion: This section should be concise. Emphasize only the new and most important aspects of the study and their conclusions. The discussion should include a brief statement of the principal findings, a discussion of the validity of the observations, a discussion of the findings in light of other published work dealing with the same or closely related subjects, and a statement of the possible significance of the work. Authors are encouraged to conclude with a brief paragraph that highlights the main findings of the study.

Acknowledgements: Authors must acknowledge individuals who do not qualify as Authors but who contributed to the research.

Abbreviations: The abbrevation of a word or word sequence is given in the first appearance within a bracket after the word or word sequence. The abbrevation is used through the main text

Tables: Tables should be numbered consecutively within the text. Provide a number and title for each table.. Tables should not be submitted as photographs or graphics files.

Figure and table legends: Cite all tables and figures in the text, numbering them sequentially as they are cited. Each figure must have a corresponding legend. The legend must be numbered with a natural number

References: References in the text must be numbered in the order of citation and must be given with natural numbers within a bracket at the end of the sentence. Use of the form of the "Uniform requirements for manuscript submitted to biomedical journals" List all Authors when six or fewer; when seven or more, list only the first three and add 'et al'. Journal titles should be cited in full. The style of references and abbreviated titles of journals must follow that of cumulated Index Medicus or one of the examples illustrated below:

Format for journal articles:

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

Format for Committees and Groups of Authors:

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.

Format for Chapter from a book:

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

Format for Books and Monographs:

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

COMMUNICATION

Doç. Dr. Tuncay KIRIŞ
Head Editor
Izmir Hastanelerine Yardım ve Bilimsel
Araştırmaları Teşvik Derneği
Yeşilyurt, İZMİR/TURKEY
Tel: 0 507 3114607
e-mail: idhdergi@yahoo.com

OUR ARTICLE SUBMITTING RULES

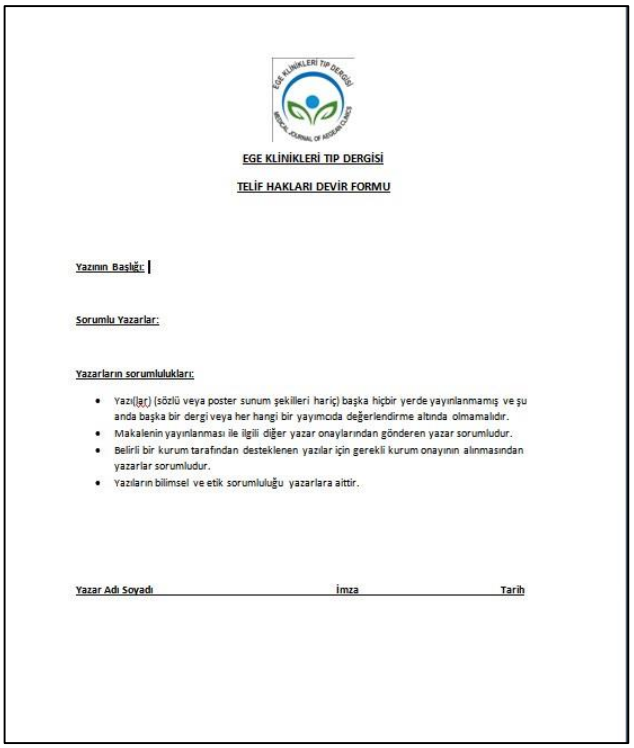
• Copyright Transfer Form must be signed by all authors.

• All authors of an article must submit their ORCID numbers.
(You can obtain and register for an ORCID ID from the website http://orcid.org for free of charge. In accordance with the layout of our journal; the author's ORCID ID must be written along with the author names and institution information in the first page of the study.)

• The Ethics Committee Consent itself (Ethics Committee Consent Document) must be sent with the study. Besides, the title of the study must be exactly the same in the Ethics Committee Document.

• The approval of ethics committe is a must for the articles to be published in our journal and a sentence denoting that the study has had ethics committee approval must be present in the material-method section of a study.

• The consent of patient/patients is a must for the case reports to be published in our journal and a sentence denoting that the case report has had 'consent from the patient/patients must be present in the introduction section of the study.



EGE KLİNİKLERİ TIP DERGİSİ

TELİF HAKLARI DEVİR FORMU

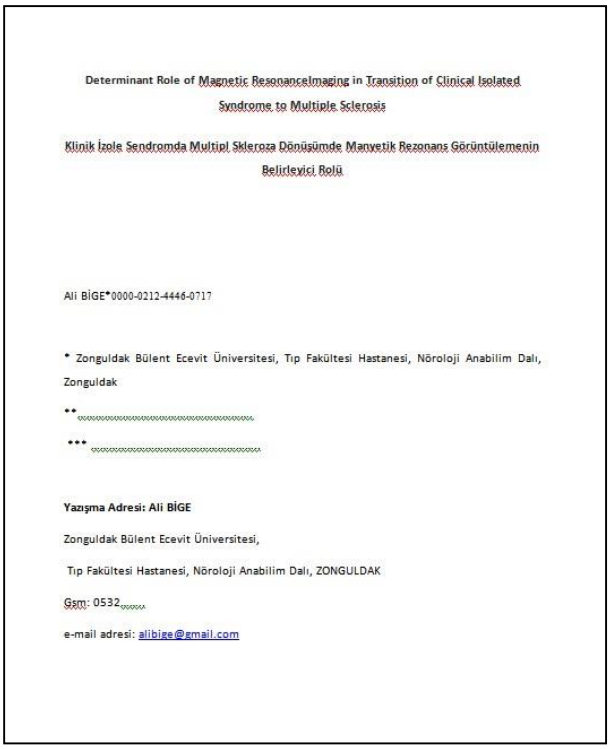
Yazının Başlığı:

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 ResonanceImaging 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

**

***

Yazışma Adresi: Ali BİGE

Zonguldak Bülent Ecevit Üniversitesi,

Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, ZONGULDAK

Gsm: 0532

e-mail adresi: alibige@gmail.com

İÇİNDEKİLER/CONTENTS

KLİNİK ÇALIŞMALAR/ CLINICAL TRIALS

1. Predictors Of Long Procedure Time in Patients With ST-Segment Elevation Myocardial Infarction ……..1

Who Underwent Primary Percutaneous Coronary Intervention

Primer Perkütan Koroner Girişim Yapılan ST Elevasyonlu Miyokard İnfarktüsü Hastalarında Uzun Prosedürel Süresinin Prediktörleri

Serdar SÖNER, Yusuf HOŞOĞLU, Oktay ŞENÖZ, Fethullah KAYAN, Tuncay GÜZEL

2. Evaluation of Congenital Diaphragmatic Hernia Cases Diagnosed Prenatally Between 2016 and 2023……8

2016-2023 Yılları Arasında Prenatal Tanı Alan Konjenital Diyafragma Hernisi Vakalarının Değerlendirilmesi

Raziye TORUN, Sevim TUNCER CAN, Ceren SAĞLAM, İlknur TOKA, İlayda GERCİK ARZIK, İlker UÇAR, Hale ANKARA AKTAŞ, Zübeyde EMİRALİOĞLU ÇAKIR, Atalay EKİN, Mehmet ÖZEREN

3. *Evaluation of Shock Appropriateness in Patients Admitted to the Emergency Department After ICD Shocking……14*

ICD Şoklaması Sonrası Acil Servise Başvuran Hastalarda Şoklama Uygunluğunun İncelenmesi

Efe KANTER, Osman Sezer ÇINAROĞLU, Ramazan Batuhan ŞAHİN, Ecem ERMETE GÜLER

4. *Evaluation Of Bifurcation Lesion Procedures Performed In A Tertiary Centre……22*

Üçüncü Basamak Bir Merkezde Yapılan Bifurkasyon Lezyon Girişimlerinin Değerlendirilmesi

Dogac Caglar GURBUZ, Emre OZDEMIR, Sadik Volkan EMREN, Cem NAZLI, Mehmet TOKAC

5. Analysis of Early Term Results of Elective Ascending Aortic Aneurysm Surgery……32

Elektif Asendan Aort Anevrizması Cerrahisinin Erken Dönem Dönem Sonuçlarının Analizi

Ahmet DOLAPOĞLU, Emin BARBARUS

6. Human Equivalent Phantom Computed Tomography Study for Foreign Body Detection in the Body……38

Vücutta Yabancı Cisim Saptanması İçin İnsan Eşdeğer Fantom Bilgisayarlı Tomografi Çalışması

Halil İbrahim ÖZDEMİR, Murat KÖYLÜ, Hatice Elif ÖZDEMİR, Mert ARSLAN, Saliha ÇETİN, Deniz YALMAN, Mustafa HARMAN

7. Relationship Between Serum Uric Acid Level And Frequency Of Gastrointestinal Bleeding……45

in Patients Using New Oral Anticoagulants

Yeni Nesil Oral Antikoagülan Kullanan Hastalarda Serum Ürik Asit Düzeyi ile Gastrointestinal Kanama Sıklığı Arasındaki İlişki

Eyyüp ERKİZ, Seda Elçim YILDIRIM, Tarık YILDIRIM, Özgen ŞAFAK, Onur ARGAN, Mehmet Tolga HEKİM, Eyüp AVCI, Halil Lütfi KISACIK

OLGU SUNUMU/ CASE REPORT

Delayed-Onset Morbilliform Drug Eruption Induced by Hydroxychloroquine: ……51

A Clinical Observation in a Patient with Systemic Sclerosis

Hidroksiklorokin Kullanımına Bağlı Gecikmiş Başlangıçlı Morbilliform İlaç Döküntüsü: Sistemik Sklerozlu Bir Hastada Klinik Gözlem

Gülşah ÇELİK

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (1):1-7

Predictors of Long Procedure Time in Patients With ST-Segment Elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention

Primer Perkütan Koroner Girişim Yapılan ST Yükselmeli Miyokard Enfarktüsü Hastalarında Uzun Prosedürel Süresinin Prediktörleri

Serdar SÖNER* 0000-0002-2807-6424
Yusuf HOŞOĞLU0000-0003-2440-9209**
Oktay ŞENÖZ*0000-0002-3847-7598**
Fethullah KAYAN*0000-0002-8875-5672
Tuncay GÜZEL*0000-0001-8470-1928

*Department of Cardiology, Health Science University, Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkey,
**Department of Cardiology, Health Science University, Dr Ersin Arslan Training and Research Hospital, Gaziantep, Turkey
**Department of Cardiology, Bakırçay University, Çiğli Training and Research Hospital, İzmir, Turkey

Corresponding Author: Serdar SÖNER
Department of Cardiology, Health Science University, Gazi Yaşargil Training and Research Hospital,Diyarbakır, Turkey
E-Mail: drserdar_89@hotmail.com

Geliş Tarihi: 03.01.2025
Kabul Tarihi: 02.02.2025

Abstract

Aim: ST-Segment Elevation Myocardial Infarction (STEMI) is a critical condition characterized by complete coronary artery occlusion, with procedural timing influencing outcomes. Our aim in this study was to investigate the factors that cause the prolongation of the procedural time.

Materials and methods: This study retrospectively evaluated factors prolonging procedural time during primary percutaneous coronary intervention (PCI) in 606 STEMI patients who admitted to our hospital between January and June 2023. Patients were divided into two groups based on median procedural times: longer (n=296) and shorter (n=310).

Results: Key predictors of prolonged procedural time included advanced age (OR=1.019, 95% CI=1.004-1.035, p=0.016), multivessel intervention (OR=15.974, 95% CI=4.737-53.867, p<0.001), off-hour admission (OR=4.655, 95% CI=2.043-10.610, p<0.001), and procedural complications (OR=1.686, 95% CI=1.160-2.449, p=0.006). Multivariable logistic regression confirmed these factors as independent predictors. Notably, patients in the prolonged procedure group exhibited higher door-to-balloon times, procedural complications, and multivessel interventions. The use of acetylsalicylic acid, beta-blockers, and coronary artery by-pass grafting operation history was associated with longer procedure times but lacked independence as predictors.

Conclusion: The findings of our investigation showed that in STEMI patients, longer procedure times were independently predicted by advanced age, multivessel intervention, off-hour admission, and procedural difficulties. Our study may be a reference for cardiologists who perform primary percutaneous coronary intervention in STEMI patients to predict the prolonged procedure.

Keywords: Fluoroscopy time, procedural time, ST-elevation myocardial infarction

Öz

Amaç: ST-Segment Yükselmeli Miyokard Enfarktüsü (STYME), tam koroner arter tıkanıklığı ile karakterize kritik bir durumdur ve işlem zamanlaması sonuçları etkilemektedir. Bu çalışmadaki amacımız, işlem süresinin uzamasına neden olan faktörleri araştırmaktı.

Yöntem: Bu çalışmada, Ocak ve Haziran 2023 tarihleri arasında hastanemize başvuran 606 STYME hastasında primer perkütan koroner girişim (PKG) sırasında işlem süresini uzatan faktörler retrospektif olarak değerlendirilmiştir. Hastalar, medyan işlem sürelerine göre iki gruba ayrılmıştır: daha uzun (n=296) ve daha kısa (n=310).

Bulgular: Çok değişkenli lojistik analizlerinde işlem süresinin uzamasının bağımsız prediktörleri arasında ileri yaş (OR=1.019, 95% CI=1.004-1.035, p=0.016), çok damarlı müdahale (OR=15.974, 95% CI=4.737-53.867, p<0.001), mesai saatleri dışında yatış (OR=4.655, 95% CI=2.043-10.610, p<0.001) ve işlem sırasında komplikasyon gelişmesi (OR=1.686, 95% CI=1.160-2.449, p=0.006) yer almıştır. Özellikle, uzamış işlem grubundaki hastalarda daha yüksek kapı-balon süreleri, işlem komplikasyonları ve çok damarlı müdahaleler görülmüştür. Asetilsalisilik asit ve beta blokörlerin kullanımı ve koroner arter by-pass greft operasyon geçmişi, daha uzun işlem süreleriyle ilişkilendirildi ancak bağımsız öngörücü değildi.

Sonuç: Araştırmamızın bulguları, STYME hastalarında daha uzun işlem sürelerinin ileri yaş, çok damarlı müdahale, mesai saatleri dışında yatış ve işlem zorlukları tarafından bağımsız olarak öngörüldüğünü gösterdi. Çalışmamız, STYME hastalarında primer perkütan koroner müdahale uygulayan kardiyologlar için uzamış işlemi öngörmek amacıyla bir referans olabilir.

Anahtar Kelimeler: Floroskopi süresi, işlem süresi, ST yükselmeli miyokard enfarktüsü

Introduction

Myocardial ischemia and consequent necrosis are the hallmarks of ST-Segment Elevation Myocardial Infarction (STEMI), a potentially fatal medical emergency that is defined by total coronary artery blockage. As a major cause of morbidity and death globally, STEMI has persisted over time, requiring a thorough comprehension of its pathogenesis, precise diagnostic techniques, and efficient treatment methods (1). The mortality rate of STEMI has decreased significantly from 13% to 4% since the development of healthcare systems, mainly due to the early opening of the culprit artery (2). Increased mortality is associated with infarct size (IS), microvascular obstruction (MVO), and any delay between symptom onset and infarct-related artery recanalization (3). According to treatment guidelines derived from many randomized controlled trials, restoring blood flow to the infarct-related artery as soon as possible is vital for STEMI patients (4). Even with primary percutaneous coronary intervention (PCI), effective reperfusion can be challenging at times (5). In primary PCI, delayed reperfusion can result in a prolonged procedure time, which may contribute to poor clinical outcomes (6, 7).

Long procedure times are also associated with a higher incidence of periprocedural complications, such as contrast-induced nephropathy, emergent coronary artery by-pass grafting (CABG), and early death (6).

The importance of ischemia time in STEMI patients has been shown in many studies (8-10). One component of ischemia time is the prolongation of the procedural time of primary percutaneous coronary angiography. Our aim in this study was to investigate the factors that cause the prolongation of the procedural time.

Materials and Methods

Study population

Our study comprised patients who received primary percutaneous coronary intervention at the Health Sciences University Gazi Yaşargil Training and Research Hospital between January and June 2023 after a diagnosis of STEMI. The study began with a total of 744 patients diagnosed with STEMI. Thirty-seven patients were excluded because PCI was performed more than 12 hours after symptom onset or more than 6 hours after hospital admission, 83 patients because data were not available, and 18 patients because PCI was not performed (surgical or medical treatment). As a result, 606 patients were included in the study. Door-to-balloon times (DTB) and total procedure times of the patients during percutaneous coronary intervention were recorded. Two groups were formed according to the total procedure time. Since there is no accepted cut-off value for procedure time in STEMI patients, groups were formed by taking into account the median procedure time of the total population. The longer procedure time group consisted of 296 patients, and the shorter group consisted of 310 patients. The study followed the guidelines outlined in the 2013 Declaration of Helsinki. The ethics committee of the Gazi Yaşargil Training and Research Hospital provided ethical approval (270-12/12/2024). Written informed consent was not obtained due to the retrospective study design.

Definitions

STEMI patients were diagnosed according to the recommendations of the European Society of Cardiology (ESC) guidelines (11). Hypertension was defined as a history of hypertension and/or medical treatment for it before hospitalization. A total cholesterol level of 200 mg/dL or a low-density lipoprotein cholesterol level of 130 mg/dL with medical treatment for dyslipidemia or a history of dyslipidemia were considered indicators of dyslipidemia. A HbA_1c level of 7%, treatment for diabetes mellitus, or a history of diabetes mellitus were considered indicators of diabetes mellitus. The Cockroft–Gault formula was used to compute the values of glomerular filtration rate (GFR).

On-or off-hour admissions were defined according to the admission times to the emergency department. On-hour admissions were defined as admissions between 08:00 and 17:00, and off-hour admissions were defined as admissions between 17:00 and 08:00. DTB was defined as the time interval from arrival at the emergency department to the first blood supply (with balloon inflation or wire crossing). Malignant arrhythmias, no-reflow phenomenon, cardiac arrest, coronary dissection, or rupture developing during the procedure were also defined as procedural complications. Bifurcation procedures or interventions for non-culprit artery lesions after culprit lesions were defined as multivessel interventions. Detailed echocardiographic measurements of the patients were performed within 24 hours of the primary PCI.

Coronary angiography records were reviewed by two qualified invasive cardiologists who were unaware of the patient's clinical status. Our center's interventional cardiologists were free to choose any PCI equipment, including stents, balloons, thrombectomy devices, rotating atherectomy devices, and guidewires. Instead of using two separate diagnostic catheters, our center uses a diagnostic catheter for the non-culprit region and a guiding catheter for the culprit region. To reduce DTB, our center has a heart team that can perform coronary angiography 24/7.

Statistical Analysis

SPSS version 27 for Windows (SPSS, Inc., Chicago, Illinois) was used to analyze the data. The continuous variables were displayed as mean ± SD or median (25th-75th percentiles). The Shapiro–Wilks test and histograms were used to confirm that the data had a normal distribution. The Pearson $\chi 2$ test was used to compare categorical variables expressed as numbers (percentages). Student's test was used to compare normally distributed continuous variables between groups, and the Mann-Whitney U test was used to compare non-normally distributed continuous variables.

Univariable and multivariable logistic regression analyses were conducted to determine the relationship between the clinical factors and longer procedure time. Parameters with p values <0.1 in univariable regression analyses were included in multivariable regression analyses. In addition, the 95% CI and odds ratio (OR) were determined. Statistical significance was defined as a p-value less than 0.05.

Results

In our study, 606 patients were included in two groups. The long procedure time group included 296 patients, and the short group included 310 patients. The majority of the population was male, the number of male patients was 462 (76.2%). The mean age of the patients was 60.5±13.4 years.

In the long procedure time group, age (62.2±13.4 vs. 58.8±13.2, p=0.002), door-to-balloon time (36 [25-50] vs. 29 [22-41], p<0.001) were higher. CABG history (10 [3.4] vs. 2 [0.6], p=0.016), Circumflex artery intervention (61 [20.6] vs. 44 [14.2], p=0.037), graft vessel intervention (10 [3.4] vs. 2 [0.6], p=0.016), off-hour admission (157 [53] vs. 132 [42.6], p=0.010), multivessel intervention (40 [13.5] vs. 3 [1], p<0.001), procedural complications (42 [14.2] vs. 12 [3.9], p<0.001), diabetes mellitus (DM) (131 [44.3] vs. 107 [34.5], p=0.014), Acetylsalicylic acid (95 [32.1] vs. 76 [24.5], p=0.038), and beta-blocker usage (92 [31.1] vs. 71 [22.9], p=0.023) rates were also higher. The LVEF (49.8±9.2 vs. 51.5±9.2, p=0.032) and Right coronary artery (RCA) intervention rate (88 [29.7] vs. 120 [38.7], p=0.020) was lower. Baseline characteristics of the total population are shown in Table 1.

Table 1: Baseline characteristics of the total population				
Parameters	**Long procedural time (≥18 min) (n=296)**	**Short procedural time (<18 min) (n=310)**	**Total (n=606)**	**p-value**
Age n, (y)	62.2±13.4	58.8±13.2	60.5±13.4	**0.002**
Female gender n, (%)	80 (27)	64 (20.6)	144 (23.8)	0.065
LVEF (%)	49.8±9.2	51.5±9.2	50.7±9.3	**0.032**
Left atrium diameter (cm)	3.8±0.46	3.8±0.43	3.8±0.45	0.243
DTB min (25th-75th percentiles)	36 (25-50)	29 (22-41)	32 (23-46)	**<0.001**
CABGO history n, (%)	10 (3.4)	2 (0.6)	12 (2)	**0.016**
PCI history n, (%)	43 (14.5)	35 (11.3)	78 (12.9)	0.234
Left anterior descending artery n, (%)	142 (48)	146 (47.1)	288 (47.5)	0.829
Circumflex artery n, (%)	61 (20.6)	44 (14.2)	105 (17.3)	**0.037**
Right coronary artery n, (%)	88 (29.7)	120 (38.7)	208 (34.3)	**0.020**
Graft vessel n, (%)	10 (3.4)	2 (0.6)	12 (2)	**0.016**
Multivessel intervention n, (%)	40 (13.5)	3 (1)	43 (7.1)	**<0.001**
Procedural complication n, (%)	42 (14.2)	12 (3.9)	54 (8.9)	**<0.001**
Off-hour admission n, (%)	157 (53)	132 (42.6)	289 (47.7)	**0.010**
Hemoglobin (g/dL)	14±2.4	13.7±3.1	13.9±2.8	0.133
HbA_1c	6.7±1.9	6.6±1.8	6.6±1.9	0.329
Glucose mg/dL, (25th-75th perc.)	139 (114-204)	139 (118-181)	139 (116-185)	0.655
Creatinine mg/dL, (25th-75th perc.)	0.91 (0.78-1.05)	0.9 (0.78-1.05)	0.9 (0.78-1.05)	0.867
GFR	77.4±17	79.2±16.2	78.3±16.6	0.173
Albumin (mg/dL)	41.4±5.4	42.1±5.4	41.7±5.4	0.293
Sodium (mmol/L)	140.2±3.9	140.3±3.6	140.2±3.7	0.714
Potassium (mmol/L)	4.3±0.50	4.3±0.53	4.3±0.51	0.507
Total cholesterol (mg/dL)	182±47.9	180±43.8	181±45.8	0.693
High-density lipoprotein (mg/dL)	39.6±10.6	38.3±9	38.9±9.8	0.108
Low-density lipoprotein (mg/dL)	113.5±36.8	112.1±36	112.8±36.4	0.656
Triglyceride mg/dL, (25th-75th perc.)	117 (81-172)	122 (82-190)	121 (82-179)	0.558
Troponin (ng/mL)	20.3±7.8	20.1±8.4	20.2±8.1	0.766
White blood cell ($10^3/\mu L$)	13.2±4.5	13.6±4.2	13.4±4.3	0.196
Neutrophil (%)	9.6±4.3	9.3±3.9	9.5±4.1	0.416
Platelet ($10^3/\mu L$)	240±85	232±92	235±88	0.293
Hypertension n, (%)	99 (33.4)	97 (31.3)	196 (32.3)	0.571
Diabetes mellitus n, (%)	131 (44.3)	107 (34.5)	238 (39.3)	**0.014**
Dyslipidemia n, (%)	120 (40.5)	121 (39)	241 (39.8)	0.705
Smoking n, (%)	128 (43.2)	154 (49.7)	282 (46.5)	0.112
Acetyl-salicylic acid n, (%)	95 (32.1)	76 (24.5)	171 (28.2)	**0.038**
Beta-blocker n, (%)	92 (31.1)	71 (22.9)	163 (26.9)	**0.023**
Statin n, (%)	81 (27.4)	77 (24.8)	158 (26.1)	0.479
ACE-I n (%)	68 (23)	63 (20.4)	131 (21.7)	0.440
ARB n, (%)	52 (17.6)	43 (13.9)	95 (15.7)	0.211
In-hospital death n, (%)	8 (2.7)	10 (3.2)	18 (3)	0.705
1-year death n, (%)	26 (8.8)	28 (9)	54 (8.9)	0.915

LVEF; Left ventricular ejection fraction, DTB; door to balloon time, CABGO; Coronary artery by-pass grafting operation, PCI; Percutaneous coronary intervention, Off-hour admission; Admission between 17:00 and 08:00 am, GFR; Glomerular filtration rate, ACE-I; Angiotensin-converting enzyme inhibitor, ARB; Aldosterone receptor blocker

No significant difference was observed between the groups in terms of gender, PCI history, Left anterior descending artery intervention, HBa_1c value, laboratory parameters, Hypertension (HT), dyslipidemia, smoking, in-hospital, and 1-year death (p>0.05 for each).

To determine the variables influencing procedure time, multivariable and univariable logistic regression analyses were conducted. In univariable logistic regression analyses, age (OR=1.020, 95% CI=1.007-1.032, p=0.002), CABGO history, or graft vessel intervention (OR=5.385, 95% CI=1.170-24.785, p=0.031), off-hour admission (OR=1.523, 95% CI=1.105-2.099, p=0.010), culprit lesion of the circumflex artery (Cx) (OR=1.569, 95% CI=1.025-2.402, p=0.038), culprit lesion of RCA (OR=0.670, 95% CI=0.478-0.939, p=0.020), multivessel intervention (OR=15.990, 95% CI=4.889-52.293, p<0.001), procedural complication (OR=4.106, 95% CI=2.116-7.969, p<0.001), diabetes mellitus (OR=1,506, 95% CI=1.085-2.090, p=0.014), using acetylsalicylic acid (OR=1.455, 95% CI=1.020-2.077, p=0.039), using beta-blocker (OR=1.518, 95% CI=1.057-2.179, p=0.024) door to balloon time (OR=1.015, 95% CI=1.007-1.024, p<0.001), and LVEF (OR=0.980, 95% CI=0.962-0.998, p=0.033) were associated with procedure time.

Parameters with p<0.1 in univariable logistic regression analyses were included in multivariable logistic regression analysis. In multivariable logistic regression analysis, age (OR=1.019, 95% CI=1.004-1.035, p=0.016), off-hour admission (OR=1.686, 95% CI=1.160-2.449, p=0.006), multivessel intervention (OR=15.974, 95% CI=4.737-53.867, p<0.001), and procedural complication (OR=4.655, 95% CI=2.043-10.610, p<0.001) were independent predictors of longer procedure time among all causes. The results of univariable and multivariable logistic regression analyses are shown in Table 2.

Table 2: Univariable and multivariable logistic regression analyses for predictors of long procedural time

Parameters	**Univariable**		**Multivariable**	
	OR (95 % CI)	**p- value**	**OR (95 % CI)**	**p- value**
Age	1.020 (1.007-1.032)	**0.002**	1.019 (1.004-1.035)	**0.016**
CABGO or graft vessel	5.385 (1.170-24.785)	**0.031**	3.514 (0.6776-18.262)	0.135
PCI history	1.335 (0.828-2.153)	0.235		
Off-hour admission	1.523 (1.105-2.099)	**0.010**	1.686 (1.160-2.449)	**0.006**
Culprit lesion of LAD	1.036 (0.753-1.425)	0.829		
Culprit lesion Cx	1.569 (1.025-2.402)	**0.038**	1.473 (0.872-2.487)	0.148
Culprit lesion of RCA	0.670 (0.478-0.939)	**0.020**	0.831 (0.534-1.291)	0.414
Multivessel intervention	15.990 (4.889-52.293)	**<0.001**	15.974 (4.737-53.867)	**<0.001**
Procedural complication	4.106 (2.116-7.969)	**<0.001**	4.655 (2.043-10.610)	**<0.001**
Female gender	0.702 (0.482-1.023)	0.066	0.837 (0.525-1.336)	0.456
Hypertension	1.104 (0.785-1.551)	0.571		
Diabetes mellitus	1.506 (1.085-2.090)	**0.014**	1.243 (0.797-1.940)	0.337
Current smoking	1.296 (0.941-1.784)	0.113		
Using acetyl-salicylic acid	1.455 (1.020-2.077)	**0.039**	1.058 (0.625-1.791)	0.835
Using beta-blocker	1.518 (1.057-2.179)	**0.024**	1.060 (0.620-1.812)	0.831
Door to balloon time	1.015 (1.007-1.024)	**<0.001**	1.006 (0.996-1.016)	0.252
LVEF	0.980 (0.962-0.998)	**0.033**	0.987 (0.966-1.009)	0.244

CABGO; Coronary artery by-pass grafting operation, LAD; left anterior descending artery, Cx; circumflex, RCA; right coronary artery, PCI; Percutaneous coronary intervention, LVEF; left ventricular ejection fraction

Discussion

In our study, advanced age, multivessel intervention, procedural complications, CABG history, culprit lesion of the graft vessel and Cx, using acetylsalicylic acid and beta blocker, door-to-balloon time, and LVEF were predictors of prolonged procedural time. Multivariable logistic regression analyses revealed that older age, multivessel intervention, and procedural complications were independent predictors of longer procedure time among all causes.

Although several studies have been conducted to find the determinants of prolonged procedure time in PCI (12, 13), there are few studies to find it in primary PCI for STEMI(14). In a study investigating the predictors of long procedure time in NSTEMI patients, Ishibashi S. et al. showed that previous CABG history was significantly associated with long procedure time (15). In our study, previous CABG history was associated with longer procedural time but was not an independent predictor. The lack of an independent predictor is likely related to the small number of patients with previous CABG history included in the study (12 patients, 5% in total).

In a study investigating predictors of prolonged procedure time in patients undergoing primary PCI for STEMI, Asada S et al. (14) found that extensive long lesions, tortuosity, and moderate to severe calcification were associated with prolonged procedure time. We do not have data on lesion characteristics in our study. However, we showed that advanced age is an independent predictor of longer procedural time. Increasing calcification with advanced age indirectly supports this study. Increased calcification in coronary arteries with increasing age may also cause increased procedural time with advanced age, as may severe calcification (16). In addition, peripheral tortuosity and anatomical changes accompanying advanced age may have also affected the prolonged procedural time.

In our study, multivessel intervention was also an independent predictor of procedural time. Di Mario et al. randomly assigned 69 STEMI patients with multivessel coronary artery disease to receive comprehensive multivessel intervention (n = 52) or treatment of the culprit lesion alone (n = 17). The multivessel intervention group required more contrast and longer procedures. Predictably, treatment of more vessels could result in longer procedural time. However, its effect on prognosis at long-term follow-up is controversial.

In the study by Wang X et al. (17), the primary predictors of malignant arrhythmias in patients with STEMI presenting within six hours of symptom onset were age and symptom-to-balloon time. In our study, procedural complications were an independent predictor of prolonged procedural time. DTB was also associated with prolonged procedural time, although it was not an independent predictor.

In our study, a significant relationship was observed between the use of acetylsalicylic acid and beta-blockers and long procedural time. However, these treatments were not independent predictors among all causes. We attribute the higher use of acetylsalicylic acid and beta-blockers in the long procedural time group to secondary causes. We attribute this to the widespread use of these treatments in patients with previous atherosclerotic cardiovascular disease, PCI, or CABG history. Therefore, the results appear to be statistically significant.

Studies on the time of admission in STEMI patients have shown that it generally does not affect long-term and short-term mortality (18-20). Although no-reflow was not seen the day following the procedure, edema of the pulmonary system and cardiogenic shock were more frequent in patients hospitalized outside of normal office hours, according to the research by Özbek M et al. (20). Clinical results were comparable amongst the groups, even though patients with STEMI hospitalized at off-peak hours had poorer medical conditions. In our study, the procedure time was significantly longer in patients admitted off-hours. We believe that this is due to their presentation to the hospital with worse clinical conditions.

Limitations

First, it could not completely rule out the possibility of patient selection bias because this was a retrospective, observational, single-center study. Secondly, as there was no set cut-off point for a longer procedure time, we determined it using the median value of the time. Third, there may be other parameters that may cause procedural time to be prolonged but are missing in our dataset, such as coronary arterial calcification level, peripheral artery anatomy, Leriche syndrome, repeated percutaneous femoral access attempts, and operator experience.

Conclusion

According to our study's results, off-hour admission, advanced age, multivessel intervention, and procedural complications were independent predictors of longer procedure time in STEMI patients. Our study may provide a reference for cardiologists performing percutaneous coronary intervention in STEMI patients to determine the difficulties of the intervention.

References

1.Elendu C, Amaechi DC, Elendu TC, et al. Comprehensive review of ST-segment elevation myocardial infarction: Understanding pathophysiology, diagnostic strategies, and current treatment approaches. Medicine (Baltimore). 2023;102(43):e35687.

2.Hausenloy DJ, Yellon DM. Myocardial ischemia-reperfusion injury: a neglected therapeutic target. J Clin Invest. 2013;123(1):92-100.

3.Doddipalli SR, Rajasekhar D, Vanajakshamma V, Sreedhar Naik K. Determinants of total ischemic time in primary percutaneous coronary interventions: A prospective analysis. Indian Heart J. 2018;70 Suppl 3(Suppl 3):S275-s9.

4.Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39(2):119-77.

5.Levi A, Kornowski R, Vaduganathan M, et al. Incidence, predictors, and outcomes of failed primary percutaneous coronary intervention: a 10-year contemporary experience. Coron Artery Dis. 2014;25(2):145-51.

6.Nikolsky E, Pucelikova T, Mehran R, et al. An evaluation of procedure time and correlation with outcomes after percutaneous coronary intervention. J Invasive Cardiol. 2007;19(5):208-13.

7.Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol. 2018;72(18):2231-64.

8.Byrne R, Coughlan JJ, Rossello X, Ibanez B. The '10 commandments' for the 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2024;45(14):1193-5.

9.Hassan MO, Ahmed SA, Hassan MS, Köprülü D. Door-to-Balloon Time and Mortality Among Patients Undergoing Primary PCI, Challenges and Experience from Somalia's Largest PCI Center. Int J Gen Med. 2024;17:237-44.

10.Park J, Choi KH, Lee JM, et al. Prognostic Implications of Door-to-Balloon Time and Onset-to-Door Time on Mortality in Patients With ST - Segment-Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention. J Am Heart Assoc. 2019;8(9):e012188.

11.Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023;44(38):3720-826.

12.Mujtaba SF, Saghir T, Sial JA, Rizvi NH. Procedural determinants of procedure time in patients undergoing cardiac catheterization. Pak J Med Sci. 2019;35(1):166-71.

13.Fazel R, Curtis J, Wang Y, et al. Determinants of procedure time for invasive coronary angiography and percutaneous coronary intervention: insights from the NCDR(®). Catheter Cardiovasc Interv. 2013;82(7):1091-105.

14.Asada S, Sakakura K, Taniguchi Y, et al. Association of the long procedure time with factors in contemporary primary percutaneous coronary interventions. PLoS One. 2020;15(8):e0237362.

15.Ishibashi S, Sakakura K, Asada S, et al. Clinical Factors Associated with Long Procedure Time in Percutaneous Coronary Interventions to the Culprit Lesion of Non-ST-Segment Elevation Myocardial Infarction. Int Heart J. 2021;62(2):282-9.

16.Javaid A, Dardari ZA, Mitchell JD, et al. Distribution of Coronary Artery Calcium by Age, Sex, and Race Among Patients 30-45 Years Old. J Am Coll Cardiol. 2022;79(19):1873-86.

17.Wang X, Wei L, Wu Y, et al. ST-segment elevation predicts the occurrence of malignant ventricular arrhythmia events in patients with acute ST-segment elevation myocardial infarction. BMC Cardiovasc Disord. 2023;23(1):61.

18.Javanshir E, Ramandi ED, Ghaffari S, et al. Association Between Off-hour Presentations and In-hospital Mortality for Patients with Acute ST-Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention. J Saudi Heart Assoc. 2020;32(2):242-7.

19.Tscharre M, Jäger B, Farhan S, et al. Impact of time of admission on short- and long-term mortality in the Vienna STEMI registry. Int J Cardiol. 2017;244:1-6.

20.Ozbek M, Ildirimli K, Arik B, et al. Dependence of clinical outcomes on time of hospital admission in patients with ST-segment elevation myocardial infarction. Ann Saudi Med. 2023;43(1):25-34.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (1): 8-13

Evaluation of Congenital Diaphragmatic Hernia Cases Diagnosed Prenatally Between 2016 and 2023

2016-2023 Yılları Arasında Prenatal Tanı Alan Konjenital Diyafragma Hernisi Vakalarının Değerlendirilmesi

Raziye TORUN* 0000-0002-0272-7196
Sevim TUNCER CAN* 0000-0003-3119-1148
Ceren SAĞLAM* 0000-0001-6013-6602
İlknur TOKA 0000-0002-3804-2826**
İlayda GERCİK ARZIK* 0000-0001-7308-352X
İlker UÇAR 0000-0002-4871-0621**
Hale ANKARA AKTAŞ* 0000-0002-0723-4948
Zübeyde EMİRALİOĞLU ÇAKIR* 0000-0002-0272-7196
Atalay EKİN* 0000-0002-4712-3927
Mehmet ÖZEREN 0000-0002-4552-9042**

* Sağlık Bilimleri Üniversitesi İzmir Şehir Hastanesi Kadın Hastalıkları ve Doğum Ana Bilim Dalı, Perinatoloji Kliniği
** Sağlık Bilimleri Üniversitesi Tepecik Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Ana Bilim Dalı, Perinatoloji Kliniği

Yazışma Adresi: Raziye TORUN
Sağlık Bilimleri Üniversitesi, İzmir Şehir Hastanesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Perinatoloji Kliniği İzmir,
E-mail: drraziyetorun@gmail.com

Geliş Tarihi: 03.01.2025
Kabul Tarihi: 14.02.2025

Abstract

Objective: The aim is to evaluate the clinical characteristics and perinatal outcomes of the cases with congenital diaphragmatic hernia (CDH) diagnosed during the prenatal period.

Materials and Methods: Fetuses with CDH between 2016 and 2023 were analyzed and compared in terms of fetal ultrasonography findings, maternal demographic characteristics, antenatal follow-up, and perinatal outcomes.

Results: Sixty-nine cases of CDH were diagnosed by antenatal ultrasonography. Sixty-seven cases of CDH (97.1%) were left-sided, and 2 (2.9%) cases were right-sided. Eleven cases (15.9%) terminated their pregnancy. There were 2 (3.4%) cases of stillbirth and 1 (1.7%) case of missed abortion. Of the 55 (79.7%) CDH cases that resulted in live births, 34 (49.2%) died in neonatal period 21 (30.4%) were survived.

Conclusion: CDH is one of the most severe birth defects, with significant morbidity and mortality. Timely antenatal diagnosis of CDH allows clinicians for detailed parental counseling, delivery planning and appropriate postpartum management.

Keywords: Congenital diaphragmatic hernia, fetal anomaly, prenatal diagnosis

Öz

Amaç: Prenatal dönemde tanı konulan konjenital diyafragma hernisi (KDH) olgularının klinik özellikleri ve perinatal sonuçlarının değerlendirilmesi.

Gereç ve yöntemler: 2016-2023 yılları arasında üçüncü basamak bir merkezde KDH tanısı alan fetüslerin ultrasonografi bulguları, maternal demografik özellikleri, antenatal takipleri ve perinatal sonuçları değerlendirilerek karşılaştırıldı.

Bulgular: Antenatal ultrasonografik değerlendirme ile KDH tanısı alan 69 vaka tespit edildi. Vakaların 67'si (%97.1) sol taraflı, 2'si (%2.9) sağ taraflı KDH idi. Vakalardan 11'i (%15.9) gebelik terminasyon seçeneğini kabul etti. İki (%3.4) vaka ölü doğum, 1 (%1.7) vaka abortus ile sonuçlandı. Canlı doğum ile sonuçlanan 55 (%79.7) KDH vakasından 34'ünde (%49.2) doğum sonrası neonatal ölüm gerçekleşti. 21 olgunun (%30.4) postnatal dönemde sağ ve sağlıklı olduğu saptandı.

Sonuç: KDH önemli ölçüde morbidite ve mortaliteyle bilikte olan en şiddetli doğum defektlerinden biridir. KDH'nin antenatal dönemde zamanında tanınması, klinisyenler için aileye ayrıntılı danışmanlık verilmesine, doğum planlamasına ve uygun postpartum yönetime olanak sağlar

Anahtar Kelimeler: Konjenital diyafragma hernisi, fetal anomali, prenatal tanı

Introduction

CDH (Congenital diaphragmatic hernia) is a rare developmental anomaly of the diaphragm characterized by the herniation of abdominal internal organs into the chest. Since the introduction of fetal anomaly screening, the prenatal evaluation of fetuses with CDH has increased; over 60% of cases can be identified by antenatal ultrasonography. The prevalence of CDH is approximately 1 to 4 cases per 10,000 live births. Herniation occurs on the left side in 80 to 85% of cases, on the right side in 10 to 15% of cases, and bilaterally in less than 2% of cases. In left-sided herniations, the stomach usually shifts position, and the liver can also herniate; in right-sided herniations, the liver almost always shifts upwards.

The sensitivity of ultrasound in detecting CDH varies significantly. Diagnosis is more likely when the defect is large, associated abnormalities are present, the pregnancy is more advanced, and the examination is conducted by experienced fetal ultrasonographers. CDH can be an isolated anomaly, part of a syndrome, or associated with other non-syndromic abnormalities. Approximately 30 to 50% of CDH cases are associated with major structural malformations, chromosomal abnormalities, and/or single-gene disorders. Associated malformations can occur in all major organ systems, including neural tube defects and cardiac anomalies. Additional anomalies are most common in cases of bilateral CDH. The presence of a large-volume liver herniation, other systemic anomalies, chromosomal abnormalities, findings suggestive of a fetal syndrome, and low fetal lung volume are factors that adversely affect the prognosis.

Fetuses affected by CDH are at significant risk of morbidity and mortality. Prenatal diagnosis of CDH provides an opportunity for the affected fetuses to be born under optimal conditions and for optimal neonatal management. Prenatal diagnosis of CDH offers parents the opportunity to receive multidisciplinary counseling about the prognosis of their children, prenatal or expected perinatal management, postnatal intervention, and the option of terminating the pregnancy.

Therefore, the purpose of this study is to examine the natural course and detailed perinatal outcomes of CDHs diagnosed during the prenatal period.

Materials and Methods

This retrospective cohort study included patients diagnosed with fetal CDH who admitted to the Perinatology Department of Izmir Tepecik Training and Research Hospital between 2016 and 2023. CDH is characterized by failed closure of the diaphragm, thereby allowing abdominal viscera (stomach, liver, intestine) to herniate into the thoracic cavity (Figure 1). Data were collected by scanning the hospital database and conducting telephone interviews with parents to gather information about the postnatal outcomes of the newborns.

Parents were informed about the chromosomal abnormality risk, and fetal karyotyping was performed upon the parents' request. Fetal genetic tests were conducted based on gestational age using samples from chorionic villus (11-14 weeks), amniotic fluid (16-20 weeks), or umbilical cord blood (after 20 weeks). Detailed counseling for perinatal prognosis was given to the parents. The termination was offered to the pregnancies under 24 weeks. Close perinatological follow-up was performed for pregnant women who decided to continue their pregnancies. Cases were compared in terms of the fetal ultrasonographic findings (side of the defect, associated anomalies), fetal karyotype results, maternal demographic characteristics (age, gravida, parity, presence of systemic diseases), and perinatal outcomes (termination of pregnancy, intrauterine death, birth, and postnatal prognosis). This study was conducted in accordance with the principles of the Helsinki Declaration. Approval was obtained from the Ethics Committee of the Health Sciences University, Izmir Tepecik Training and Research Hospital (2024/05-06). Informed consent was obtained from all patients.

Statistical data were analyzed using SPSS (Statistical Package for the Social Sciences) software version 27.0. Categorical data were obtained using frequency analysis and presented as counts and percentages. Numerical data were obtained using descriptive analysis and presented as mean, standard deviation, and minimum-maximum values. A p-value of less than 0.05 was considered statistically significant.

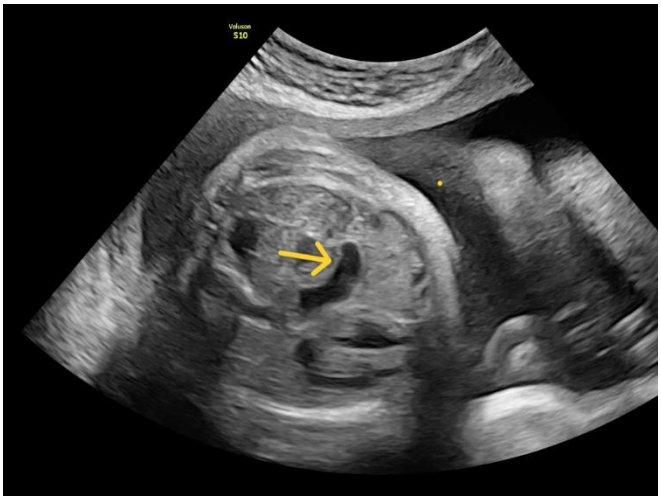


Figure 1. Ultrasonographic image of a patient with left-sided CDH, the heart is pushed to the right side and a gastric air pocket (yellow arrow) is observed behind the heart.

Results

Over an 8-year period, 69 cases of CDH were identified antenatally, with 67 (97.1%) being left-sided and 2 (2.9%) right-sided. The average maternal age was 29.11 ± 6.44 years (range 17-45). Thirty-eight cases (55.1%) were diagnosed before 24 weeks of gestation, and 31 cases (44.9%) were diagnosed at or beyond 24 weeks. A significant relationship was found between the week of diagnosis and fetal prognosis ($p<0.05$). Among cases with CDH, 19 (27.5%) were primigravida and 50 (72.4%) were multigravida. Forty-three (62.3%) cases declined invasive fetal karyotyping. Among the 26 (37.6%) cases who accepted karyotyping, chromosomal abnormalities included trisomy 18 in 2 (7.6%) cases, trisomy 9 in 1 (3.8%) case, 46der3t(3;7) in 1 (3.8%) case, Emanuel Syndrome in 1 (3.8%) case, and normal karyotype in 21 (80.7%) cases.

Eleven pregnancies (15.9%) were terminated due to the parents' request. Two (2.8%) pregnancies resulted in intrauterine death and 1 (1.4%) missed abortion. There were 34 (49.2%) cases of neonatal death in 55 live births, while 21 cases (30.4%) were alive and healthy in the postnatal period. The average gestational week at birth was 36.7 ± 2.9 weeks (range 24 to 39[5] weeks). The average birth weight was 2735.6 ± 632.9 grams (range 1000 to 4000 grams).

Antenatal ultrasonographic findings included 11 (15.94%) liver herniation: 4 (5.7%) total herniation of the liver and gallbladder, and 7 (10.1%) partial liver herniation.

In cases with partial herniation, 5 (7.2%) resulted in neonatal death, and 2 (2.8%) were alive and healthy. In cases with total herniation, 1 (1.4%) resulted in neonatal death, 1 (1.4%) in missed abortion, 1 (1.4%) was terminated at the parents' request, and 1 (1.4%) was alive and healthy.

CDH was found as an isolated condition in 38 cases (55%). Most common anomalies associated with CDH were cardiovascular system anomalies (35.48%), followed by central nervous system anomalies (29%). A significant negative relationship was found between the presence of additional anomalies and perinatal prognosis ($p<0.01$).

There were 34 (49.3%) female, and 35 (50.7%) male fetuses. In female fetuses with CDH, 15 (44.1%) dead in neonatal period, 1 (2.9%) aborted, 6 (17.6%) terminated, and 12 (35.2%) were alive and healthy in the postnatal period. In male fetuses with CDH, 19 (54.2%) dead in neonatal period, 2 (5.7%) had stillbirth, 5 (14.2%) terminated, and 9 (25.7%) were alive and healthy in the postnatal period. Of the 34 female fetuses, 22 (64.7%) had isolated CDH, while 12 (35.3%) had associated anomalies. Of the 35 male fetuses, 16 (45.7%) had isolated CDH, while 19 (54.2%) had associated anomalies. The amniotic fluid was within normal ranges in most of the cases with CDH (86.9%). Polyhydramnios was observed in 8 cases (11.5%), and oligohydramnios in 1 case (1.4%).

Table 1. Relationship between prognostic indicators and perinatal outcomes in cases with CDH.

		Perinatal outcomes				
		Neonatal death (n=34)	**Alive and healthy (n=21)**	**Abortus+stillbirth+TOP (n=14)**	**Total (n=69)**	**p-value**
Additional anomaly	None	22	14	2	38	<0.01
	CVS	5	1	6	12	
	CNS	4	0	4	8	
	Others	3	6	2	11	
Time of diagnosis (w)	<24 weeks	17	9	12	38	<0.05
	≥24 weeks	17	12	2	31	
Liver herniation	None	28	18	12	58	0.583
	Partial	5	2	0	7	
	Total	1	1	2	4	
Gender	Female	15	12	7	34	0.642
	Male	19	9	7	35	

CDH, congenital diaphragmatic hernia; CVS, cardiovascular system; CNS, central nervous system; TOP, termination of pregnancy.

Table 2. The relationship between additional anomalies in CDH cases and prognostic factors and perinatal outcomes.

	Total	Isolated	Additional anomaly					
	n = 69	n = 38	n = 31					
			CVS	CNS	Urinary	Face	Others	Total
			n = 12	n = 8	n = 3	n = 3	n = 5	n = 31
Aneuploidy								
n (%)	5 (7.2)	1 (2.6)	1 (25)	2 (50)	0 (0)	1 (25)	0 (0)	4 (12.9)
p- value		0.102	0.872	0.039	0.621	0.075	0.533	0.102
Liver herniation								
n (%)	11 (15.9)	8 (21.1)	0 (0)	1 (33.3)	0 (0)	2 (66.6)	1 (33.3)	3 (9.7)
p-value		0.199	0.097	0.779	0.441	0.014	0.796	0.199
Gender								
F/M	34/35	22/16	5/6	3/6	1/2	1/2	2/3	12/19
p-value		0.113	0.562	0.478	0.572	0.572	0.666	0.562
TOP								
n (%)	11 (15.9)	0(0)	5 (45.4)	4 (36.3)	0 (0)	2 (18.1)	0 (0)	11 (35.5)
p-value		<0.001	0.007	0.005	0.441	0.014	0.312	<0.001
Delivery								
n (%)	55 (79.7)	36 (94.7)	5 (26.3)	5 (26.3)	3 (15.7)	1 (5.2)	5 (26.3)	19 (61.3)
p-value		<0.001	<0.001	0.198	0.371	0.041	0.242	<0.001
Alive								
n (%)	21 (30.4)	14 (36.8)	1 (14.2)	0 (0)	2 (28.5)	0 (0)	4 (57.1)	7 (22.6)
p-value		0.200	0.093	0.047	0.163	0.241	0.012	0.200

CDH, congenital diaphragmatic hernia; CVS, cardiovascular system; CNS, central nervous system; F, female; M, male; TOP, termination of pregnancy.

Table 3. Comparison of prognostic factors and perinatal outcomes in CDH cases according to the time of prenatal diagnosis.

	Time of diagnosis			
	< 24 weeks	≥ 24 weeks	p- value	Total
	n = 38	n = 31		n = 69
Additional anomaly	16 (42.1)	15 (48.4)	0.748	31 (44.9)
Liver herniation	7 (18.4)	4 (12.9)	0.595	11 (15.9)
Aneuploidy	5 (13.2)	0 (0)	0.049	5 (7.2)
TOP	10 (26.3)	1 (3.2)	0.024	11 (15.9)
Abortus	1 (2.6)	0 (0)	0.369	1 (1.5)
Stillbirth	2 (5.3)	0 (0)	0.207	2 (2.9)
Neonatal death	2 (5.3)	1 (3.2)	0.718	34 (49.3)
Alive	3 (7.9)	2 (6.5)	0.830	5 (7.2)

CDH, congenital diaphragmatic hernia; TOP, termination of pregnancy.

Discussion

We retrospectively assessed and compared the fetal and neonatal outcomes of pregnancies diagnosed with prenatal CDH. Previous studies do not show an association between prevalence of CDH and maternal age (3). Similarly, in our study, the average maternal age was 29.11 ± 6.44 years (range 17-45). According to the literature, more than 60% of CDH cases are initially diagnosed during routine sonographic fetal anatomical examination between 18 and 22 weeks. In our study, 55.1% of cases were diagnosed before 24 weeks, consistent with these findings (2). The diagnosis of CDH can be made at a later stage of pregnancy due to small defects that do not cause early herniation of abdominal contents into the fetal thorax, or due to technical or interpretation issues during earlier examinations. Furthermore, the diagnosis of CDH could be missed until delivery and the time of development of neonatal respiratory distress depends on delivery mode, resuscitation of the infant, size of the defect and pressure in the abdominal cavity. However, we could not able to obtain the data regarding postnatal diagnosis of CDH and therefore, pre-and postnatal comparison could not be performed.

While some studies have reported a slightly higher prevalence in males, most do not observe a gender relationship in CDH (5). In our study, the ratio of female (49.3%) to male (50.7%) fetuses was similar. Previous studies reported that herniations occur on the left side in 80 to 85% of cases, on the right side in 10 to 15% of cases, and bilaterally in less than 2% of cases (2, 5, 6). Our study showed a much higher prevalence of left-sided CDH with an incidence of 97.1% compared to right-sided CDH (2.9%). This difference with the literature could be explained by the ultrasound equipment used for the study population. Left-sided herniations typically involve the displacement of the stomach and may include the liver; right-sided herniations almost always involve upward displacement of the liver. In our study, 13.4% of left-sided CDH cases were accompanied by liver herniation.

Over the past decade, magnetic resonance imaging (MRI) has become complementary to ultrasonography for antenatal prognostication of CDH in most referral centers. MRI allows for more accurate imaging of most fetal structures than ultrasonography because of its superior tissue contrast, wider field of view, and image quality that is independent of maternal body habitus, fetal position, or abnormalities of amniotic fluid. MRI provides a more reliable measurement of lung area, especially on the ipsilateral side, for assessing the total fetal lung volume, that is, the sum of both lung volume.

CDH can be an isolated anomaly, part of a syndrome, or associated with other non-syndromic abnormalities.

The group with non-isolated CDH comprises about 30-50% of cases and is associated with major structural malformations and chromosomal abnormalities. Associated malformations can occur in all major organ systems including neural tube defects and cardiac anomalies (5).

Previous research has shown that a significant percentage of CDH cases, around 68%, are associated with major extra cardiac malformations (15). A previous systematic review found that 15% of fetuses with CDH have congenital heart disease, while in our study, 45% of cases with CDH had other system anomalies, with cardiac malformations making up 35.4% and consistent with the literature, 64.5% were associated with extra cardiac malformations. Prenatally detected cases show conventional karyotype abnormalities in 10 to 20% of cases, with the most common aneuploidies being trisomy 18, 13, and 21 (9,16). The most frequently detected aneuploidy in our study was trisomy 18 (40%). Submicroscopic copy number variations potentially associated with CDH are detected using microarrays (17,18), and in our study, microarray analysis diagnosed 2 cases (40%) with abnormal karyotypes. We provide evidence supporting the recommendation that genetic testing should be offered for all fetuses with diaphragmatic hernia, regardless of whether the cases are isolated or non-isolated.

In the literature, the general survival rate for isolated CDH cases is reported between 44% and 53%. Our study found a lower rate at 36.8% compared to the literature (19,20). Liver herniation is a poor prognostic factor, and the absence of liver herniation is one of the most reliable prenatal indicators of postnatal survival. A study in 2010 assessing 710 fetuses with CDH found survival rates with and without liver herniation to be 45% and 74%, respectively (21). In our study, survival rates for cases with liver herniation were 27.2%, and for those without were 31%, both lower than reported in the literature.

This study had some limitations. First, the sample size was small with only 69 fetuses of CDH analyzed retrospectively. Second, the retrospective design of the study prevents us to identify other prognostic factors such as fetal lung volume and magnetic resonance imaging. However, the study's strengths lie in its design at a single center and the availability of long-term outcomes.

In conclusion, when a fetus with CDH is diagnosed, concurrent possible anomalies should be investigated. Our study revealed that the postnatal survival rate for CDH without liver herniation is higher compared to cases with liver herniation. Detailed counseling is crucial as parents may choose to terminate the pregnancy if a severe anomaly or abnormal karyotype is detected.

References

1. Cordier AG, Russo FM, Deprest J, Benachi A. Prenatal diagnosis, imaging, and prognosis in Congenital Diaphragmatic Hernia. *Semin Perinatol*. 2020;44(1):51163. doi:10.1053/j.semperi.2019.07.002
2. Deprest J, Brady P, Nicolaides K, et al. Prenatal management of the fetus with isolated congenital diaphragmatic hernia in the era of the TOTAL trial. *Semin Fetal Neonatal Med*. 2014;19(6):338-348. doi:10.1016/j.siny.2014.09.006
3. McGivern MR, Best KE, Rankin J, et al. Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. *Arch Dis Child Fetal Neonatal Ed*. 2015;100(2):F137-F144. doi:10.1136/archdischild-2014-306174
4. Burgos CM, Frenckner B. Addressing the hidden mortality in CDH: A population-based study. *J Pediatr Surg*. 2017;52(4):522-525. doi:10.1016/j.jpedsurg.2016.09.061
5. Dott MM, Wong LY, Rasmussen SA. Population-based study of congenital diaphragmatic hernia: risk factors and survival in Metropolitan Atlanta, 1968-1999. *Birth Defects Res A Clin Mol Teratol*. 2003;67(4):261-267. doi:10.1002/bdra.10039
6. Torfs CP, Curry CJ, Bateson TF, Honoré LH. A population-based study of congenital diaphragmatic hernia. *Teratology*. 1992;46(6):555-565. doi:10.1002/tera.1420460605
7. Graham G, Devine PC. Antenatal diagnosis of congenital diaphragmatic hernia. *Semin Perinatol*. 2005;29(2):69-76. doi:10.1053/j.semperi.2005.04.002
8. Sweed Y, Puri P. Congenital diaphragmatic hernia: influence of associated malformations on survival. *Arch Dis Child*. 1993;69(1 Spec No):68-70. doi:10.1136/adc.69.1_spec_no.68
9. Crane JP. Familial congenital diaphragmatic hernia: prenatal diagnostic approach and analysis of twelve families. *Clin Genet*. 1979;16(4):244-252. doi:10.1111/j.1399-0004.1979.tb00996.x
10. Puri P, Gorman F. Lethal nonpulmonary anomalies associated with congenital diaphragmatic hernia: implications for early intrauterine surgery. *J Pediatr Surg*. 1984;19(1):29-32. doi:10.1016/s0022-3468(84)80010-x
11. Witters I, Legius E, Moerman P, et al. Associated malformations and chromosomal anomalies in 42 cases of prenatally diagnosed diaphragmatic hernia. *Am J Med Genet*. 2001;103(4):278-282.
12. Neff KW, Kilian AK, Schaible T, Schütz EM, Büsing KA. Prediction of mortality and need for neonatal extracorporeal membrane oxygenation in fetuses with congenital diaphragmatic hernia: logistic regression analysis based on MRI fetal lung volume measurements. *AJR Am J Roentgenol*. 2007;189(6):1307-1311. doi:10.2214/AJR.07.2434
13. Javid PJ, Jaksic T, Skarsgard ED, Lee S; Canadian Neonatal Network. Survival rate in congenital diaphragmatic hernia: the experience of the Canadian Neonatal Network. *J Pediatr Surg*. 2004;39(5):657-660. doi:10.1016/j.jpedsurg.2004.01.022
14. Benachi A, Cordier AG, Cannie M, Jani J. Advances in prenatal diagnosis of congenital diaphragmatic hernia. *Semin Fetal Neonatal Med*. 2014;19(6):331-337. doi:10.1016/j.siny.2014.09.005
15. Hautala J, Karstunen E, Ritvanen A, et al. Congenital diaphragmatic hernia with heart defect has a high risk for hypoplastic left heart syndrome and major extra-cardiac malformations: 10-year national cohort from Finland. *Acta Obstet Gynecol Scand*. 2018;97(2):204-211. doi:10.1111/aogs.13274
16. Taylor GA, Atalabi OM, Estroff JA. Imaging of congenital diaphragmatic hernias. *Pediatr Radiol*. 2009;39(1):1-16. doi:10.1007/s00247-008-0917-7
17. Brady PD, DeKoninck P, Fryns JP, Devriendt K, Deprest JA, Vermeesch JR. Identification of dosage-sensitive genes in fetuses referred with severe isolated congenital diaphragmatic hernia. *Prenat Diagn*. 2013;33(13):1283-1292. doi:10.1002/pd.4244
18. Burgos CM, Gupta VS, Conner P, et al. Syndromic congenital diaphragmatic hernia: Current incidence and outcome. Analysis from the congenital diaphragmatic hernia study group registry. *Prenat Diagn*. 2023;43(10):1265-1273. doi:10.1002/pd.6407
19. Jani J, Nicolaides KH, Keller RL, et al. Observed to expected lung area to head circumference ratio in the prediction of survival in fetuses with isolated diaphragmatic hernia. *Ultrasound Obstet Gynecol*. 2007;30(1):67-71. doi:10.1002/uog.4052
20. DeKoninck P, Gomez O, Sandaite I, et al. Right-sided congenital diaphragmatic hernia in a decade of fetal surgery. *BJOG*. 2015;122(7):940-946. doi:10.1111/1471-0528.13065
21. Mullassery D, Ba'ath ME, Jesudason EC, Losty PD. Value of liver herniation in prediction of outcome in fetal congenital diaphragmatic hernia: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2010;35(5):609-614. doi:10.1002/uog.7586

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (1): 14-21

Evaluation of Shock Appropriateness in Patients Admitted to the Emergency Department After ICD Shocking

ICD Şoklaması Sonrası Acil Servise Başvuran Hastalarda Şoklama Uygunluğunun İncelenmesi

Efe KANTER* 0000-0002-0208-950X
Osman Sezer ÇINAROĞLU* 0000-0002-3860-2053
Ramazan Batuhan ŞAHİN 0009-0009-8957-0344**
Ecem ERMETE GÜLER* 0000-0002-1490-8840

* Izmir Katip Celebi University, Faculty of Medicine, Department of Emergency Medicine, Izmir
** Izmir Katip Celebi University, Faculty of Medicine

Correspondence Address: Efe KANTER
Izmir Katip Celebi University, Ataturk Training and Research Hospital, Emergency Room, 35150, Karabaglar/Izmir
E-mail : efekanter@hotmail.com

Geliş Tarihi: 22.01.2025
Kabul Tarihi: 10.03.2025

Abstract

Aim: Implantable cardioverter-defibrillators (ICDs) are crucial for preventing sudden cardiac death in high-risk patients by delivering shocks during life-threatening arrhythmias. However, inappropriate ICD shocks can lead to unnecessary emergency department (ED) visits and patient distress. This study aims to evaluate the appropriateness of ICD shocks in patients presenting to the ED and assess their relationship with patient demographics, clinical characteristics, and outcomes.

Methods: This retrospective study included patients who presented to emergency department following an ICD shock between January 2023 and July 2023. Subsequent analysis involved examining general patient characteristics, comorbidities, the relationship between shock appropriateness and other parameters. We used statistical analysis to determine key predictors of inappropriate shocks by examining general patient characteristics, comorbidities, and their relationship with shock appropriateness.

Results: Of the 175 patients analyzed, inappropriate shocks were identified in 49.1% of cases. These inappropriate shocks were significantly associated with supraventricular tachycardia and atrial fibrillation with rapid ventricular response ($p<0.001$). Patients with inappropriate shocks demonstrated significantly lower ejection fraction (EF) ($p=0.013$) and higher rates of comorbidities, particularly diabetes and smoking history ($p=0.011$ and $p=0.024$).

Conclusion: This study highlights the significant incidence of inappropriate ICD shocks in patients presenting to the ED. The findings emphasize the importance of thorough device interrogation, careful evaluation of patient-specific factors, and individualized management to prevent unnecessary interventions and optimize patient outcomes. Future research should focus on refining ICD programming and identifying patient-specific risk factors to reduce inappropriate shocks and improve the quality of care in the ED setting.

Keywords: Apropriateness, ICD, shock

Öz

Amaç: İmplante edilebilir kardiyoverter-defibrilatörler (ICD'ler), yüksek riskli hastalarda hayatı tehdit eden aritmiler sırasında şok uygulayarak ani kardiyak ölümü önlemede hayati öneme sahiptir. Bununla birlikte, uygunsuz ICD şokları gereksiz acil servis (AS) başvurularına ve hasta stresine yol açabilir. Bu çalışma, ICD şoku ile AS'ye başvuran hastalarda şokların uygunluğunu değerlendirmeyi ve bu şokların hasta demografisi, klinik özellikleri ve sonuçları ile olan ilişkisini incelemeyi amaçlamaktadır.

Yöntem: Bu retrospektif çalışmaya, Ocak 2023 ile Temmuz 2023 tarihleri arasında ICD şoku sonrası acil servise başvuran hastalar dahil edilmiştir. Sonraki analizde, genel hasta özellikleri, komorbiditeler, şok uygunluğu ile diğer parametreler arasındaki ilişki incelenmiştir. Bu faktörler, anlamlı etkileyici faktörleri belirlemek amacıyla uygun istatistiksel yöntemler kullanılarak analiz edilmiştir.

Bulgular: Analiz edilen 175 hastanın %49,1'inde uygunsuz şoklar tespit edilmiştir. Bu uygunsuz şokların, supraventriküler taşikardi ve hızlı ventriküler yanıtlı atriyal fibrilasyon ile anlamlı şekilde ilişkili olduğu bulunmuştur ($p<0.001$). Uygunsuz şok alan hastalarda ejeksiyon fraksiyonunun (EF) anlamlı derecede daha düşük olduğu ($p=0.013$) ve özellikle diyabet ve sigara öyküsü gibi komorbiditelerin daha yüksek oranlarda görüldüğü belirlenmiştir ($p=0.011$ ve $p=0.024$).

Sonuçlar: Bu çalışma, acil servise başvuran hastalarda uygunsuz ICD şoklarının önemli bir insidansa sahip olduğunu ortaya koymaktadır. Bulgular, gereksiz müdahaleleri önlemek ve hasta sonuçlarını optimize etmek için cihazın titizlikle incelenmesinin, hasta özelinde faktörlerin dikkatlice değerlendirilmesinin ve bireyselleştirilmiş yönetim yaklaşımlarının önemini vurgulamaktadır. Gelecekteki araştırmalar, uygunsuz şokların azaltılması ve acil servis ortamında bakım kalitesinin artırılması amacıyla ICD programlamasının iyileştirilmesine ve hasta bazlı risk faktörlerinin belirlenmesine odaklanmalıdır.

Anahtar Kelimeler: ICD, şoklama, uygunluk

Introduction

Implantable Cardioverter Defibrillators (ICDs) are critical devices for preventing sudden cardiac death in patients at high risk for malignant ventricular arrhythmias by delivering therapeutic shocks when life-threatening rhythms are detected (1,2). While ICDs significantly improve survival rates, inappropriate shocks remain a major concern, particularly in the emergency department (ED), where the initial evaluation and disposition of patients with ICD discharges must be made rapidly and accurately (3).

Inappropriate ICD shocks—defined as shocks delivered in the absence of life-threatening ventricular arrhythmias, often triggered by supraventricular tachycardia (SVT), atrial fibrillation with rapid ventricular response (AFRVR), or device-related artifacts—can lead to unnecessary ED visits, prolonged hospitalizations, and increased healthcare utilization (4,5). Additionally, these shocks may cause significant psychological distress, including heightened anxiety and depression, which can negatively impact long-term quality of life (3). Despite these well-documented concerns, the evaluation of ICD shock appropriateness in the ED setting remains highly variable, with limited standardized protocols guiding management decisions.

Current literature indicates that ICD shock appropriateness is influenced by multiple factors, including the triggering rhythm, left ventricular ejection fraction (EF), presence of comorbidities, and device programming strategies (4,5). However, data specific to the ED setting—where clinicians often lack access to immediate device interrogation results and must make time-sensitive decisions—remain scarce. Given the increasing number of patients presenting to the ED following ICD shocks, a more structured approach to distinguishing appropriate from inappropriate shocks is essential to prevent unnecessary hospitalizations and optimize patient outcomes.

This study aims to assess the appropriateness of ICD shocks in patients presenting to the ED and to identify key clinical parameters associated with inappropriate shocks. By elucidating the predictors of inappropriate ICD discharges, this study seeks to provide evidence-based guidance for ED physicians, enhance risk stratification, and improve patient-centered management strategies.

Materials and Methods

Study design and setting

This retrospective study was conducted following approval from the Izmir Katip Celebi University Clinical Research Ethics Committee (Approval No: 0430, Date: 21.09.2023). The study aimed to evaluate the appropriateness of ICD shocks in patients presenting to the emergency department (ED) between January 2023 and July 2023. The findings of this study are expected to contribute to the optimization of clinical decision-making processes regarding ICD management in the ED.

Study Population

All adult patients (≥18 years) who presented to the ED due to ICD shocks within the study period were included. Patients were excluded if they:

- Were under 18 years of age (n=2),
- Could not be evaluated due to a lack of access to the device manufacturer (n=11),
- Had incomplete data (n=17),
- Were referred to another institution or refused further treatment, precluding follow-up (n=7).

The patient selection process is illustrated in **Figure 1**.

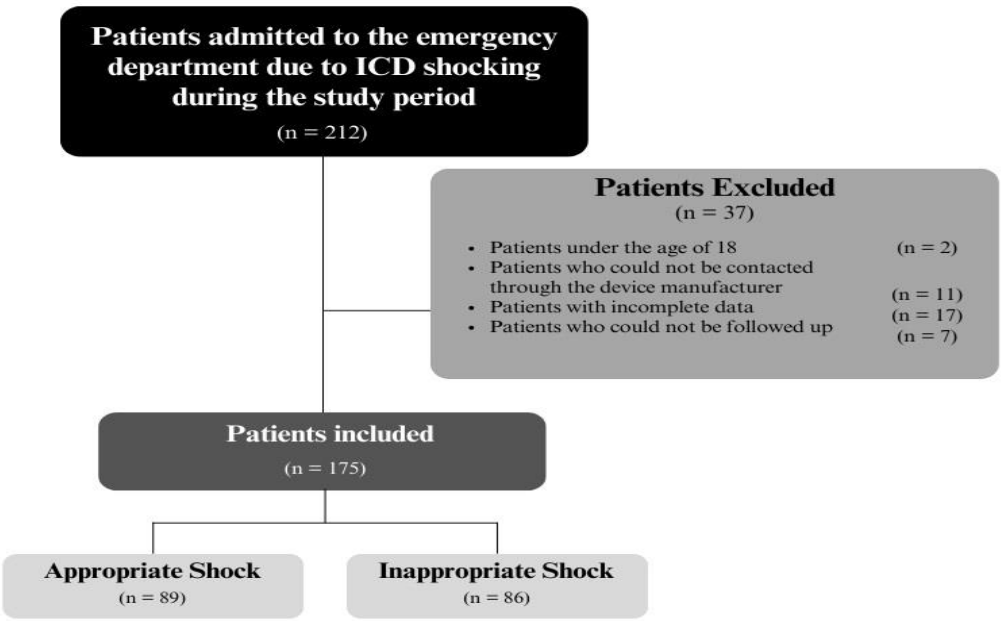


Figure 1. Flowchart of the Study

Evaluation of Shock Appropriateness

ICD shock appropriateness was determined based on established criteria in the literature and manufacturer-defined algorithms. Shocks were classified as:

- **Appropriate**: When triggered by documented life-threatening arrhythmias, such as ventricular tachycardia (VT) or ventricular fibrillation (VF), confirmed via device interrogation and clinical correlation.
- **Inappropriate**: When occurring due to non-life-threatening arrhythmias (e.g., atrial fibrillation with rapid ventricular response (AFRVR), supraventricular tachycardia (SVT)) or device-related issues (e.g., lead malfunction, oversensing).

Device interrogation reports, stored electrograms, and ECG findings were reviewed by an electrophysiologist and an experienced emergency physician for validation.

Although ICD device types (single-chamber, dual-chamber, biventricular, subcutaneous) were documented, further analysis regarding their impact on shock appropriateness was not performed.

Data Collection

Patient data were extracted from hospital electronic medical records and ICD interrogation reports. To ensure consistency and minimize bias, data were collected systematically under the following categories:

Demographic and Clinical Characteristics:

- Age, gender and comorbidities (diabetes mellitus, hypertension, congestive heart failure and coronary artery disease).
- Smoking history (self-reported during ED admission).

ICD Shock Data:

- Shock appropriateness classification based on manufacturer reports and clinical correlation.
- Presenting rhythm at ED admission (sinus rhythm, atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, or ventricular fibrillation).
- Shock-triggering rhythm identified by the ICD (corroborated with device interrogation).
- ECG evaluation at ED presentation, performed by an emergency physician and electrophysiologist.

Laboratory and Physiological Data:

- Heart rate (first documented measurement in the ED; subsequent readings not analyzed).
- Ejection Fraction (EF) (most recent echocardiographic measurement within three months prior to ED admission).

Patient Outcomes:

- Disposition: Discharge, inpatient admission, or ICU transfer.
- Mortality, determined via hospital records and follow-up data when available.

Patients with missing data for critical variables were excluded to maintain data integrity.

Statistical Analysis

In this study, descriptive statistics were presented as mean ± standard deviation and median (min-max) for continuous variables, and frequency and percentage (%) for categorical variables. For group comparisons, an independent samples t-test was used for continuous variables with a normal distribution, and the Mann-Whitney U test was applied for continuous variables that did not follow a normal distribution. The relationships between categorical variables were assessed using the Chi-square test. All statistical analyses were performed using SPSS version 26.0, with a p-value of <0.05 considered statistically significant.

Results

In this study, a total of 175 patients admitted to the ED following ICD shocks were analyzed. Among the patients, 135 (77.1%) were male, and 40 (22.9%) were female, with a mean age of 63.40 ± 13.51 years, ranging from 22 to 90 years. The initial rhythm recorded in the ED revealed that sinus rhythm was the most common (64%), followed by atrial fibrillation (27.4%), and to a lesser extent, pacemaker rhythm (5.7%). Notably, ventricular tachycardia was the predominant shock rhythm in 28.6% of the cases, while ventricular fibrillation and atrial fibrillation with rapid ventricular response (AFRVR) were observed in 16% and 39.4% of the patients, respectively **(Table 1)**.

The evaluation of the appropriateness of ICD shocks showed that 89 patients (50.9%) received appropriate shocks, while 86 patients (49.1%) received inappropriate shocks, as indicated in **Table 1**. Regarding the cardiac function, the mean ejection fraction was calculated as 33.37% ± 12.52, with a median value of 30%. The patient outcomes varied significantly, with 76 patients (43.4%) being discharged, 83 patients (47.4%) transferred to the ICU, and 16 patients (9.1%) admitted to the inpatient ward. Additionally, mortality outcomes revealed that 141 patients (80.6%) survived, while 34 patients (19.4%) did not survive.

Table 1: General Characteristics and Shock Appropriateness of the Patients

	n	%
Gender		
Female	40	22,9
Male	135	77,1
Age		
$\bar{x}$±ss	63,40±13,51	
M (min-max)	65 (22-90)	
Rhythm in ER		
Sinus rhythm	112	64,0
Atrial fibrillation	48	27,4
Pace rhythm	10	5,7
Supraventricular tachycardia	2	1,1
Ventricular tachycardia	3	1,7
Shock rhythm		
No shock	13	7,4
AFRVR	69	39,4
Supraventricular tachycardia	15	8,6
Ventricular tachycardia	50	28,6
Ventricular fibrillation	28	16,0
Appropriateness of shock		
Appropriate	89	50,9
Inappropriate	86	49,1
Ejection fraction		
$\bar{x}$±ss	33,37±12,52	
M (min-max)	30 (15-70)	
Outcome		
Discharged	76	43,4
Admitted to Inpatient Ward	16	9,1
Transferred to ICU	83	47,4
Mortality		
None	141	80,6
Present	34	19,4

ER: emergency room, AFRVR: atrial fibrillation with rapid ventricular response, ICU: intensive care unit

Table 2 provides a detailed account of the comorbidities present in the study population. Diabetes mellitus (DM) was present in 36% of the patients, hypertension (HT) in 52%, congestive heart failure (CHF) and coronary artery disease (CAD) each in 62%, while malignancy was noted in only 2.9% of the patients. Smoking history was present in 32.6% of the cases.

Table 2: Comorbidity Status of the Patients

Variables	*n*	%
DM		
None	112	64,0
Present	63	36,0
HT		
None	84	48,0
Present	91	52,0
CHF		
None	66	37,7
Present	109	62,3
CAD		
None	66	37,7
Present	109	62,3
Malignancy		
None	170	97,1
Present	5	2,9
Smoking history		
None	118	67,4
Present	57	32,6

DM: diabetes mellitus, HT: hypertension, CHF: congestive heart failure, CAD: coronary artery disease

A deeper analysis of the relationship between shock appropriateness and clinical parameters revealed several important findings **(Table 3)**. Firstly, the rhythm observed in the ED was significantly correlated with the appropriateness of the shocks (p=0.008). Sinus rhythm was associated with a higher likelihood of appropriate shocks (59,8% in the appropriate group versus 40,2% in the inappropriate group), while atrial fibrillation was more common in patients who received inappropriate shocks (68,8% in the inappropriate group versus 31,3% in the appropriate group).

The type of shock rhythm, as also shown in **Table 3**, played a particularly critical role in determining shock appropriateness. Ventricular tachycardia and ventricular fibrillation were almost exclusively associated with appropriate shocks, with 90% and 100% of these rhythms leading to appropriate interventions. On the other hand, AFRVR and supraventricular tachycardia (SVT) were predominantly associated with inappropriate shocks, as approximately 76,8% and 100% of patients with this rhythm received inappropriate ICD shocks. This association between shock rhythm and shock appropriateness was highly statistically significant (p<0.001).

Further exploration into cardiac function showed that patients who experienced inappropriate shocks had a significantly higher mean ejection fraction than those with appropriate shocks (35.59 ± 13.12 vs. 31.23 ± 11.58, p=0.013), as illustrated in **Table 3**. Additionally, the mean heart rate was significantly found to be elevated in the inappropriate shock group (97.79 ± 27.61 bpm) compared to the appropriate shock group (87.98 ± 21.02 bpm, p=0.048), suggesting that higher heart rates may contribute to the misinterpretation of the need for shock.

The presence of comorbid conditions, specifically diabetes mellitus (DM), was another factor significantly associated with shock appropriateness. As shown in **Table 3**, patients with DM were more likely to receive inappropriate shocks (61,9% vs. 38,1% in the appropriate group, p=0.011). A history of smoking also showed a significant association, with a higher prevalence of smoking in patients who received appropriate shocks (63,2% vs. 36,8% in the inappropriate group, p=0.024). However, no significant differences were found between shock appropriateness and other factors such as gender, age, hypertension (HT), congestive heart failure (CHF), coronary artery disease (CAD), or malignancy.

Table 3: Comparison of Clinical Characteristics Based on Shock Appropriateness

	Appropriateness of Shock		**Test Statistics**	
	Appropriate	Inappropriate	Test value	*p* value
Gender				
Female	17 (42,5)	23 (57,5)	1,449	0,229
Male	72 (53,3)	63 (46,7)		
Age				
$\bar{x}$±ss	62,64±12,50	64,18±14,52	0,805	0,421
M (min-max)	65 (22-84)	65 (23-90)		
Rhythm in ER				
Sinus rhythm	67 (59,8)	45 (40,2)	13,757	**0,008**
Atrial fibrillation	15 (31,3)	33 (68,8)		
Pace rhythm	6 (60,0)	4 (40,0)		
Supraventricular tachycardia	0 (0,0)	2 (100,0)		
Ventricular tachycardia	1 (33,3)	2 (66,7)		
Shock rhythm				
No shock	0 (0,0)	13 (100,0)	107,821	**<0,001**
AFRVR	16 (23,2)	53 (76,8)		
Supraventricular tachycardia	0 (0,0)	15 (100,0)		
Ventricular tachycardia	45 (90,0)	5 (10,0)		
Ventricular fibrillation	28 (100,0)	0 (0,0)		
Ejection fraction				
$\bar{x}$±ss	31,23±11,58	35,59±13,12	2,491	**0,013**
M (min-max)	30 (15-60)	35 (15-70)		
Heart rate				
$\bar{x}$±ss	87,98±21,02	97,79±27,61	1,978	**0,048**
M (min-max)	90 (45-160)	92 (55-180)		
DM				
None	65 (58,0)	47 (42,0)	6,415	**0,011**
Present	24 (38,1)	39 (61,9)		
HT				
None	47 (56,0)	37 (44,0)	1,678	0,195
Present	42 (46,2)	49 (53,8)		
CHF				
None	33 (50,0)	33 (50,0)	0,031	0,860
Present	56 (51,4)	53 (48,6)		
CAD				
None	33 (50,0)	33 (50,0)	0,031	0,860
Present	56 (51,4)	53 (48,6)		
Malignancy				
None	87 (51,2)	83 (48,8)	0,243	0,622
Present	2 (40,0)	3 (60,0)		
Smoking history				
None	53 (44,9)	65 (55,1)	5,118	**0,024**
Present	36 (63,2)	21 (36,8)		

ER: emergency room, AFRVR: atrial fibrillation with rapid ventricular response, DM: diabetes mellitus, HT: hypertension, CHF: congestive heart failure, CAD: coronary artery disease

Discussion

This study provides a detailed analysis of the appropriateness of ICD shocks in patients presenting to the emergency department (ED) and examines its association with various clinical parameters. The findings highlight key factors influencing ICD shock appropriateness, contributing to improved patient management and risk stratification in the ED setting.

A significant association was found between the presenting rhythm and shock appropriateness. Sinus rhythm was more frequently associated with appropriate shocks, whereas atrial fibrillation (AF) was strongly linked to inappropriate shocks. This finding aligns with previous studies suggesting that AF, particularly with rapid ventricular response (AFRVR), may trigger unnecessary ICD shocks due to misclassification of atrial arrhythmias as life-threatening ventricular events (6,7). Given the high prevalence of AF among ICD recipients, these results underscore the need for AF-specific detection algorithms in ICD programming to minimize inappropriate shocks.

One of the most striking findings of this study is the relationship between the arrhythmic trigger and shock appropriateness. ICD shocks triggered by ventricular tachycardia (VT) or ventricular fibrillation (VF) were almost exclusively appropriate, confirming that these rhythms are correctly classified as life-threatening by the ICD. In contrast, AFRVR and supraventricular tachycardia (SVT) were the primary contributors to inappropriate shocks. This suggests that ICD programming refinements are required to improve differentiation between supraventricular and ventricular arrhythmias (8,9).

Additionally, a strong correlation was observed between left ventricular ejection fraction (EF) and shock appropriateness. Patients with lower EF were more likely to receive appropriate shocks, whereas those with preserved EF had a higher incidence of inappropriate shocks. This may reflect more aggressive ICD programming in patients with reduced EF, which increases the likelihood of appropriate shock delivery when needed (10,11). However, in patients with relatively preserved EF, inappropriate shocks may occur due to misinterpretation of high-rate supraventricular arrhythmias as malignant ventricular events. These findings suggest that adjustments in detection thresholds and algorithm refinement may be necessary for ICD recipients with preserved EF. Heart rate also emerged as a significant factor in shock appropriateness. Higher heart rates at presentation were associated with inappropriate shocks, likely due to misclassification of sinus tachycardia or supraventricular arrhythmias as VT (12,13). Given this association, careful consideration of heart rate trends and episode duration thresholds in ICD programming could help reduce unnecessary shocks. Among comorbid conditions, diabetes mellitus (DM) was identified as a key factor associated with inappropriate shocks. Patients with DM were significantly more likely to experience inappropriate ICD discharges. Although the exact pathophysiological mechanisms remain unclear, autonomic dysfunction in diabetic patients may contribute to altered arrhythmic triggers and inappropriate ICD activation (14,15). These findings emphasize the importance of individualized ICD programming in patients with DM to mitigate the risk of unnecessary shocks.

Clinical Implications

The results of this study underscore the need for improved ICD detection algorithms, particularly in patients with AF, preserved EF, or diabetes mellitus. Optimizing ICD programming by refining detection parameters and incorporating advanced rhythm discrimination algorithms could significantly reduce inappropriate shocks and improve patient outcomes.

One of the most effective strategies to reduce inappropriate ICD shocks is the optimization of device programming parameters. Specifically, adjusting the nominal rate detection thresholds and detection durations can significantly improve rhythm discrimination. For example, increasing the ventricular tachycardia detection rate above 180 beats per minute and extending detection intervals may help differentiate supraventricular arrhythmias from true ventricular arrhythmias, thereby reducing inappropriate therapies. Additionally, enabling advanced discrimination algorithms, such as morphology discrimination or onset and stability criteria, can enhance the specificity of arrhythmia detection. These adjustments should be individualized based on the patient's arrhythmic profile and comorbidities.

To minimize unnecessary hospital admissions, we suggest a structured algorithm for managing patients presenting with ICD shocks in the ED. This approach should include immediate 12-lead ECG, bedside echocardiography, symptom assessment, and, if available, rapid device interrogation. Patients with confirmed inappropriate shocks, stable hemodynamics, and no evidence of myocardial ischemia or structural decompensation could potentially be discharged with close outpatient follow-up. Implementation of such an algorithm may reduce resource utilization while maintaining patient safety.

Study Limitations

This study has several limitations. As a retrospective study, data collection was dependent on existing medical records, which may have introduced incomplete documentation or selection bias. Additionally, the study was conducted at a single center, which may limit the generalizability of the findings. While ICD device types (single-chamber, dual-chamber, biventricular, and subcutaneous) were recorded, a detailed analysis of their impact on shock appropriateness was beyond the scope of this study. Future multicenter prospective studies are needed to validate these findings and assess the potential role of device-specific programming adjustments.

Conclusion

This study identifies key factors influencing the appropriateness of ICD shocks in patients presenting to the ED. AF, AFRVR, preserved EF, high heart rate, and DM were significant predictors of inappropriate shocks, highlighting the need for refinements in ICD detection algorithms and individualized device programming. These findings have important clinical implications for improving ICD therapy, reducing unnecessary ED visits, and optimizing patient outcomes.

References

1. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. The New England Journal of Medicine. 2005;352(3):225-237.
2. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. The New England Journal of Medicine. 2002;346(12):877-883.
3. Poole JE, Johnson GW, Hellkamp AS, et al. Prognostic importance of defibrillator shocks in patients with heart failure. The New England Journal of Medicine. 2008;359(10):1009-1017.
4. Sweeney MO, Wathen MS, Volosin K, et al. Appropriate and inappropriate ventricular therapies, quality of life, and mortality among primary and secondary prevention implantable cardioverter-defibrillator patients: results from the PREDICTOR trial. Journal of Cardiovascular Electrophysiology. 2010;21(12):1343-1349.
5. van Rees JB, Borleffs CJ, de Bie MK, et al. Inappropriate implantable cardioverter-defibrillator shocks: incidence, predictors, and impact on mortality. Journal of the American College of Cardiology. 2011;57(5):556-562.
6. Jalife J, Berenfeld O, Skanes A, Mandapati R. Mechanisms of atrial fibrillation: mother rotors or multiple daughter wavelets, or both? Journal of Cardiovascular Electrophysiology. 1998 Aug;9(8 Suppl):S2-12. PMID: 9727669.
7. Gillis AM, Unterberg-Buchwald C, Schmidinger H, Massimo S, Wolfe K, Kavaney DJ, et al. Safety and efficacy of advanced atrial pacing therapies for atrial tachyarrhythmias in patients with a new implantable dual chamber cardioverter-defibrillator. Journal of the American College of Cardiology. 2002; 40: 1653-59.
8. Lin G, Nishimura RA, Gersh BJ, et al. Device complications and inappropriate implantable cardioverter defibrillator shocks in patients with hypertrophic cardiomyopathy. Heart. 2009; 95: 709-14.
9. Nazer B, Dale Z, Carrassa G, Owens A, Olivotto I, Heitner SB. Appropriate and inappropriate shocks in hypertrophic cardiomyopathy patients with subcutaneous implantable cardioverter-defibrillators: An international multicenter study. Heart Rhythm. 2020; 17: 1107-14.
10. Daubert JP, Zareba W, Cannom DS, McNitt S, Rosero SZ, Wang P, et al. Inappropriate implantable cardioverter-defibrillator shocks in MADIT II: Frequency, mechanisms, predictors, and survival impact. Journal of the American College of Cardiology. 2008; 51: 1357-65.
11. Gehi AK, Mehta D, Gomes JA. Evaluation and management of patients after implantable cardioverter-defibrillator shock. The Journal of the American Medical Association. 2006; 296: 2839-47.
12. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NAM, Freedman RA, Gettes LS, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. Circulation. 2008; 117: e350-408.
13. Sweeney MO, Wathen MS, Volosin K, Abdalla I, DeGroot PJ, Otterness MF, et al. Appropriate and inappropriate ventricular therapies, quality of life, and mortality among primary and secondary prevention implantable cardioverter defibrillator patients. Circulation. 2005; 111: 2898-2905.
14. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. The New England Journal of Medicine. 2002; 346: 1845-53.
15. Steinberg JS, Fischer A, Wang P, Schuger C, Daubert J, McNitt S, et al. The clinical implications of cumulative right ventricular pacing in the Multicenter Automatic Defibrillator Trial II. Journal of Cardiovascular Electrophysiology. 2005; 16: 359-65.

Ege Klin Tıp Derg 2025;63 (1): 22-31

Evaluation Of Bifurcation Lesion Procedures Performed In A Tertiary Centre

Üçüncü Basamak Bir Merkezde Yapılan Bifurkasyon Lezyon Girişimlerinin Değerlendirilmesi

Dogac Caglar GURBUZ* 0000-0002-0517-8612
Emre OZDEMIR 0000-0003-0034-3022**
Sadik Volkan EMREN0000-0002-7652-1123**
Cem NAZLI 0000-0003-2231-3780**
Mehmet TOKAC 0000-0002-3223-7497**

*Istanbul Sisli Kolan International Hospital, Cardiology ISTABUL/TURKEY
**Izmir Katip Celebi University, Cardiology Department IZMIR/TURKEY

Yazışma Adresi: Doğaç Çağlar GÜRBÜZ
Istanbul Sisli Kolan International Hospital,
Cardiology ISTABUL/TURKEY
E-Mail: drdogacgurbuz@gmail.com

Geliş Tarihi: 11.03.2024
Kabul Tarihi: 02.04.2025

Abstract

Introduction: We aimed to learn the results of coronary bifurcation lesions that underwent intervention and to investigate awareness of what can be done to reduce morbidity and mortality.

Methods: Patients who underwent coronary intervention between January 2013 and May 2018 were retrospectively screened and patients who underwent bifurcation lesion procedures were collected. A total of 151 eligible patients were identified. Demographic information, risk factors, clinical presentations, medication use, laboratory values, imaging findings, and complications were recorded retrospectively. Primary endpoints were determined as all-cause mortality, myocardial infarction, TVR, TLR, and all events.

Results: Being above the calculated mean age (age>59.6, p: 0.017), having multi-vessel disease (>1.98 vessel count, p: 0.027), not performing final kissing angioplasty during coronary intervention (p: 0.013) were statistically found to be the most important causes of all-cause mortality in patients who underwent coronary bifurcation intervention. In addition, the most common complication after the procedure was acute renal failure, which was observed to cause an increase in all-cause mortality. In multiple analyses; it was determined that in patients who did not undergo final kissing balloon angioplasty, there was a 1.74-fold increase in all events (p: 0.043), in patients with acute renal failure, there was a 5.93-fold increase in all events after the procedure (p: 0.107), and in patients with multi-vessel disease, there was a 2.171-fold increase in mortality and morbidity in all events.

Conclusion: In elderly patients who are planned for complex coronary intervention; in order to reduce mortality and morbidity, the most appropriate technique (PCI or CABG) should be selected for the lesion, final kissing balloon angioplasty should be performed, and opaque material should be used carefully.

Keywords: Intervention of coronary bifurcation lesion, acute renal failure, multi-vessel coronary lesion, final kissing angioplasty

Öz

Giriş: Girişim uygulanan koroner bifurkasyon lezyonlarının sonuçlarını öğrenmeyi, morbidite ve mortaliteyi azaltmak için neler yapılabileceği konusunda farkındalığı araştırmayı amaçladık.

Yöntem: Ocak 2013 ile Mayıs 2018 arasında koroner müdahale geçiren hastalar retrospektif olarak tarandı ve bifurkasyon lezyon prosedürü geçiren hastalar toplandı. Toplam 151 uygun hasta tespit edildi. Demografik bilgiler, risk faktörleri, klinik başvurular, ilaç kullanımı, laboratuvar değerleri, görüntüleme bulguları, komplikasyonlar retrospektif olarak kaydedildi. Birincil son noktaları tüm nedenlere bağlı ölüm, miyokard enfarktüsü, TVR, TLR ve tüm olaylar olarak belirlendi.

Bulgular: Hesaplanan ortalama yaşın üzerinde ve (yaş>59.6,p: 0,017) çoklu damar hastalığına sahip olmak(>1.98 damar sayısı, p: 0,027), koroner girişim sırasında final kissing anjiyoplasti yapılmaması(p: 0,013) istatiksel olarak koroner bifurkasyon girişimi yapılan hastalarda tüm nedenlere bağlı ölümlerin en önemli nedenleri olarak bulunmuştur. Ayrıca işlem sonrası en sık görülen komplikasyon akut böbrek yetmezliği olup ve tüm nedenlere bağlı ölümlerde artışa sebep olduğu gözlenmiştir. Çoklu analizlerde; final kissing balon anjiyoplastisi yapılmayan hastalarda, tüm olaylarda 1,74 kat artış (p: 0,043), akut böbrek yetmezliği olan hastalarda işlem sonrası tüm olaylarda 5,93 kat artış (p: 0,107) ve çok damar hastalarında tüm olaylarda 2,171 kat mortalite ve morbiditede artışa neden olduğu belirlenmiştir.

Sonuç: Kompleks koroner girişim planlanan ileri yaş hastalarda; Mortalite ve morbiditeyi azaltmak için hastalarda lezyona en uygun teknik seçilmeli, final öpüşme balon anjiyoplastisi yapılmalı ve opak materyal dikkatli kullanılmalıdır.

Anahtar Kelimeler: Koroner bifurkasyon lezyonlarına girişim, akut böbrek yetmezliği, çok damar koroner arter hastalığı, final kissing anjiyoplasti

Introduction

Atherosclerosis may develop in the regions of coronary bifurcation due to turbulent flow and high shear stress (1). Bifurcation lesions (BL); It is a member of the complex coronary intervention family, prolongs the procedure and increases the complication rate, and decreases the success rates of percutaneous coronary interventions (PCI) (2). BL investigates about 50% for PCI, but BL usually requires multiple and complex stenting techniques (3).

The use of multiple stents increases stent complications (restenosis, thrombosis) and mortality rates (4). New stent technology results and results on BL show a decrease in the success rates of BL (5).

In this title, we aimed to report the results of BL in the middle follow-up period, which was a successful PCI in tertiary health centres.

Material and method

Patients who had two or more coronary intervention wires (floppy wires) used in the angiography laboratory and who underwent intervention between January 2013 and May 2018 at the İzmir Katip Çelebi University Atatürk Education and Research Hospital Faculty of Medicine were retrospectively scanned via the 'Probel' system and recorded as an Excel file. 3100 patients were identified, and their angiogram papers were scanned. 151 patients were reported to have undergone coronary bifurcation intervention and were included in our study.

Retrospectively; age, gender, diabetes mellitus (known diabetes treated with diet or medication), arterial hypertension (known hypertension, treated with antihypertensive drugs), smoking history, percutaneous coronary intervention and / or coronary artery bypass grafting, history of cerebrovascular event and peripheral arterial disease; clinical condition of the patient, hospitalization stable angina pectoris (SAP), unstable angina pectoris (USAP), non-ST elevation myocardial infarction (NSTEMI), ST elevation myocardial infarction (STEMI), hyperlipidaemia (according to ATP III guidelines), ongoing antiaggregant therapy , Ejection fraction (EF) in echocardiography, balloon - stent dimensions and intervention technique, basal glomerular filtration rate (GFR) (calculated by MDRD method), low density (LDL) and high density (HDL) protein levels, lymphocyte and neutrophil values were scanned.

In angiographic image; an anatomically important myocardium using blood supply, bifurcation angle, tortuosity, MEDINA classification, SYNTAX scores with main vessel diameter ≥ 2.5 mm and side branch diameter ≥ 2.0 mm; In-hospital mortalities were recorded.

From the hospital records, Follow-up time after discharge was calculated as the time from discharge to the last outpatient clinic visit. Out-of-hospital mortality was found by scanning records in the national mortality system.

The main purpose of the study was to investigate these data to compare with all-cause death, myocardial infarction, total vascular revascularization (TVR) and total lesion revascularization (TLR) after BL (bifurcation lesion) procedure of our clinic. The study was performed with the approval of the local ethics committee and all procedures with written informed consent.

Statistical Analysis

The "Statistical Package for Social Sciences (SPSS) for Windows 22" program was used for data analysis. Descriptive statistics were expressed as mean±standard deviation for continuous variables, and categorical variables were expressed as number of cases and (%). Continuous variables with normal distribution were compared using the student t test, and continuous variables without normal distribution were compared using the Mann Whitney-U test. Chi-square test or Fischer Exact test was used for comparison of categorical variables, and multiple logistic regression analysis was used to determine independent predictors of coronary artery disease. A P value of <0.05 was considered significant.

Results

In our study, 110 of the patients were male (72.8%) and 41 were female (27.2%). The age distribution between 35 and 86 was observed in the recruited patients. The average age of the population was found to be 59.6 years. Those who are above the average age have statistical significance in death due to all causes compared to those below (p value: 0.017), but statistical significance was not observed in MI, TVR and all events. Thirty-seven (24.5%) of the patients had a family history, and those with or without a family history were not statistically significant with death from all causes, MI, TVR, TLR all events. Hypertension was observed in 87 (57.6%) volunteers in the population. Those with and without a history of hypertension did not verbally write about all-cause death, MI, TVR, TLR all events. In the evaluation made based on LDL value as hyperlipidaemia, LDL was found to be> 70mg / dL in 115 (78.2%) patients. No statistical significance was found in patients with all-cause death, MI, TVR, TLR, and all events, values below and above 70 mg / dL. 48 (31.8%) diabetes mellitus was detected; significance varying between all cause death, MI, TVR, TLR and all events was not detected. 48 (55.6%) of the patients were found to be active or passive smokers.

No correlation was found between all causes of death, MI, TVR, TLR and all events.

45 of our patients (29.8%) had a history of coronary percutaneous intervention for any reason before and 8 (5.3%) patients had a history of previous coronary artery bypass graft.

No statistical significance was found among patients who underwent percutaneous coronary intervention (stent, balloon angioplasty or coronary bypass) with all causes of death, MI, TVR, TLR and all events. 4 (2.6%) had a revised history of cerebrovascular events, and 7 (4.6%) had a history of peripheral disease. No statistical significance was found among patients. It was found that 60 (39.7%) patients used acetylsalicylic acid, 30 (19.9%) patients used clopidogrel in the maintenance single antiaggregant treatment after dual antiaggregant treatment of patients diagnosed with atherosclerosis. It was determined that he did not have a statistical advantage among all-cause

death, MI, TVR,TLR and all event (Table-1).

Table -1 Demographic Data of Patients Included in The Study

	Value (n)	**Value (Rate %)**	**Death (P value)**	**MI (P value)**	**TVR (value)**	**TLR (p value)**	**All event (p value)**
Sex							
Male	110	%72.8	0.491	0.447	0,405	0,318	0,375
Female	41	%27.2	0.756	0.582	0,389	0,287	0,482
Age	59,6 ±21,6		**0,017**	0,213	0,625	0,738	0,680
Family History	37	%24.5	0.124	0.238	0.287	0,753	0,414
Hypertension	87	%57.6	0.375	0.304	0.644	0,669	0,699
Hyperlipidaemia	115	%78.2	0.570	0.326	0.545	0,438	0,602
Diabetes Mellitus	48	%31.8	0.602	0.318	0,575	0,558	0,790
Smoking	84	%55.6	0.654	0.092	0,759	0,271	0,481
PRİOR PCI	45	%29.8	0.579	0.135	0.439	0,125	0,074
PRİOR CABG	8	%5.3	0.478	0.566	0.365	0,585	0,444
Use of Acetylsalicylic Asid	60	%39.7	0.277	0.336	0.491	0,240	0,257
Use of Clopidogrel	30	%19.9	0.087	0.303	0.105	0,126	0,070
Cerebrovascular Event	4	%2.6	0.534	0.245	0.681	0,676	0,371
Peripheral Arterial Disease	7	%4.6	0.475	0.608	0.790	0,099	0,105

52 (34.4%) of the patients were hospitalized with STEMI, 25 (16.6%) patients were NSTEMI, 11 (7.3%) patients were USAP, and 63 (41.7%) patients were hospitalized with a pre-diagnosis of SAP and a coronary bifurcation was attempted. In our study, STEMI and other reasons for hospitalization (SAP, USAP, NSTEMI) were compared due to the greater effect of STEMI on mortality.

Statistically, according to this comparison, STEMI in 52 (34.4%) patients and other clinical presentations in 99 (65.6%) patients were observed. When all-cause death, MI, TVR, TLR and all events were compared with STEMI and their clinical presentations, no statistical difference was found (Table 2).

Table – 2 Type of Clinical Presentations of Patients Included in The Study		
	Value(n)	**Value (Rate %)**
STEMİ	52	%34.4
NSTEMİ	25	%16.6
USAP	11	%7.3
SAP	63	%41.7

The mean GFR value of the patients was 92, the maximum GFR value was 195 and the minimum value was 24. When all-cause death, MI, TVR, TLR and all events were compared with GFR (those below and above the mean), no significance was found in the p value. The mean neutrophil / lymphocyte ratio was 6.73, the maximum was 24, and the minimum was 1.16. When MI, TVR, TLR and all events were compared with neutrophil / lymphocyte ratio (below and above the mean), no statistical difference was found, but death due to causes and neutrophil / lymphocyte ratio were found to be statistically significant (p: 0.035). EF rate of the patients was found to be maximum 70%, minimum 20%, average 51.9%. A statistical significance was found due to all causes, TVR, TLR and all events were compared with patients with EF below or above the average (p: 0.048). The SYNTAX II rate in our study was found to be maximum 67.6, minimum 15.4, and average 36.3.

When the MI, TVR, TLR and all events were compared with the patients below and above the mean SYNTAX score, no statistical significance was found. However, those below the mean value of SYNTAX II were found to be statistically significant in all-cause deaths compared to those above the SYNTAX II value (p: 0.049) (Table -3).

Coronary lesions consist of 3 (1.9%) LMCA, 90 (59.7%) LAD, 50 (33.1%) CX, 8 (5.3%) RCA. Patients with coronary bifurcation lesions; The least diseased vessels were 1, the most diseased vessels were 4, and the mean number of lesions in 151 patients was 1.98. When comparing MI, TVR TLR, it was not statistically significant. However, death due to all causes and all events were found when compared with the involved vascular disease and it was found to be statistically significant (p value: 0.027-0.005, respectively) (Table-4).

Table -3 Laboratory, Scanning and SYNTAX II Data Analysis of Patients Included in The Study								
	Max	**Min**	**Avr**	**Death**	**MI (P value)**	**TVR (P value)**	**TLR (p value)**	**All event (P value)**
Glomerular filtration rate	195	24	92	0,185	0.584	0.323	0.537	0.930
Neutrophil/leukocyte ratio	24.4	1.16	6.73	**0.035**	0.255	0.687	0.614	0,578
Ejection Fraction	70	20	51,9	0,830	**0,048**	0,078	0,124	0,181
SYNTAX II	67,6	15,4	36,3	**0,049**	0,602	0,098	0,330	0,465

Table -4 Number of Significant Diseased Coroner Artery	**Max**	**Min**	**Avr**	**Death (P value)**	**MI (P value)**	**TVR (p value)**	**TLR (P value)**	**All event (P Value)**
	4	1	1,98	**0,027**	0,087	0,276	0,375	**0,005**

Table -5 MEDİNA Classification of Patients Included in The Study		
	Value(n)	**Value (Rate %)**
1-0-1	20	%13.2
0-1-1	18	%11.9
1-1-1	47	%31.1
1-1-0	33	%21.9
1-0-0	10	%6.6
0-1-0	17	%11.3
0-0-1	6	%4

The carina is the inflection point at which the proximal MB bifurcates into the distal MB and SB. The European Bifurcation Club defines a bifurcation lesion as a significant stenosis (i.e., >50%) in a coronary artery adjacent to and/or involving the origin of an SB that is clinically significant According to this definition; Coronary angiography images of our patients were monitored, Medina classification was made. In true bifurcation lesions, statistical significance was found in deaths due to all causes (p: 0.05) (Table 5-6).

Coronary angiography images of 151 patients were monitored one by one over the 'DICOM VIEWER' and QCA measurements were taken. (Before coronary balloon angioplasty main branch lesion diameter, side branch lesion diameter; after coronary balloon angioplasty main branch lesion diameter, after coronary balloon angioplasty side branch lesion diameter, main branch reference vessel diameter, lateral branch reference vessel diameter).

The maximum, minimum and average results of the parameters were obtained in millimetres. According to these calculations, when compared with the values above the average value before (maximum 70 mm, minimum 0 mm, average 17.91) and after (maximum 74 mm, minimum 0 mm, average 17.22) main vessel balloon angioplasty, the p value was determined as 0.05 and 0.027, respectively. It was significant in death due to all causes. In other QCA measurements, the p value was not found to be significant between all causes of death, MI, TVR, TLR and all events(table-7). Provisional techniques were applied to 131 patients, and other techniques were applied to 20 patients. All-cause death, MI, TVR, TLR and all events were investigated, no statistically significant difference was found.

Table -6 True Bifurcation Lesions Occur Within the Medina Classification							
	Value (n)	**Value (Rate %)**	**Death**	**MI (p value)**	**TVR (p value)**	**TLR (p value)**	**All event (p value)**
***True bifurcation lesions* (1-1-1, 0-1-1, 1-0-1)**	85	%53.3	**0.050**	0,078	0,748	0,252	0,403

Table -7. Quantitative Coronary Angiography

	Max (mm	Min (mm)	Avr (mm)	Death (P value)	MI (P value)	TVR (P value)	TLR (P value)	All event (P value)
Pre- Ptca main vessel lesion length	70	0	17,91	**0,050**	0,364	0,247	0,587	0,736
Pre-ptca Side branch lesion length	22	0	10,43	0,168	0,336	0,325	0,887	0,582
Post ptca main branch lesion length	74	0	17,22	**0,027**	0,567	0,874	0,864	0,604
Post-ptca side branch lesion length	18	0	10,6	0,141	0,559	0,652	0,378	0,979
Pre-ptca main branch lesion diameter	2,1	0	1,52	0,561	0,515	0,325	0,665	0,852
Post-ptca main branch lesion diameter	3,08	0	2,09	0,282	0,534	0,741	0,938	0,852
Pre -ptca side branch lesions diameter	2,09	0	1,74	0,696	0,144	0,069	0,241	0,593
Post-ptca side branch lesion diameter	3,12	0	1,61	0,581	0,318	0,106	0,841	0,880
Main branch reference diameter	4,64	0	3,1	0,456	0,416	0,216	0,268	0,930
Side branch reference diameter	4,0	0	2,2	0,169	0,169	0,222	0,107	0,072

Table 8- Proximal optimization technique and Final kissing angioplasty of Patients Included in The Study

	Value (n)	Value (Rate %)	Death (P value)	MI (P value)	TVR (P value)	TLR (P value)	All event (P value)
Proximal optimization technique	36	%23.8	0,421	0,412	0,214	0,434	0,304
Without Final kissing angioplasty	74	%49	0,830	0,147	0,592	**0,007**	**0,013**

When the patients with and without proximal optimization and final kissing balloon angioplasty were evaluated after the bifurcation procedure, POT was applied to 36 (23.8%) of 151 patients and Final kissing balloon angioplasty was not applied to 77 (51%) of them. In patients without final kissing balloon angioplasty, a relationship was found between TLR and all events and was evaluated as statistically significant (p value 0.007-0.013, respectively) (Table 8). No tamponade, mechanical complication or cerebrovascular event were observed in any of the patients.

Arrhythmia complications, death from all causes, MI, TVR, TLR and all events were not statistically significant. In patients who developed acute renal failure after the procedure, statistical significance was found among all causes of death, recurrent MI and all events (p value: <0.001 - 0.021-0.048, respectively). Statistical significance was found between ventricular arrhythmia observed during or within 48 hours of the procedure, death due to all causes and recurrent MI (p value, 0.044-0.018, respectively) (Table -9).

Tablo 9 – Complication of Patients Included in The Study

	Value (n)	**Value (Rate%)**	**Death (P Value)**	**MI (P Value)**	**TVR (P Value)**	**TLR (P Value)**	**All event (P Value)**
Cardiac tamponade	0	%0					
Mechanical complications	0	%0					
Cerebrovascular event	0	%0					
Atrial arrhythmia	1	%0.66	0,086	0,071	0,815	0,828	0,513
Sinoatrial And Atrioventricular Block	5	%3.3	0,307	0,146	0,680	0,681	0,825
Ventricular arrhythmia	7	%4.6	0,044	0,018	0,230	0,346	0,942
Acute Kidney Failure	11	%7.2	**<0,001**	**0,021**	0,333	0,097	**0,048**

All events that are statistically significant as p (<0.05) value are evaluated, according to multivariate analysis results; 2.17 (OR) times in patients with multiple vascular disease, above average, compared to the average below and above; There was an increase in all events by 1.74 (OR) times in patients who did not apply final kissing, and 5.93 (OR) times in patients with acute renal failure.

The p value was found to be 0.043 in patients who did not undergo final kissing balloon angioplasty and 0.019 in patients with a p value above the average, and it was considered significant according to multiple analysis results (table -10)

Table- 10 Multivariate analysis of Significant Value (p<0.05)

	OR	**%95 CI**	**P Value**
Final kissing balloon angioplasty			
- (Ref: +)	**1,74**	1,193-7,101	**0,043**
Acute Kidney Failure			
+Var (Ref:-)	**5,93**	0,789-11,412	0,107
Diseased coronary artery count			
Average and above (Ref: below average)	**2,171**	1,193-7,101	**0,019**

Discussion

In the literature review; Ravi et al. Emphasized the importance of increasing age as an independent risk factor for CVD and observed that the incidence and mortality of coronary artery disease increased as age increased (1). In our study, as in the study of Ravi et al, it was found that there was an increase in mortality due to all causes in the age group above average.

Long-term mortality in patients with low ejection fraction, with or without coronary lesions; It was higher than short term mortality. Therefore, ejection fraction plays a role as a prognostic factor in the short or long term after acute MI, and there is a very strong relationship between the EF value in the first 3 days and the prognosis of the disease in patients with acute MI (2). In our study, the frequency of recurrent MI after the procedure was increased in patients with low ejection fraction. No such study was found in the literature review, and the parameter may be misleading, showing an increase in troponin value in patients with low ejection fraction, and an incidental bifurcation lesion may have been observed as an acute MI infarction (3).

Syntax II is a calculation system designed by adding 8 different parameters to Syntax I. The largest study conducted in the literature review; Farooq et al.'s prospective, randomized controlled study of 1800 patients, with a SYNTAX I score below 33 and above were divided into 2 groups. The 4-year follow-up of the patients who underwent CABG and PCI were followed up, 8 different comorbidities were added, and all possible dependent / independent clinical events were accepted as the primary endpoint. As a result of the study, it was argued that SYNTAX II was more predictive than SYNTAX I in elderly patients with major coronary lesions and chronic obstructive lung disease, while there was no difference between SYNTAX I and SYNTAX II in young, female and low ejection fraction patients during their 4-year follow-up (4). On the contrary, in the EXCEL study by Campos et al; Patients with left main coronary lesions with stent and CABG were compared according to SYNTAX II scoring. According to the results of the study, no significant difference was found between SYNTAX I and SYNTAX II (5). According to the ESC 2018 revascularization guideline, SYNTAX II scoring was not taken as a definite indication criterion in daily practice because it is less predictive than SYNTAX I scoring. In our study, the SYNTAX II score, which was above the average (> 36.3), was found to be significant in the increase in deaths due to all causes in single analysis. This result is not numerically like the result in the SYNTAX II scoring, but the value we obtained> 33 indicates that the SYNTAX II scoring may be significant in bifurcation lesions. More data and meta-analysis are needed to prove this.

True bifurcation lesions are differentiated from other bifurcation lesions with no lesions in the lateral branch mouth. In addition, the duration and difficulty of the actual bifurcation lesions and the number of stent burden and balloon angioplasty increases even more in lesions above their processing. In the literature; The 'Medina' classification made by Medina et al. Distinguished true (true) and false (pseudo) bifurcation lesions. In this separation, it was observed that true bifurcation lesions last longer than other bifurcation lesions and the complication rate were higher, resulting in short- or long-term mortality (6). Similar results were obtained in our study, and the all-cause mortality of true bifurcation lesions was found to be higher. However, a prospective study of true and true bifurcation lesions has not been found in the literature. Therefore, a randomized controlled study is required.

In coronary bifurcation lesions, main branch balloon angioplasty and the length of the lesion before/ after all causes were observed to be significant in deaths. In the "European Bifurcation Coronary TWO" study, the provisional T stenting technique Culotte technique was compared and QCA was performed. Main branch pre-dilatation was statistically insignificant (n: 200, p: 0.758), post dilatation was found to be statistically significant (n: 200, p: 0.022), and a significant increase in the rate of death due to all causes, recurrent MI and TVR within 12 months of the study observed (7). Provisional stenting and bifurcation double stent technique were compared in the "TYRTON" study conducted on 704 patients, randomly and prospectively. According to the QCA results, predilatation (n: 704 p: 0.82) and post dilatation (n: 704 p: 0.70) were not found to be significant (8). In the SMART study, no statistical value was established for the main branch predilatation and post dilatation lumen diameters (9). Among the above studies, SMART is the most appropriate study to compare with our study, and the main branch lesion length could not be compared because it was not given statistically in the data. However, our post dilation results are like the “European Bifurcation Coronary’’ study, and more prospective / randomized studies are required for both parameters.

As known; In patients with multiple coronary artery disease, higher mortality is observed in long-term studies compared to single vessel diseases. SYNTAX classification is recommended for patients with multiple vessel or main coronary lesions according to the revascularization classification. It is not recommended for patients with SYTNAX I value> 33 with PCI class III indication. According to the ESC 2018 Revascularization classification, SYNTAX classification is recommended for patients with multiple vessel or main coronary lesions. It is not recommended for patients with SYTNAX I value> 33 with PCI class III indication.

The reason for this is related to stent thrombosis, recurrent MI and increased mortality in patients with multiple vessels, with or without bifurcation lesions (10,11). In our study, a correlation was found between death due to all causes and all events in patients with multiple vascular disease, and a 2.17-fold increase in all events was observed in multiple analysis. The results of our study with the ESC 2018 guide were found to be similar.

Final kissing balloon angioplasty should be performed for carinal reconstruction, especially in patients with double stenting after coronary bifurcation or lateral branch balloon plaque shift after the main branch procedure. Biondi et al. on final kissing, it is not recommended for patients who underwent a provisional procedure in which a single stent was placed and a side-branch lesion was not intervention, whereas it is recommended because it reduces the rates of recurrent interventions and MACCE in patients undergoing main branch and side branch stenting (12). According to the meta-analysis results of 1264 patients taken from 5 suitable studies with the provisional stenting technique performed by Zhong et al. In 2018; It was observed that patients without final kissing balloon angioplasty remained non-inferior when the end points were compared compared to patients who had final kissing, and it was emphasized that routine final kissing balloon angioplasty should be avoided (13).

In our study, unlike other studies, it was found that there was an increase in all-cause events in provisional stenting without final kissing. Even this has been proven with multiple analyses, when comparing the ones with and without final kissing balloon angioplasty, it was observed that all events increased 1.74 (p: 0.043) times in the arm that was not performed.

Conclusion

In patients who underwent complex coronary intervention for diagnosis and treatment and who did not undergo final kissing balloon angioplasty during coronary bifurcation intervention, the all-cause mortality rate increased significantly. However, since these patients were exposed to a heavy opaque material load, an increase in acute renal failure was observed. For this reason, especially older patients for intervention in bifurcation lesions should be carefully selected and, if necessary, coronary artery bypass grafting should be considered.

References

1. Dhingra R, Vasan RS. Age as a risk factor. Med Clin North Am. 2012 Jan;96(1):87-91. doi: 10.1016/j.mcna.2011.11.003. Epub 2011 Dec 12. PubMed PMID: 22391253; PubMed Central PMCID: PMC3297980.

2. The Multicenter Postinfarction Research G. Risk stratification and survival after myocardial infarction. N Engl J Med 1983; 309:331-336.

3. Felker GM, Mentz RJ, Teerlink JR et al. Serial high sensitivity cardiac troponin T measurement in acute heart failure: insights from the RELAX-AHF study. Eur J Heart Fail 2015; 17:1262–70

4. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. Lancet (London, England). 2013;381(9867):639-50.

5. Campos CM, van Klaveren D, Farooq V, Simonton CA, Kappetein AP, Sabik JF III et al. Long-term forecasting and comparison of mortality in the Evaluation of the Xience Everolimus Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial: Prospective validation of the SYNTAX Score II. Eur Heart J 2015; 36:1231–1241.

6. Medina, A, Suarez de Lezo, J, Pan, M. "A new classification of coronary bifurcations lesions". Rev Esp Cardiol. vol. 59. 2006. pp. 183.

7. Hildick-Smith D, Behan MW, Lassen JF, Chieffo A, Lefevre T, Stankovic G, et al. The EBC TWO Study (European Bifurcation Coronary TWO): A Randomized Comparison of Provisional T-Stenting Versus a Systematic 2 Stent Culotte Strategy in Large Caliber True Bifurcations. Circulation Cardiovascular interventions. 2016;9(9).

8. Genereux P, Kumsars I, Lesiak M, Kini A, Fontos G, Slagboom T, et al. A randomized trial of a dedicated bifurcation stent versus provisional stenting in the treatment of coronary bifurcation lesions. Journal of the American College of Cardiology. 2015;65(6):533-43.

9. Song YB, Park TK, Hahn JY, Yang JH, Choi JH, Choi SH, et al. Optimal Strategy for Provisional Side Branch Intervention in Coronary Bifurcation Lesions: 3-Year Outcomes of the SMART-STRATEGY Randomized Trial. JACC Cardiovascular interventions. 2016;9(6):517-26.

10. Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: A meta-analysis of randomized clinical data. J Am Coll Cardiol 2011; 58:1426–1432

11. Ahn JM, Roh JH, Kim YH, Park DW, Yun SC, Lee PH et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease: 5-Year outcomes of the PRECOMBAT study. J Am Coll Cardiol 2015; 65:2198–2206.

12. Biondi-Zoccai G, Sheiban I, De Servi S, Tamburino C, Sangiorgi G, Romagnoli E. To kiss or not to kiss? Impact of final kissing-balloon inflation on early and long-term results of percutaneous coronary intervention for bifurcation lesions. Heart and vessels. 2014;29(6):732-42.

13. Zhong M, Tang B, Zhao Q, Cheng J, Jin Q, Fu S. Should kissing balloon inflation after main vessel stenting be routine in the one-stent approach? A systematic review and meta-analysis of randomized trials. PLoS One. 2018 Jun 27;13(6): e0197580. doi: 10.1371/journal.pone.0197580. PubMed PMID: 29949587; PubMed Central PMCID: PMC6021082.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (1):32-37

Analysis of Early Term Results of Elective Ascending Aortic Aneurysm Surgery

Elektif Asendan Aort Anevrizması Cerrahisinin Erken Dönem Dönem Sonuçlarının Analizi

Ahmet DOLAPOĞLU* 0000-0001-9161- 2632
Emin BARBARUS 0000-0001-8586-9810**

*Balıkesir Üniversitesi, Tıp Fakültesi Hastanesi , Kalp ve Damar Cerrahisi Anabilim Dalı, Balıkesir
** Balıkesir Üniversitesi, Tıp Fakültesi Hastanesi, Kalp ve Damar Cerrahisi Anabilim Dalı, Balıkesir

Yazışma Adresi: Emin BARBARUS
Balıkesir Üniversitesi, Tıp Fakültesi Hastanesi
Kalp ve Damar Cerrahisi Anabilim Dalı, Balıkesir
E-mail: eminbarbarus@gmail.com

Geliş Tarihi: 13.02.2025
Kabul Tarihi: 15.03.2025

Abstract

Objective: Ascending aortic aneurysms carry a high mortality risk with increased aortic diameter and accompanying genetic risk factors. In this study, we aimed to share our surgical results in our patients who were operated for this reason.

Methods: Demographic, operative, preoperative and postoperative data of 45 patients who were electively operated for ascending aortic aneurysm between August 2018 and February 2024 were retrospectively analysed.

Results: The mean age of the 45 patients included in the study was 58.98 years, 60% were male and 40% were female. The most common associated risk factors were HT (55.6%) and smoking (52.4%). Preoperative echocardiography revealed severe aortic regurgitation in 17 patients and severe aortic stenosis in 9 patients. The most common surgical procedures were Weath (42.2%) and Bentall (40%) procedures. Permanent pacemaker requirement and stroke development were not observed in the postoperative period. In 3 patients, reexploration was performed due to bleeding. 30-day in-hospital mortality was 6.7% and 1-year survival of discharged patients was 92.8%.

Conclusion: In-hospital mortality and 1-year survival rates of the operations performed in our clinic are compatible with the studies in the literature, but more patient data and longer follow-up periods are required.

Keywords: Aortic Aneurysm, Elective, Surgery

Öz

Amaç: Asendan aort anevrizmaları aort çapının artması ve eşlik eden genetik risk faktörleri ile yüksek mortaliete riski taşımakta olup çalışmamızda bu nedenle opere edilen hastalarımızda cerrahi sonuçlarımızı paylaşmayı amaçladık.

Yöntem: Ağustos 2018- Şubat 2024 tarihleri arasında asendan aort anevrizması nedeniyle elektif olarak opere edilen 45 hastanın demografik, operasyonel ve preoperatif ile postoperatif verileri retrospektif olarak incelendi.

Bulgular: Çalışmaya dahil edilen 45 hastanın yaş ortalaması 58.98 olup %60'ı erkek %40 ise kadın idi. En sık eşlik eden risk faktörleri HT(%55.6) ve sigara kullanımı (%52.4) olarak gözlendi. Preoperatif ekokardiyografide 17 hastada ileri Aort Yetmezliği 9 hastada ise ciddi aort darlığı mevcuttu.

Anahtar Kelimeler: Aort anevrizması, Elektif, Cerrahi

En sık uygulanan cerrahi proesedürler Weath(%42.2) ve Bentall(%40) prosedürü idi. Postoperatif dönemde kalıcı pacemaker gereksinimi ve inme gelişimi gözlenmedi. 3 hastada kanama nedeniyle reeksplorasyon yapıldı. 30 günlük hastane içi mortalite %6.7 olarak saptanmış olup taburcu edilen hastaların 1 yıllık sağkalımı %92.8 olarak saptandı.

Sonuç: Kliniğimizde yapılan operasyonların hastane içi mortalite ve 1 yıllık sağkalım oranları literatürdeki çalışmalarla uyumlu olup daha fazla hasta verisi ve daha uzun takip süreleri gereksinimi mevcuttur.

Material Methods

Ethics committee approval for the study was obtained from the Balıkesir University Health Sciences Non-Interventional Research Ethics Committee, with decision number 2024/141.

The demographic, operative, preoperative, and postoperative data of 45 patients who underwent elective surgery for ascending aortic aneurysm in our clinic between August 2018 and February 2024 were retrospectively analyzed. Patients requiring emergency surgery due to aortic dissection, penetrating aortic ulcer, rupture, or intramural hematoma were excluded from the study.

The surgical indication thresholds for ascending aortic aneurysm were set at 45 mm for patients with aortic valve pathology (aortic stenosis/insufficiency), 50 mm for those with a bicuspid aortic valve, and 55 mm for patients without high-risk factors and an annual dilatation rate below 5 mm. Surgical procedures performed for the ascending aorta included the Wheat procedure, Bentall operation, supracoronary ascending aortic replacement, and hemiarch/total arch replacement.

Routine antegrade cerebral perfusion was employed in patients requiring total circulatory arrest (TCA). Systemic cooling was applied at 22–26°C when TCA was necessary and at 32°C when TCA was not required, depending on the specific characteristics of the procedure. Del Nido solution was used for cardioplegia. Postoperative in-hospital and one-year all-cause mortality, as well as one-year survival analyses, were conducted.

Statistical Method

The data were analyzed using IBM SPSS Statistics 26 software (IBM Corp., Released 2019). The results were presented as mean ± standard deviation (Mean ± SD) for quantitative variables and as frequency (n) and percentage (%) for categorical variables. A p-value of <0.05 was considered statistically significant in all calculations and interpretations. (4)

Results

The mean age of the 45 patients included in the study was 58.98 years (range: 28–84). Male patients accounted for 60% of the study population. The mean body mass index (BMI) was 28.05, while the mean body surface area (BSA) was 1.88 m^2. A total of 52.4% of the patients were smokers. Regarding chronic conditions, hypertension (HT) was present in 55.6% of the patients, diabetes mellitus (DM) in 11.1%, dyslipidemia in 31.1%, chronic obstructive pulmonary disease (COPD) in 11.1%, a history of cerebrovascular events (CVE) in 4.4%, and atrial fibrillation (AF) in 17.8%. The mean EuroSCORE II was calculated as 8.71, while the mean glomerular filtration ratio (GFR) was 77.24. (Table 1) (Tablo 1)

Table 1. Demographic data of the patients

	n / Mean ± SD	**Median (min.-max.)**
Age	58.98 ± 12.39	59 (28- 84)
Gender		
Female	18	40
Male	27	60
Body Mass Index(BMI)	28.05 ± 4.39	27.7 (18.37- 35.2)
Body Surface Area (m2)	1.88 ± 0.19	1.86 (1.43-2.28)
Smoking	22	52.4
HT	25	55.6
DM	5	11.1
Dyslipidemia	14	31.1
COPD	5	11.1
CVA	2	4.4
AF	8	17.8
EuroScore 2	8.71 ± 2.11	9 (6 - 13)
GFR (creatinine clearance)	77.24 ± 21.08	80.26 (0.68 - 118)

Mean: Average, SD: Standard deviation, min: Minimum, max: Maximum

Severe aortic regurgitation was observed in 37.8% of the patients. Bicuspid aortic valve was detected in 24.4%. Preoperative aortic stenosis was detected in 20% of the patients and the mean gradient was 42.33±17.36 in these patients. The mean preoperative left ventricular ejection fraction (LVEF) value was 57.11. When preoperative Pulmonary Artery Pressure (PAP) levels were analysed, it was observed that 68.9% were normal, 13.3% were moderate and 8.9% were severe.

The mean sinus valsalva diameter was 42.68 mm, the mean ascending aorta diameter was 52.79 mm and the mean arcus aorta diameter was 40.53 mm in CT angiography evaluation. The mean aortic height index (AHI) was 3.24 and the mean aortic body surface area index (ASI) was 2.9. The mean postoperative EF was 56.67 and the mean postoperative gradient was 12.65 in 37 patients who underwent aortic valve replacement. (Table 2)

When the surgical procedures were analysed, it was observed that wheat procedure was performed with the highest rate of 42.2%, Bentall procedure with 40%, and ascending aorta procedure with the lowest rate of 2.2%. In concomitant surgeries, CABG was the most common procedure with a rate of 50%.

Total circulatory arrest (TCA) was applied in all cases in which deep hypothermia was applied and the mean duration was 28.56 min, X-clamp mean was 122.07 min, Cardiopulmonary Bypass (CPB) mean was 158.93 min and antegrade cerebral perfusion mean was 28.6 min. Operations were performed in deep hypothermia in 10 patients (22.2%), moderate hypothermia in 5 patients (11.1%) and mild hypothermia in 30 patients (66.6%) who were resuscitated to TCA and intervened in the arch aorta. Composite graft was used in 18 patients who underwent Bentall procedure and the most commonly used graft was 23 no composite graft (55.5%). Among the tubular grafts used in other procedures, the most commonly used graft was 32 mm dacron graft (40.7%).

Whilst haemorrhage revision was observed in 6.7% of patients and new AF was observed in 8.9% of patients, no patient required permanent pacemaker and no stroke was observed. 30-day mortality was 6.7% and 1-year survival was 92.8% in the group without 30-day mortality (Table 3).

Table 2. Angiographic and Echocardiographic data

	n / Mean ± SD	**Median (min.-max.)**
Aortic Regurgitation		
Mild	7	%15.5
Moderate	16	%35.6
Severe	17	%37.8
Bicuspid Aortic Valve	11	24.4
Aortic Stenosis (mean gradient)	9	%20
	42.33 ± 17.36	46 (17 - 72)
Preoperative LVEF	57.11 ± 6.26	60 (35 - 65)
PAP (mmHg)		
Normal	31	68.9
Mild	4	8.9
Moderate	6	13.3
Severe	4	8.9
Sinüs Valsalva Diameter (mm)	42.68 ± 7.44	41.9 (29.3 - 63.5)
Ascendan Aorta Diameter (mm)	52.79 ± 8.81	51.6 (33.8 - 78)
Arcus Aorta Diameter (mm)	40.63 ± 7.22	39.7 (28.3 - 68.5)
AHI	3.24 ± 0.5	3.11 (2.51 - 4.48)
ASI	2.9 ± 0.57	2.69 (2.19 - 4.5)
Postoperative LVEF	56.67 ± 6.76	57.5 (35 - 65)
Postoperative mean gradient	37	%82.2
	12.65 ± 4.92	12 (6 - 29)

Mean: Average, SD: Standard deviation, min: Minimum, max: Maximum

Table 3. Surgical data of the patients

	n / Mean ± SD	Median (min.-max.)
Surgical Procedure*		
Bentall	18	40
Hemiarcus Replacement	9	20
Supracoronary AA Replacement	9	20
Wheat Procedure	19	42.2
Concomminant Surgery*		
CABG	6	50
MVR	4	33.3
Tricuspid Valve Repair	2	16.7
VSD Repair	1	8.3
TCA (min.)	28.56 ± 16.68	24 (14 - 81)
X-Clamp (min.)	122.07 ± 32.48	121 (57 - 210)
CPB (min.)	158.93 ± 36.11	155 (82 - 287)
Antegrad Cerebral Perfusion (min.)	28.56 ± 16.68	24 (14 - 81)
Deep Hypothermia (18-22 C°)	10	22,2
Moderate Hypothermia (24-30 C°)	5	11,1
Mild Hypothermia (32-34 C°)	30	66,6
Composite Graft (18 patients)		
23	10	55,5
25	5	27,8
27	3	16,7
Tubular Graft (27 patients)		
28	2	7,4
30	10	37
32	11	40,7
34	4	14,8
Permanent Pacemaker requirement	0	0
Reexploratin for bleeding	3	6.7
New on-set AF	4	8.9
Stroke	0	0
30 day Mortality	3	6.7
1 Year Survey	39	92,8

*: Multiple response, more than one response in a case. Mean: Average, SD: Standard deviation, min: Minimum, max: Maximum

Discussion

Ascending aortic aneurysm is an important factor in clinical follow-up because it causes symptoms such as rupture, dissection and sudden death and the only treatment is surgery. The Wheat procedure was the most common procedure performed in the operations performed by us, followed by the Bentall procedure, supracoronary ascending aortic replacement and hemiarcus replacement procedures. The mean age was 58.89 years and 60% of the patients were male and 40% were female. The most common associated morbidity was HT. Smoking was also present in 52.4% of the patients. In a study by Beller et al. in which gender and elective AAA surgery outcomes were investigated, 29% of the patients were female, which was lower than in our study.

In this study, normalised aortic diameter (aortic diameter/VAD) was found to be higher in female patients, they were operated at an older age, the duration of intensive care unit stay was longer and postoperative haemodialysis requirement was found to be higher.(5) In the study conducted by Memiş et al. patients under and over 70 years of age were divided into two groups. In the group over 70 years of age, cardiovascular risk factors were found to be higher and aortic diameter was observed to be higher. In-hospital mortality was found to be 3.5% in the group above 70 years of age and 1.5% in the group below 70 years of age and no statistically significant difference was observed. (p=0.16) When 5-year survival was analysed, it was 81.4% in the group above 70 years of age and 93.9% in the group below 70 years of age and a statistically significant difference was observed (p<0.001) (6)

Preoperative echocardiographic findings revealed aortic stenosis in 9 patients and severe aortic regurgitation in 17 patients. Bicuspid aortic valve is an important pathology in determining the prognosis of aortic surgery and was observed in 11 patients (24.4%). Tomographic measurements were performed separately in the sinus of valsalva, ascending aorta and arch and the largest diameter was observed in the ascending aorta with 52.79 ± 8.81. AHI (3.24 ± 0.5) and ASI (2.9 ± 0.57) measurements included in the new guideline were measured in our study. In the aortic/height index (AHI) study by Zafar et al., 5-year expected survival without dissection, rupture and death was reported as 85.5% in the ASI<2.00 group and 86.6% in the AHI<2.40 group, which decreased to 4.9% in the ASI>4.25 cm/m2 group and to 9.5% in the AHI>4.35 cm/m group and was found to be effective in determining expected survival (7)

When the postoperative echocardiograms of the patients who underwent Wheat procedure and Bentall procedure were analysed, the mean gradient was 12.65 ± 4.92 and no patient-prosthesis incompatibility was observed. TSA was performed in all patients who underwent arcus/hemiarctus intervention or in whom X-clamp could not be placed because the aneurysm extended to the arcus aorta, and standard antegrade cerebral prefusion was applied to these patients during the TCA period. The duration of TCA was 28.56 ± 16.68 min and was performed with deep hypothermia.

No postoperative stroke or need for permanent pacemaker was observed in our patients.

New AF was observed in only 6.3% of our patients and sinus rhythm was achieved with medical cardioversion. 30-day in-hospital mortality was 6.7% in 3 patients and 1-year follow-up of the discharged patients was 92.8%.

Vaquero et al. found a postoperative in-hospital mortality of 5.96% in a study of 738 patients. In the long-term follow-up, 3, 5 and 8-year cumulative survival was 94.07%, 89.96% and 82.72%, respectively, and was found to be similar to the life expectancy of the general population.(8) Again, Van Duffel et al. reported in-hospital mortality as 9.7% and 5-year survival as 80.9% in the mortality and survival results of elective ascending aortic operations. (9) In the elective Modified Bentall operations performed by Maureira et al., in-hospital mortality was found to be 4.4% and 5-10 year survival was reported as 93.8±2.3% and 80.5±4.5%, respectively.(10) In comparison with the literature, 30-day in-hospital mortality and 1-year survival rates of the operations performed in our clinic were found to be similar.

The primary limitations of our study include the relatively small sample size, which prevented a comprehensive analysis of factors influencing mortality and morbidity. Additionally, the retrospective nature of the study may introduce selection bias and limit the ability to establish causal relationships. Furthermore, long-term follow-up data are not yet available, restricting our ability to assess late complications, survival outcomes, and the durability of surgical interventions.

References

1. Davies, R. R., Gallo, A., Coady, M. A., Tellides, G., Botta, D. M., Burke, B., Coe, M. P., Kopf, G. S., & Elefteriades, J. A. (2006). Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. The Annals of thoracic surgery, 81(1), 169–177. https://doi.org/10.1016/j.athoracsur.2005.06.026
2. Saeyeldin, A. A., Velasquez, C. A., Mahmood, S. U. B., Brownstein, A. J., Zafar, M. A., Ziganshin, B. A., & Elefteriades, J. A. (2019). Thoracic aortic aneurysm: unlocking the "silent killer" secrets. *General thoracic and cardiovascular surgery*, *67*(1), 1–11. https://doi.org/10.1007/s11748-017-0874-x
3. Isselbacher, E. M., Preventza, O., Hamilton Black, J., 3rd, Augoustides, J. G., Beck, A. W., Bolen, M. A., Braverman, A. C., Bray, B. E., Brown-Zimmerman, M. M., Chen, E. P., Collins, T. J., DeAnda, A., Jr, Fanola, C. L., Girardi, L. N., Hicks, C. W., Hui, D. S., Schuyler Jones, W., Kalahasti, V., Kim, K. M., Milewicz, D. M., … Peer Review Committee Members (2022). 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*, *146*(24), e334–e482. https://doi.org/10.1161/CIR.0000000000001106
4. - IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp
5. Beller, C. J., Farag, M., Wannaku, S., Seppelt, P., Arif, R., Ruhparwar, A., Karck, M., Weymann, A., & Kallenbach, K. (2015). Gender-specific differences in outcome of ascending aortic aneurysm surgery. PloS one, 10(4), e0124461. https://doi.org/10.1371/journal.pone.0124461
6. Memis, F., Thijssen, C. G. E., Gökalp, A. L., Notenboom, M. L., Meccanici, F., Mokhles, M. M., van Kimmenade, R. R. J., Veen, K. M., Geuzebroek, G. S. C., Sjatskig, J., Ter Woorst, F. J., Bekkers, J. A., Takkenberg, J. J. M., & Roos-Hesselink, J. W. (2023). Elective Ascending Aortic Aneurysm Surgery in the Elderly. Journal of clinical medicine, 12(5), 2015. https://doi.org/10.3390/jcm12052015
7. Zafar, M. A., Li, Y., Rizzo, J. A., Charilaou, P., Saeyeldin, A., Velasquez, C. A., Mansour, A. M., Bin Mahmood, S. U., Ma, W. G., Brownstein, A. J., Tranquilli, M., Dumfarth, J., Theodoropoulos, P., Thombre, K., Tanweer, M., Erben, Y., Peterss, S., Ziganshin, B. A., & Elefteriades, J. A. (2018). Height alone, rather than body surface area, suffices for risk estimation in ascending aortic aneurysm. *The Journal of thoracic and cardiovascular surgery*, *155*(5), 1938–1950. https://doi.org/10.1016/j.jtcvs.2017.10.140
8. Hernandez-Vaquero, D., Silva, J., Escalera, A., Álvarez-Cabo, R., Morales, C., Díaz, R., Avanzas, P., Moris, C., & Pascual, I. (2020). Life Expectancy after Surgery for Ascending Aortic Aneurysm. Journal of clinical medicine, 9(3), 615. https://doi.org/10.3390/jcm9030615
9. Van Duffel, D., Van Gemert, R., Starinieri, P., Pauwels, J. L., Natukunda, A., Rakhmawati, T. W., Chirehwa, M. T., Orwa, J., Thys, H., Deboosere, P., Robic, B., Mees, U., & Hendrikx, M. (2013). Elective reconstruction of the ascending aorta for aneurysmal disease restores normal life expectancy. An analysis of risk factors for early and late mortality. *Acta cardiologica*, *68*(4), 349–353. https://doi.org/10.1080/ac.68.4.2988887
10. Maureira, P., Vanhuyse, F., Martin, C., Lekehal, M., Carteaux, J. P., Tran, N., & Villemot, J. P. (2012). Modified Bentall procedure using two short grafts for coronary reimplantation: long-term results. The Annals of thoracic surgery, 93(2), 443–449. https://doi.org/10.1016/j.athoracsur.2011.11.003

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (1): 38-44

Human Equivalent Phantom Computed Tomography Study for Foreign Body Detection in the Body

Vücutta Yabancı Cisim Saptanması İçin İnsan Eşdeğer Fantom Bilgisayarlı Tomografi Çalışması

Halil İbrahim ÖZDEMİR* 0000-0002-3336-6848
Murat KÖYLÜ 0000-0003-0439-8768**
Hatice Elif ÖZDEMİR* 0009-0005-9821-2048**
Mert ARSLAN** 0009-0000-3516-6359**
Saliha ÇETİN*** 0009-0007-7351-5514**
Deniz YALMAN 0000-0002-4010-8353**
Mustafa HARMAN* 0000-0001-9234-887X

* Ege Üniversitesi Tıp Fakültesi Radyoloji AD, Bornova/İzmir
** Ege Üniversitesi Radyasyon Onkolojisi AD, Bornova/İzmir
*** Ege Üniversitesi Tıp Fakültesi Biyofizik AD, Bornova/İzmir
**** Ege Üniversitesi Ege MYO, Biyomedikal Cihaz Teknolojisi Programı, Bornova/İzmir
***** Ege Üniversitesi Atatürk Sağlık Hizmetleri MYO, Tıbbi Görüntüleme Teknikleri Programı, Bornova/İzmir

Yazışma Adresi: Halil İbrahim ÖZDEMİR
Ege Üniversitesi Tıp Fakültesi, Radyoloji AD, Bornova/İzmir,
E-mail: ozdemir.egeli@gmail.com

Geliş Tarihi: 14.03.2025
Kabul Tarihi: 02.04.2025

Abstract

Introduction: In our lives, some foreign bodies can be taken into the body unintentionally or accidentally. This situation has an important place in emergency injuries. In order to provide appropriate treatment for foreign bodies that have entered the body for any reason, it is very important to correctly identify the type of these substances. This research was conducted to identify foreign bodies that have entered the body using standard human equivalent phantoms with Computed Tomography Haunsfield Unit values.

Material and Method: In the research, 23 foreign bodies were placed in cylindrical holes in the human equivalent Rando Phantom. Routine whole body protocol and single phase CT examination were performed on the Rando phantom. Haunsfield values of foreign bodies were measured from the images taken to the Sectra archive system. The results were evaluated with the SPSS statistical program.

Findings: The tube potential energy in the protocol used could not create sufficient attenuation value in metals and since it generally showed high HU values (3071), their distinction could not be made. It has been observed that glass (1735), rubber (1453), plastics (between 112-1021) and wood product-based materials (between -138 and -476) can be roughly distinguished. Computed Tomography Haunsfield Unit value ranges are quite variable.

Conclusion: In order to fully distinguish foreign bodies in the body, different post-processing image analysis methods should be investigated and tested in addition to Haunsfield Unit values.

Keywords: Computed Tomography, Alderson Rando Phantom, Foreign Body, Haunsfield Unit.

Öz

Giriş: Yaşamımızda bazı yabancı cisimler istem dışı ya da kaza ile vücut içerisine alınabilmektedir. Bu durum acil yaralanmalar içerisinde önemli bir yer tutmaktadır. Herhangi bir neden ile vücuda girmiş olan yabancı maddelerin uygun tedavilerinin yapılabilmesi için bu maddelerin türünün doğru bir şekilde saptanması oldukça önem taşımaktadır. Bu araştırma, vücuda girmiş olan yabancı maddelerin standart insan eşdeğer fantom kullanılarak Bilgisayarlı Tomografi Haunsfield Unit değerleri ile tanımlanabilmesi amacıyla yapılmıştır.

Materyal ve Metod: Araştırmada, insan eşdeğer Rando Fantom içerisindeki silindirik hollere 23 adet yabancı cisim yerleştirilmiştir. Rando fantoma rutin tüm vücut protokolünde ve tek faz BT tetkiki yapılmıştır. Sectra arşiv sistemine alınan görüntüler üzerinden yabancı cisimlerin Haunsfield değerleri ölçülmüştür. Sonuçlar, SPSS istatistik programı ile değerlendirilmiştir.

Bulgular: Kullanılan protokoldeki tüp potansiyel enerjisi metallerde yeterli attenüasyon değeri oluşturamamış ve genelde yüksek HU değerleri (3071) gösterdiğinden ayrımları yapılamamıştır. Cam (1735), kauçuk (1453), plastiklerin (112-1021 arasında) ve odun ürünleri temelli materyallerin ise (-138 ila -476 arasında) ayrımlarının kabaca yapılabildiği görülmüştür. Bilgisayarlı Tomografi materyallerin Haunsfield Unit değer aralıkları oldukça varyatiftir.

Sonuç: Vücut içerisindeki yabancı cisimlerin tam olarak ayrımlarının yapılabilmesi için Haunsfield Unit değerleri yanında farklı post prosessing görüntü analiz yöntemleri araştırılmalı ve denenmelidir.

Anahtar Kelimeler: Bilgisayarlı Tomografi, Alderson Rando Fantom, Yabancı cisim, Haunsfield Unit.

Introduction

Foreign bodies can unintentionally or accidentally enter the human body, making this issue a significant concern in emergency injuries. According to a study, cases involving foreign bodies of external origin account for approximately 7-15% of all emergency injury cases (1-2). These external foreign bodies that cause emergency injuries can be composed of various materials and exhibit different morphologies. Such foreign bodies may include materials such as metal, glass, and wood, among others (3). Identifying the type, structure, and morphology of the foreign substance is crucial for appropriate treatment.

Non-invasive imaging methods, including Radiography, Computed Tomography (CT), Ultrasonography (US), and Magnetic Resonance Imaging (MRI), are used for detecting such foreign bodies inside the human body. However, Radiography and Computed Tomography are the most commonly and efficiently used imaging modalities in hospitals. Both imaging techniques utilize X-rays, which enable differentiation of foreign bodies based on their atomic number and density through absorption. Higher atomic numbers and densities facilitate better imaging of foreign bodies inside the body. Conversely, low-density materials with small atomic numbers are more challenging to visualize and identify (4-7). For instance, in a study involving 72 patients with wood foreign bodies, radiography was reported to detect only 15% of cases (8). CT offers detailed cross-sectional and three-dimensional imaging without superimposition of foreign materials and anatomical structures. If a foreign body can not be visualized using radiography or ultrasonography, CT serves as the next best imaging modality for more detailed assessment. CT is 5-15 times more sensitive than radiography and is considered the best imaging technique for foreign bodies such as plastic, glass, and stones. However, for small, superficially located fragments, ultrasonography is more sensitive than CT (9). Although numerous case reports on foreign bodies in the human body exist in the literature, no standardized scientific research has been conducted using a human-equivalent phantom. In this study, a human-equivalent phantom embedded with 23 different foreign bodies underwent whole-body CT scanning to distinguish the foreign bodies. Therefore, this research aims to classify foreign bodies retained in the human body using CT scans and Hounsfield Units (HU).

Materials and Methods

This study was conducted with permission from the Departments of Radiation Oncology and Radiology. The human equivalent Rando Phantom in the Radiation Oncology inventory and the CT device in the Radiology inventory were used. Since no human, experimental animal or archive data were used, ethics committee approval was not required. The Alderson Rando phantom used in the study can be divided into 2 cm slices and contains multiple cylindrical spaces of 0.5x2 cm in each slice (Figure 1).

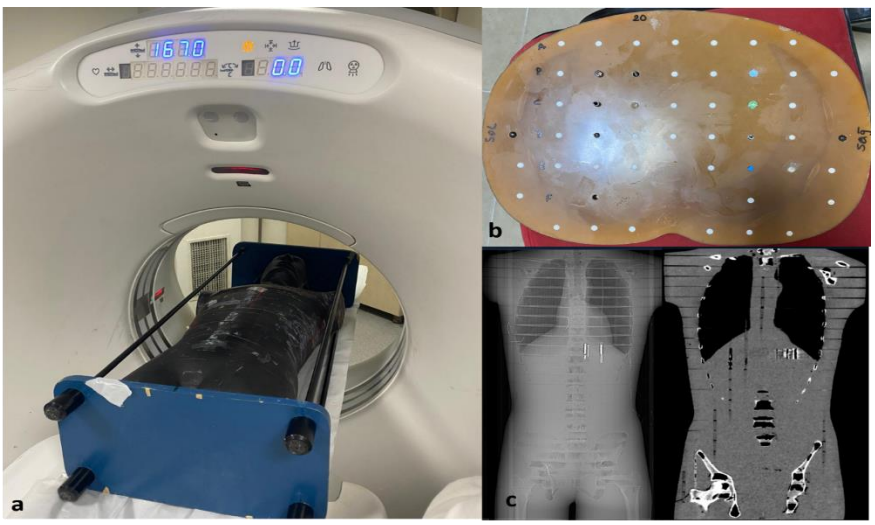


Figure 1. Rando Phantom: **a)** Whole-body CT examination, **b)** Holes within a phantom slice, **c)** Scanogram and coronal section image.

A total of 23 different foreign bodies, adjusted to fit within these cavities, were embedded in the phantom. To ensure uniformity and ease of detection, these foreign bodies were placed in the liver region of the abdominal section. The embedded foreign bodies included lead, titanium medical screw, steel medical screw, iron construction screw, tin wire, chalk, candle, graphite of pencil, wood of pencil, pastel crayons, dry tree branch (mulberry), plastic (PVC), plastic (3D printer filament), plastic (ABS), rubber, aerated concrete (Ytong), glass, construction foam, wood (MDF), plastic bead, plastic button, rubber eraser, and watermelon seed. Additionally, background measurements were taken from the liver region of the phantom.

After reassembling the phantom with the embedded foreign bodies, a whole-body CT scan was performed using a GEHC Discovery CT750 HD (California, USA) 64-slice CT scanner. The standard abdominal CT protocol was applied, utilizing 120 kV and an mA value adjusted according to body density. To ensure uniform radiation dose application, the average abdominal CT mA value was fixed at 400 mA. The scanning parameters included 120 kV, 400 mA, 1.25 mm slice interval, 0.4 s rotation time, 32 cm DFOV, and a 512x512 matrix. Using the Sectra IDS7 (Medical Imaging, Sweden) archive system, five separate measurements were taken from each foreign body on 1.25 mm CT slices using a 1 mm^2 circular region of interest (ROI), and the average HU values were recorded.

Furthermore, the total radiation dose absorbed by the phantom was calculated by multiplying the CT device's dose-length product (DLP) value with the standard dose coefficient for an adult male whole-body scan (abdomen coefficient of 0.0134 for 120 kV) (10,11) (Table 1).

Descriptive statistics and graphical analyses were conducted using the SPSS statistical software.

Results

Measurements were obtained in Hounsfield Units (HU) for each foreign body using a 1mm^3 circular region of interest (ROI) on 1.25 mm slices acquired from the human-equivalent phantom.

At least five measurements were taken for each foreign object, and the means, standard deviations, maximum, and minimum values were calculated using the SPSS software (Table 1).

The measurements revealed that lead, titanium medical screws, steel medical screws, iron screw, copper wire, and tin wire exhibited the maximum HU values, all recorded at 3071 HU. Differentiation among these metals was not possible. However, some interpretations could be made based on the scattering artifacts they produced in response to X-rays. When ranking these metals based on their degree of scattering, from highest to lowest, the order was as follows: lead, steel, tin, iron screws, copper, and titanium. Following the metals, glass had the next highest HU value (1735 HU), followed by rubber (1452 HU), plastic (PVC) (1021 HU), the carbon portion of a lead pencil (832 HU), rubber eraser (497 HU), and chalk (475 HU). Other materials with positive HU values included plastic (3D printing filament) (302 HU), pastel crayon (151 HU), plastic (ABS) (112 HU), plastic button (92 HU), and plastic bead (85 HU). The liver region of the phantom exhibited an approximate HU value of 12. As known, pure water has a HU value of 0. Foreign objects with lower density than water were recorded as follows: construction foam (-64 HU), candle (-73 HU), watermelon seed (-138 HU), wood (MDF) (-220 HU), dry wood branch (-265 HU), wooden portion of a pencil (-476 HU), and Ytong (-550 HU) (Table 2). Moreover, a cluster plot of HU values for all foreign objects, excluding metals, is presented in Table 3, while their appearances within the hepatic uniformity of the Rando Phantom CT slices are shown in Figure 2. As seen in Figure 2, since the tube potential we used (120 kV/400 mA) was not sufficient to determine the attenuation values of metals, HU distinctions were not observed. However, HU values of other materials except metals could be distinguished. Although the phantom and tube potentials used are standard, it is seen that the range between 5 HU values measured from the same material is wide. The HU value range varies according to the type of material used. For example, the minimum and maximum HU value range of the plastic 3D printer filament known as standard was found to be 265-346 (Table 2).

Table 1. Dose conversion coefficients for adult patient protocols examined in the study (10,11).

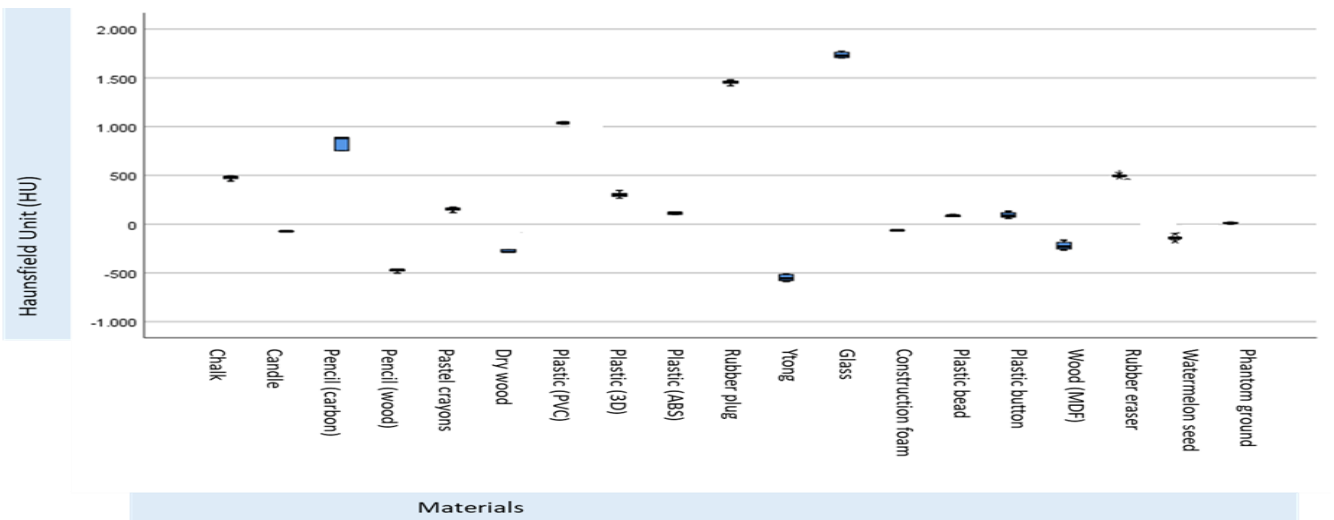
Gender	kV (kilovolt)	Thorax (mSv.mGy^{-1}.cm^{-1})	Abdomen (mSv.mGy^{-1}.cm^{-1})	Pelvis (mSv.mGy^{-1}.cm^{-1})
Female	80	0,0188	0,017	0,0157
	100	0,0183	0,017	0,0155
	120	0,0185	0,0173	0,0157
	140	0,0188	0,0173	0,016
Male	80	0,0107	0,0132	0,01
	100	0,0104	0,0132	0,0099
	120	0,0105	0,0134	0,01
	140	0,0107	0,0134	0,0102

Table 2. Descriptive statistics of the foreign bodies used, measured as Haunsfield Unit.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Lead	5	3071	3071	3071,00	,000
Medical titanium screw	5	3071	3071	3071,00	,000
Tin	5	3071	3071	3071,00	,000
Medical steel screw	5	3071	3071	3071,00	,000
Iron screw	5	3071	3071	3071,00	,000
Copper	5	3071	3071	3071,00	,000
Chalk	5	442	495	475,20	21,040
Candle	5	-78	-71	-73,80	2,775
Pencil (carbon)	5	754	884	832,00	71,204
Pencil (wood)	5	-502	-465	-476,60	15,534
Pastel crayons	5	118	173	151,40	21,443
Dry wood	5	-288	-210	-265,20	32,790
Plastic (PVC)	5	944	1051	1021,00	43,926
Plastic (3D)	5	265	346	302,40	30,713
Plastic (ABS)	5	99	124	112,00	11,683
Rubber	5	1418	1479	1452,60	23,352
Ytong	5	-589	-514	-550,80	34,809
Glass	5	1704	1775	1735,20	31,531
Construction foam	5	-67	-62	-64,20	1,924
Plastic bead	5	77	99	85,80	9,203
Plastic button	5	60	131	92,80	29,609
Wood (MDF)	5	-265	-164	-220,20	43,517
Rubber eraser	5	485	521	497,80	13,609
Watermelon seed	5	-171	-97	-138,80	26,527
Phantom ground	5	2	20	11,80	7,050
Valid N (listwise)	5				

Table 3. Cluster plot graph of the measurement values of the foreign objects used in Haunsfield Unit (HU).



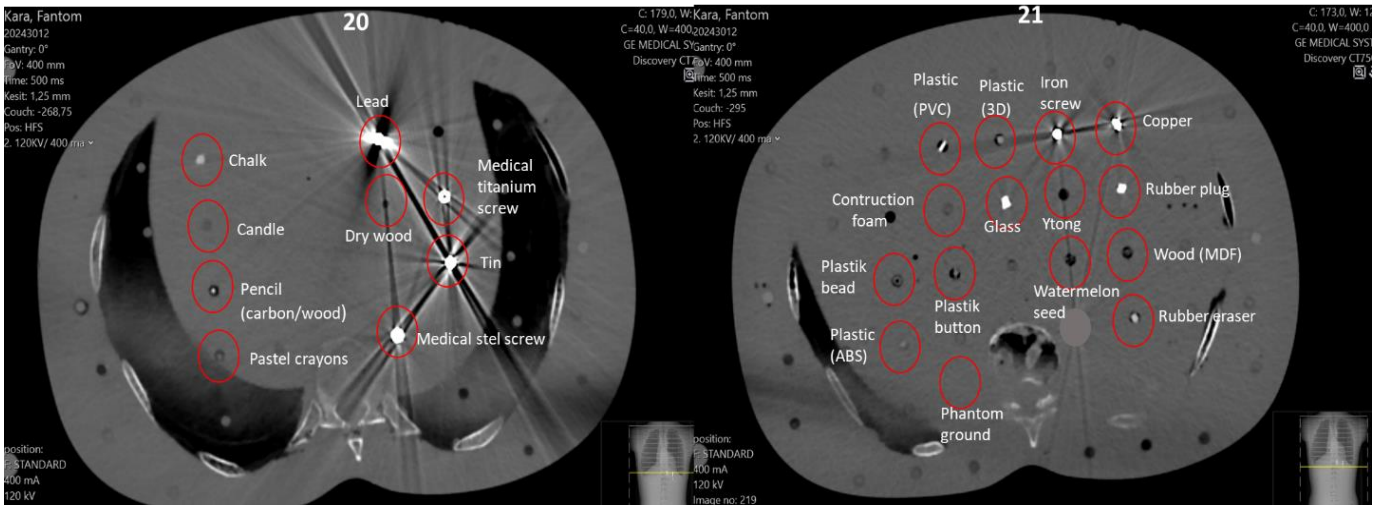


Figure 2. CT slices demonstrating the appearance of foreign bodies in the abdominal region.

Additionally, radiation dose calculations were performed using the DLP values obtained from the CT device. The DLP values were multiplied by the standard abdominal CT dose coefficient (10) for 120 kV-400mA settings to compute the effective radiation dose in milisieverts (mSv).

The total body CT scan (thorax, abdomen, pelvis) performed on the phantom resulted in a total DLP dose of 826.25. When multiplied by the abdominal CT dose coefficient of 0.0134 (Table 1), the total radiation dose absorbed by the phantom was calculated to be 11.071 mSv (Table 4).

Table 4. Dose card created after Rando Phantom Whole Body CT examination.

Kara, Fantom
20243012
Pos: HFS
999. Dose Report

Patient Name: KARA FANTOM
Accession Number:
Patient ID: 20243012
Exam Description: Abdomen

Exam no: 709
30 Dec 2024
Discovery CT750 HD

C: -512,0, W: 1024,0
C=-512,0, W=1024,0 1/7
GE MEDICAL SYSTEMS
Discovery CT750 HD

Dose Report

kV/mA	Series	Type	Scan Range (mm)	CTDIvol (mGy)	DLP (mGy-cm)	Phantom cm	DLP xCoefficient= Dose(mSv)
	1	Scout	-	-	-	-	
120/400	2	Helical	122.500-1682.500	11.67	826.25	Body 32	826,25x0,0134 = 11,071
				Total Exam DLP:	826.25		

Discussion

CT imaging allows easy visualization of metals with high atomic weight and density (3,9,12,13), yet distinguishing between different metals proves challenging. This is because once a certain density threshold is exceeded, CT assigns the highest HU value of 3071. The tube potential used could not create sufficient attenuation difference in metals. Using thin metal may be sufficient to create attenuation, but HU values will not be measured with sufficient sensitivity. Additionally, metals generate significant beam hardening artifacts in CT images (9,13). In our study, lead, steel, iron, tin, and titanium exhibited various degrees of beam hardening artifacts. This will not be a scientific determination and will vary depending on the person evaluating.

However, materials of intermediate density, such as glass, rubber, various plastics, carbon-based substances, and mineral-based materials, were well visualized. Multiple studies have also reported that CT is an effective imaging method for detecting glass (3,8,9,14), stones, and plastics (9). Glass has been documented to produce high attenuation values in CT, ranging from approximately 500 to 1900 HU, with an average of 1800 HU (13,15). In our study, the glass sample we used had an average HU of 1750. A commonly used plastic material, polyvinyl chloride (PVC), exhibits higher attenuation values (approximately 400 HU) and can be easily identified on CT without generating beam hardening artifacts (16). The plastics we tested showed HU values ranging from 302 to 1021.

Wooden and plant-based materials, due to their high air content, low density, and radiolucency, are more difficult to visualize and differentiate. However, when assessed using wide-window HU settings, they can be distinguished from other tissues in CT (17,18). The aerated concrete sample, which contains a high amount of gas, demonstrated a very low attenuation value of -550 HU.

Some researchers have also reported that dual-energy CT systems are highly effective in distinguishing different materials (19,20).

Although the phantom and tube potential used in our study are standard, when the minimum and maximum values of the measured HU values are examined (Figure 2), the HU value ranges are quite wide. In order to determine the types and suballoys of other materials, except metals, different methods and techniques must be used. It may be more useful to conduct research on determining the electron density values of materials.

Conclusion

As demonstrated in our study, CT imaging can broadly categorize foreign materials introduced into the body into metals, glass, plastics, and wood-based materials. However, due to the wide range of HU values these materials exhibit, determining their specific type or form can be challenging. Future studies should explore and evaluate different post-processing imaging analysis methods to enhance material differentiation.

Acknowledgements

We would like to thank the Radiology Department and Radiation Oncology Department managers and staff for their support in carrying out this study.

References

1. Potini VC, Francisco R, Shamian B, Tan V. Sequelae of foreign bodies in the wrist and hand. Hand (N Y) 2013;8(1):77–81.
2. Davis J, Czerniski B, Au A, Adhikari S, Farrell I, Fields JM. Diagnostic Accuracy of Ultrasonography in Retained Soft Tissue Foreign Bodies: a Systematic Review and Metaanalysis. Acad Emerg Med 2015;22(7):777–787.
3. Jarraya M, Hayashi D, de Villiers RV, et al. Multimodality imaging of foreign bodies of the musculoskeletal system. AJR Am J Roentgenol 2014;203(1):W92–W102.
4. Ipaktchi K, Demars A, Park J, Ciarallo C, Livermore M, Banegas R. Retained palmar foreign body presenting as a late hand infection: proposed diagnostic algorithm to detect radiolucent objects. Patient Saf Surg 2013;7(1):25.
5. Manthey DE, Storrow AB, Milbourn JM, Wagner BJ. Ultrasound versus radiography in the detection of soft-tissue foreign bodies. Ann Emerg Med 1996;28(1):7–9.
6. Turkcuer I, Atilla R, Topacoglu H, et al. Do we really need plain and soft-tissue radiographies to detect radiolucent foreign bodies in the ED? Am J Emerg Med 2006;24(7):763–768.
7. Reiner B, Siegel E, McLaurin T, et al. Evaluation of softtissue foreign bodies: comparing conventional plain film radiography, computed radiography printed on film, and computed radiography displayed on a computer workstation. AJR Am J Roentgenol 1996;167(1):141–144.
8. Anderson MA, Newmeyer WL 3rd, Kilgore ES Jr. Diagnosis and treatment of retained foreign bodies in the hand. Am J Surg 1982;144(1):63–67.
9. Aras MH, Miloglu O, Barutcugil C, Kantarci M, Ozcan E, Harorli A. Comparison of the sensitivity for detecting foreign bodies among conventional plain radiography, computed tomography and ultrasonography. Dentomaxillofac Radiol 2010;39(2):72–78.
10. Martin CJ. Effective dose: how should it be applied to medical exposures? Br J Radiol 2007; 80: 639-47.
11. Öncü T, Ataç GK, İnal T, Bulgurlu F, Bulur E. Bilgisayarlı tomografi incelemelerinde PraCTdose Calculator ile etkin dozun saptanması. Türk Radyoloji Derg 2016; 35: 44-51.
12. Hunter TB, Taljanovic MS. Foreign bodies. RadioGraphics 2003;23(3):731–757.
13. Haghnegahdar A, Shakibafard A, Khosravifard N. Comparison between Computed Tomography and Ultrasonography in Detecting Foreign Bodies Regarding Their Composition and Depth: an In Vitro Study. J Dent (Shiraz) 2016;17(3):177–184.
14. Fordham SD. The detection of glass foreign bodies. South Med J 1976;69(11):1484–1485.
15. Tseng HJ, Hanna TN, Shuaib W, Aized M, Khosa F, Linnau KF. Imaging Foreign Bodies: Ingested, Aspirated, and Inserted. Ann Emerg Med 2015;66(6):570–582.e5.
16. Modjtahedi BS, Rong A, Bobinski M, McGahan J, Morse LS. Imaging characteristics of intraocular foreign bodies: a comparative study of plain film X-ray, computed tomography, ultrasound, and magnetic resonance imaging. Retina 2015;35(1):95–104.
17. Yoon JH, Kim SH, Lee Y, et al. Detection of an accidentally implanted wooden foreign body using CT: case report and literature review. Clin Imaging 2015;39(1):158–160.
18. Peterson JJ, Bancroft LW, Kransdorf MJ. Wooden foreign bodies: imaging appearance. AJR Am J Roentgenol 2002;178(3):557–562.
19. Ruder TD, Thali Y, Bolliger SA, et al. Material differentiation in forensic radiology with single-source dualenergy computed tomography. Forensic Sci Med Pathol 2013;9(2):163–169.
20. Gascho D, Zoelch N, Richter H, Buehlmann A, Wyss P, Schaerli S. Identification of Bullets Based on Their Metallic Components and X-Ray Attenuation Characteristics at Different Energy Levels on CT. AJR Am J Roentgenol 2019;213(3):W105–W113.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2025;63 (1): 45-50

Relationship Between Serum Uric Acid Level And Frequency Of Gastrointestinal Bleeding in Patients Using New Oral Anticoagulants

Yeni Nesil Oral Antikoagülan Kullanan Hastalarda Serum Ürik Asit Düzeyi ile Gastrointestinal Kanama Sıklığı Arasındaki İlişki

Eyyüp ERKİZ * 0000-0001-7648-2884
Seda Elçim YILDIRIM 0000-0001-5175-0491**
Tarık YILDIRIM ** 0000-0002-6314-7371
Özgen ŞAFAK ** 0000-0001-8245-0117
Onur ARGAN ** 0000-0001-7745-7736
Mehmet Tolga HEKİM ** 0000-0001-6540-2244
Eyüp AVCI ** 0000-0002-7790-8450
Halil Lütfi KISACIK ** 0000-0003-1102-8239

* Batman Bölge Hastanesi
**Balıkesir Üniversitesi Tıp Fakültesi Hastanesi

Yazışma Adresi: Tarık YILDIRIM
Balıkesir Üniversitesi Tıp Fakültesi Hastanesi,
Kardiyoloji Anabilim Dalı, Balıkesir,
E-mail: kdrtarik@gmail.com

Geliş Tarihi: 16.09.2024
Kabul Tarihi: 10.02.2025

Abstract

Introduction: The primary objective of utilising non-vitamin K antagonist oral anticoagulants is to inhibit the onset of stroke. Gastrointestinal bleeding represents the most prevalent form of bleeding, and bleeding prediction scoring systems have been devised. Nevertheless, none of these scoring systems are specific or sensitive in detecting bleeding risk. Elevated uric acid levels have been demonstrated to impact endothelial function. This study sought to ascertain whether uric acid levels exert an influence on the prediction of gastrointestinal bleeding.

Methods: This retrospective study comprised 501 patients who were undergoing treatment with direct oral anticoagulants. These patients were screened for a history of gastrointestinal bleeding. The serum uric acid levels of the patients were evaluated during their previous outpatient visit. The control group comprised patients treated with direct oral anticoagulants who did not have a history of gastrointestinal bleeding.

Results: A total of 68 patients (13.6%) exhibited evidence of gastrointestinal bleeding, with no discernible difference between the various direct oral anticoagulant types. The mean uric acid level was 7.87 mg/dL in the gastrointestinal bleeding group and 6.30 mg/dL in the control group ($p < 0.001$). A correlation was observed between uric acid level and HAS-BLED score ($r = 0.387$).

Conclusion: The presence of elevated uric acid levels has been correlated with gastrointestinal bleeding in patients on direct oral anticoagulant therapy. In light of the uric acid levels observed in these patients, it is recommended that those deemed to be at elevated risk of bleeding undergo more frequent monitoring.

Keywords: Uric acid, gastrointestinal bleeding, direct oral anticoagulants

Öz

Giriş Yeni nesil oral antikoagülan alan hastalarda ilaç kullanımının primer hedefi hastada inme gelişimini önlemek olup, bu tedavinin en sık görülen komplikasyonu kanamadır. Bu hastalarda görülen kanamalar incelendiğinde gastrointestinal istem kanamaları en fazla görülen kanama türü olup, kanamayı öngörücü skorlama sistemleri geliştirilmiştir. Fakat bu skorlama sistemlerinin hiçbirisi kanama riskini saptamada spesifik ve sensitif değildir. Yüksek ürik asit seviyelerinin endotel disfonksiyonuna neden olduğu gösterilmiştir. Bu çalışmada ürik asit düzeylerinin gastrointestinal kanama tahmini üzerinde bir etkisi olup olmadığı araştırılmıştır.

Yöntemler Bu retrospektif çalışma, yeni nesil oral antikoagülan tedavisi gören 501 hastayı içermektedir. Bu hastalar gastrointestinal kanama öyküsü açısından tarandı. Hastaların serum ürik asit düzeyleri bir önceki poliklinik ziyaretleri sırasında değerlendirildi. Kontrol grubunda ise önceden gastrointestinal kanama geçirmemiş yeni nesil oral antikoagülan kullanan hastalar değerlendirildi.

Bulgular Toplam 68 hastada (%13.6) gastrointestinal kanama bulguları görüldü ve çeşitli direkt oral antikoagülan tipleri arasında belirgin bir fark yoktu. Ortalama ürik asit düzeyi gastrointestinal kanama grubunda 7.87 mg/dL iken kontrol grubunda 6.30 mg/dL idi ($p < 0.001$). Ürik asit düzeyi ile HAS-BLED skoru arasında bir korelasyon gözlendi ($r = 0.387$).

Sonuç Yüksek ürik asit seviyelerinin varlığı, doğrudan oral antikoagülan tedavisi gören hastalarda gastrointestinal kanama ile korele olarak saptanmıştır. Bu hastaların takibinde ürik asit seviyelerinin göz önünde bulundurularak, kanama riskinin yüksek olduğu düşünülen hastaların daha yakından takibinin uygun olduğu kanısındayız.

Anahtar Kelimeler: Ürik asit, gastrointestinal kanama, yeni nesil oral antikoagülan ilaçlar

Foreword

Atrial fibrillation (AF) represents the most prevalent cardiac arrhythmia globally. The prevalence of this condition is estimated to be between 2 and 4% in adults (1). It is recommended that antithrombotic therapy be considered for all patients with atrial fibrillation in order to prevent systemic embolism. In comparison to patients undergoing anticoagulant therapy, the risk of stroke is 2-3 times higher in patients not undergoing anticoagulant therapy (2). Direct oral anticoagulants (DOACs) have been demonstrated to be as effective as warfarin in the prevention of stroke and are associated with a reduced risk of bleeding. The most common type of bleeding in these patients is gastrointestinal bleeding. In order to predict the likelihood of such bleeding, scoring systems have been developed. The HAS-BLED score is the most evidence-based method for assessing the risk of bleeding in these patients. However, no single bleeding scoring system is both specific and sensitive.

Uric acid represents the final product of purine metabolism (3). Uric acid plays a role in scavenging free radicals and has been linked to a pro-oxidant effect in hyperuricemia (4). Endothelial dysfunction plays a role in the development and progression of atherosclerosis, which can result in cardiovascular complications (5). The evidence from experimental studies indicates that hyperuricemia causes endothelial dysfunction (6, 7). The precise role of uric acid in the context of vascular disease remains a topic of contention. The relationship between uric acid levels and the incidence of gastrointestinal bleeding in patients receiving new-generation oral anticoagulants has yet to be investigated. The objective of our study was to investigate whether there is an association between uric acid levels and the occurrence of gastrointestinal bleeding.

Materials and methods

Patients

A total of 501 patients who received DOACs for atrial fibrillation between January 2018 and August 2022 were included in this study. The patients were divided into two groups: the gastrointestinal bleeding group (n = 68) and the control group (n = 433). Patients with haematological disorders, oesophageal varices, cirrhosis, renal insufficiency, rheumatic diseases, use of non-steroidal anti-inflammatory drugs and ACS within the last year were excluded from the study. Laboratory tests, including uric acid, liver and kidney function, haemogram, albumin, and clinical and demographic characteristics, were obtained from the patients' medical records. The study was initiated following the approval of the ethics committee. (Ethics Committee approval number: 2022-78)

Definition of gastrointestinal bleeding bleeding and bleeding scoring systems

Gastrointestinal bleeding can occur at any point along the digestive tract, from the mouth to the rectum. Patients presenting with acute gastrointestinal bleeding often present with melena or haematochezia. Bleeding above the ligament of Treitz is referred to as upper gastrointestinal (GI) bleeding, whereas haematemesis indicates the presence of bleeding in a location proximal to the ligament of Treitz. Haematochezia typically signifies lower GI bleeding, although it may also be indicative of significant upper GI bleeding. It is estimated that 50% of all GI bleeds originate from the upper GI tract, 40% are lower GI bleeds, and 10% are bleeds with an indeterminate focus (8).

HAS-BLED scoring system

A comprehensive assessment of the risk of bleeding is essential prior to the commencement of anticoagulant therapy. A number of bleeding risk scores have been developed that utilise both modifiable and non-modifiable risk factors, and these are generally capable of predicting bleeding events at a moderate level of accuracy. Similarly, as there are scoring systems for the risk of stroke in patients with atrial fibrillation, there are also scoring systems for the risk of bleeding. The HAS-BLED scoring system is recommended for use as it is a more straightforward and reliable method of assessing bleeding risk than other systems, and it has a higher predictive value for intracranial bleeding. The HAS-BLED scoring system comprises six criteria: hypertension, abnormal liver or kidney function, stroke, previous bleeding, unstable INR and drug or alcohol use. In accordance with the HAS-BLED scoring system, a score of ≥3 signifies that the patient is at elevated risk of bleeding. It is therefore advised to exercise greater caution when initiating and monitoring anticoagulant therapy in these individuals (10, 11).

Statistical analysis

The data were analysed using the Statistical Package for the Social Sciences (SPSS) 21.0. The Kolmogorov-Smirnov test was employed for the purpose of testing the normality of the data.

Descriptive statistics included the number and percentage of distributions, as well as the mean, standard deviation, or minimum-maximum values. The chi-square test, t-test for independent groups, Mann-Whitney U test and one-way ANOVA analysis were employed. The level of the type 1 error was set at α=0.05.

Results

The mean age of the cohort was 69.5±8.0 years, with 56.7% of patients being female. No statistically significant differences were observed in the mean age of patients included in the study according to gender, heart failure, diabetes mellitus, or vascular disease. A total of 68 patients (13.6%) experienced gastrointestinal bleeding. Of the patients included in the study, 132 (26.3%) were on rivaroxaban, 186 (37.1%) on edoxaban, 143 (28.5%) on apixaban and 40 (8%) on dabigatran (Table 1).

Table 1. Demographic characteristics of the patients

		n	%
Sex	Women Men	284 217	56,7 43,3
Age	18-65 65-75 >75	128 235 138	25,5 46,9 27,5
DOACs	Rivaroxaban Edoxaban Apixaban Dabigatran	132 186 143 40	26,3 37,1 28,5 8
GI bleeding	Yes No	68 433	13,6 86,4
HF	Yes No	150 351	29,9 70,1
HT	Yes No	401 100	80 20
DM	Yes No	197 304	39,3 60,7
Strok	Yes No	60 441	12 88
Vascular disease	Yes No	313 188	62,5 37,5

DM; Diabetes mellitus; GI: Gastrointestinal; HF: Heart failure; HT: Hypertension; DOACs: Direct oral anticogulants

No statistically significant difference was observed in the mean CHA_2DS_2-VASc and HAS-BLED scores among the DOACs groups (Table 2). A comparison of the groups in terms of HAS-BLED score revealed no significant difference between the dabigatran and rivaroxaban groups (p=0.1). However, a statistically significant difference was observed when dabigatran was compared with edoxaban (p<0.01).

Table 2. CHA_2DS_2-VASc and HAS-BLED scores of the DOACs groups

DOACs	CHA_2DS_2-VASc	HAS-BLED
Rivaroxaban	3,91	2,37
Edoxaban	4,15	2,54
Apixaban	4,13	2,55
Dabigatran	3,82	2,02
Total	4,05	2,46

DOACs: Direct oral anticogulants

The median uric acid level was 5.61 mg/dL, which is above the normal reference value of <5.6 mg/dL. The mean uric acid levels were 6.85±2.37 mg/dl in men and 6.25±2.24 mg/dl in women, demonstrating a statistically significant difference (p<0.005). The mean uric acid level was 7.87 mg/dL in patients with GI bleeding and 6.87 mg/dL in those without, yielding a statistically significant difference between the two groups (p < 0.001). The uric acid/albumin ratio was 2.27 in patients with gastrointestinal bleeding and 1.67 in patients without gastrointestinal bleeding, yielding a statistically significant result (p < 0.001).

An evaluation of the DOACs groups revealed no significant differences with regard to gastrointestinal bleeding (Table 3).

Table 3. Association between DOACs groups and gastrointestinal bleeding

DOACs	GI bleeding (n, %)	Without GI bleeding (n, %)	χ2	p
Rivaroxaban	21 (30,9)	111 (25,6)	7,84	0,058
Edoxaban	21 (30,9)	165 (38,1)		
Apixaban	25 (36,7)	118 (27,3)		
Dabigatran	1 (1,5)	39 (9)		
Total	68 (100)	433 (100)		

DOACs: Direct oral anticogulants

A correlation was observed between the HAS-BLED score and the incidence of GI bleeding in the patients included in the study (k:0.387, p<0.001). A positive correlation was observed between uric acid levels and the HAS-BLED score in this patient cohort (k: 0.197, p < 0.001) (Table 4).

Table 4. Correlation between CHA_2DS_2-VASc and HAS-BLED scores and uric acid level

	correlation coefficient	p
CHA_2DS_2-VASc score and uric acid level	0,178	<0,001
HAS-BLED score and uric acid level	0,197	<0,001

Discussion

The use of vitamin K antagonists has been demonstrated to be an effective method for the prevention of stroke in patients diagnosed with atrial fibrillation. However, due to the narrow therapeutic window of vitamin K antagonists and the inter-individual variability observed among patients, lifelong monitoring of coagulation is necessary. Maintaining the INR within the therapeutic range is challenging, which diminishes the potential benefit of vitamin K antagonist treatment and increases the risk of stroke (12). DOACs represent a promising alternative for this patient group. As the use of these drugs increases, so too does the importance of monitoring for and managing the side effects associated with these drugs.

In a retrospective study of 501 patients with non-valvular atrial fibrillation on DOACs, a significant association was identified between elevated uric acid levels and gastrointestinal bleeding (p < 0.001). In this patient cohort, independent predictors of GI bleeding were identified as the CHA_2DS_2-VASc score, HAS-BLED score, uric acid level and uric acid to albumin ratio. Prior research has demonstrated that the CHA2DS2-VASc score is an effective predictor of ischemic stroke, with an increased risk of bleeding observed with elevated scores (13). The mean CHA_2DS_2-VASc score was 4.05, with no significant difference in CHA_2DS_2-VASc score between the DOACs groups (p=0.43). In alignment with the aforementioned findings, our results demonstrated a statistically significant correlation between a high CHA_2DS_2-VASc score and an increased risk of GI bleeding (correlation coefficient: 0.089, p < 0.05).

The HAS-BLED score is a straightforward and pragmatic scoring system for evaluating the individual risk of bleeding in patients with atrial fibrillation (AF). It is currently recommended for use in clinical practice. In a study by Lip and colleagues, it was demonstrated that the risk of gastrointestinal bleeding was elevated in patients with a HAS-BLED score of 3 or above. Furthermore, the use of DOACs was shown to be more effective than warfarin in reducing the risk of bleeding (14).

The results of our study demonstrated a statistically significant correlation between the HAS-BLED score and GI bleeding, with a correlation coefficient of 0.387 and a p-value less than 0.001. No significant difference was observed between the HAS-BLED scores of the NOAC groups. Nevertheless, a distinction was observed between the dabigatran cohort and the remaining three DOACs groups. No significant difference was observed between the HAS-BLED scores of patients in the dabigatran group and those in the rivaroxaban group (p=0.1). However, a notable discrepancy was evident when dabigatran was compared with edoxaban and apixaban (p=0.01). The discrepancy in the HAS-BLED score for dabigatran may be attributed to the relatively limited number of patients who were administered this medication. A review of the literature revealed that the use of dabigatran 150 mg, edoxaban 60 mg and rivaroxaban 20 mg was associated with an elevated risk of gastrointestinal bleeding. Among the DOACs groups, rivaroxaban was associated with the highest incidence of gastrointestinal bleeding, while edoxaban and dabigatran exhibited comparable rates of this adverse event. Apixaban demonstrated the lowest incidence of gastrointestinal bleeding among the DOACs. In the ROCKET AF trial, the incidence of major GI bleeding was 3.2% in the rivaroxaban group and 2.2% in the warfarin group (15). The incidence of GI bleeding observed in our study was comparable to that reported in the ROCKET AF study. The incidence of GI bleeding among patients treated with rivaroxaban was comparable to that observed in other DOACs groups. This may be attributed to the absence of a notable discrepancy between the CHA_2DS_2-VASc and HAS-BLED scores of the DOACs cohorts. In the ARISTOTLE trial, apixaban was demonstrated to reduce the incidence of bleeding by 27% in comparison to warfarin (p < 0.001) (16). In the RE-LY trial, dabigatran was observed to be associated with a higher incidence of GI bleeding compared to warfarin (p=0.001) (17). The ENGAGE AF-TIMI study demonstrated that rivaroxaban was associated with a higher incidence of GI bleeding compared to warfarin (18). A prospective study comparing DOACs head-to-head in terms of bleeding has yet to be performed. However, a meta-analysis has indicated that apixaban may be associated with a lower incidence of GI bleeding than dabigatran and rivaroxaban (19). A breakdown of the DOACs groups used by patients who experienced GI bleeding in the study revealed that 30.9% were on rivaroxaban, 30.9% on edoxaban, 36.5% on apixaban and 1.5% on dabigatran. No significant difference was identified between the DOACs groups in the development of GI bleeding (p=0.058). The disparate number of patients in the DOACs groups and the absence of patients on warfarin may have exerted an influence on the results.

In particular, the limited number of patients on dabigatran does not allow for an adequate assessment of the propensity for GI bleeding in the DOACs groups. In their study, Jansen et al. demonstrated that elevated levels of uric acid, a natural antioxidant and anti-inflammatory agent, are associated with an increased risk of GI bleeding (20). Similarly, an association between elevated uric acid levels and GI bleeding was identified in patients with colonic diverticula (21). The relationship between elevated uric acid levels and bleeding in patients using DOACs has yet to be investigated. The present study yielded statistically significant results with regard to the correlation between elevated uric acid levels and GI bleeding, a finding that is consistent with the existing literature ($p < 0.001$).

It has been demonstrated that hypoalbuminaemia is linked to complicated GI bleeding (22). The uric acid to albumin ratio has been demonstrated to predict contrast-induced nephropathy and is associated with the prevalence of coronary and peripheral arterial disease. In their study, Ozgur et al. demonstrated that the uric acid to albumin ratio was associated with acute renal failure and mortality. In the present study, a significantly higher uric acid-to-albumin ratio was observed in patients with GI bleeding compared to those without ($p < 0.001$).

In conclusion, our findings suggest that elevated uric acid levels may serve as a predictor of GI bleeding in patients undergoing treatment with DOACs. It may be advisable to subject high-risk patients to closer monitoring, with uric acid levels included in the follow-up protocol.

Limitation Although we found significance in the correlation analysis between elevated uric acid and gastrointestinal bleeding, we think that the fact that we did not perform regression analysis is a limitation of our study.

References

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. Circulation. 2019;139(10):e56-e528. doi: 10.1161/CIR.0000000000000659.
2. Nielsen PB, Chao TF. The risks of risk scores for stroke risk assessment in atrial fibrillation. Thromb Haemost. 2015;113(6):1170-3. doi: 10.1160/TH15-03-0210.
3. Chaudhary K, Malhotra K, Sowers J, Aroor A. Uric Acid - key ingredient in the recipe for cardiorenal metabolic syndrome. Cardiorenal Med. 2013;3(3):208-220. doi: 10.1159/000355405.
4. Sautin YY, Johnson RJ. Uric acid: the oxidant-antioxidant paradox. Nucleosides Nucleotides Nucleic Acids. 2008;27(6):608-19. doi: 10.1080/15257770802138558.
5. Gimbrone MA Jr, García-Cardeña G. Endothelial Cell Dysfunction and the Pathobiology of Atherosclerosis. Circ Res. 2016;118(4):620-36. doi: 10.1161/CIRCRESAHA.115.306301.
6. Khosla UM, Zharikov S, Finch JL, et al. Hyperuricemia induces endothelial dysfunction. Kidney Int. 2005;67(5):1739-42. doi: 10.1111/j.1523-1755.2005.00273.x.
7. Borgi L, McMullan C, Wohlhueter A, Curhan GC, Fisher ND, Forman JP. Effect of Uric Acid-Lowering Agents on Endothelial Function: A Randomized, Double-Blind, Placebo-Controlled Trial. Hypertension. 2017 Feb;69(2):243-248. doi: 10.1161/HYPERTENSIONAHA.116.08488.
8. Moledina SM, Komba E. Risk factors for mortality among patients admitted with upper gastrointestinal bleeding at a tertiary hospital: a prospective cohort study. BMC Gastroenterol. 2017;17(1):165. doi: 10.1186/s12876-017-0712-8.
9. Yao X, Gersh BJ, Sangaralingham LR, et al. Comparison of the CHA2DS2-VASc, CHADS2, HAS-BLED, ORBIT, and ATRIA Risk Scores in Predicting Non–Vitamin K Antagonist Oral Anticoagulants-Associated Bleeding in Patients With Atrial Fibrillation. Am J Cardiol . 2017;120(9):1549-1556.
10. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Europace. 2010;12(10):1360-420. doi: 10.1093/europace/euq350.
11. Caldeira D, Costa J, Fernandes RM, Pinto FJ, Ferreira JJ. Performance of the HAS-BLED high bleeding-risk category, compared to ATRIA and HEMORR2HAGES in patients with atrial fibrillation: a systematic review and meta-analysis. J Interv Card Electrophysiol. 2014;40(3):277-84. doi: 10.1007/s10840-014-9930-y.
12. Fang MC, Go AS, Chang Y, et al. Warfarin discontinuation after starting warfarin for atrial fibrillation. Circ Cardiovasc Qual Outcomes. 2010;3(6):624-31. doi: 10.1161/CIRCOUTCOMES.110.937680.
13. Maeda T, Nishi T, Funakoshi S, et al. Risks of Bleeding and Stroke Based on CHA2DS2-VASc Scores in Japanese Patients With Atrial Fibrillation: A Large-Scale Observational Study Using Real-World Data. J Am Heart Assoc. 2020;9(5):e014574. doi: 10.1161/JAHA.119.014574.
14. Lip GYH, Keshishian AV, Zhang Y, et al. Oral Anticoagulants for Nonvalvular Atrial Fibrillation in Patients With High Risk of Gastrointestinal Bleeding. JAMA Netw Open. 2021;4(8):e2120064. doi: 10.1001/jamanetworkopen.2021.20064.
15. Halperin JL, Hankey GJ, Wojdyla DM, et al; ROCKET AF Steering Committee and Investigators. Efficacy and safety of rivaroxaban compared with warfarin among elderly patients with nonvalvular atrial fibrillation in the Rivaroxaban Once Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF). Circulation. 2014;130(2):138-46. doi: 10.1161/CIRCULATIONAHA.113.005008.
16. Granger CB, Alexander JH, McMurray JJ, et al; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981-92. doi: 10.1056/NEJMoa1107039.
17. Connolly SJ, Ezekowitz MD, Yusuf S, et al; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361(12):1139-51. doi: 10.1056/NEJMoa0905561.
18. Giugliano RP, Ruff CT, Braunwald E, et al; ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2013;369(22):2093-104. doi: 10.1056/NEJMoa1310907.
19. Menichelli D, Del Sole F, Di Rocco A, et al. Real-world safety and efficacy of direct oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of 605 771 patients. Eur Heart J Cardiovasc Pharmacother. 2021;7(FI1):f11-f19. doi: 10.1093/ehjcvp/pvab002.
20. Jansen A, Harenberg S, Grenda U, Elsing C. Risk factors for colonic diverticular bleeding: a Westernized community based hospital study. World J Gastroenterol . 2009;15(4):457-61. doi: 10.3748/wjg.15.457.
21. Sugihara Y, Kudo SE, Miyachi H, et al. Analysis of Risk Factors for Colonic Diverticular Bleeding: A Matched Case-Control Study. Gut Liver. 2016;10(2):244-9. doi: 10.5009/gnl14407.
22. Tung CF, Chow WK, Chang CS, Peng YC, Hu WH. The prevalence and significance of hypoalbuminemia in non-variceal upper gastrointestinal bleeding. Hepatogastroenterology. 2007;54(76):1153-6.
23. Özgür Y, Akın S, Yılmaz NG, Gücün M, Keskin Ö. Uric acid albumin ratio as a predictive marker of short-term mortality in patients with acute kidney injury. Clin Exp Emerg Med. 2021 ;8(2):82-88. doi: 10.15441/ceem.20.024.

OLGU SUNUMU /CASE REPORT
Ege Klin Tıp Derg 2025;63 (1):51-54

Delayed-Onset Morbilliform Drug Eruption Induced by Hydroxychloroquine: A Clinical Observation in a Patient with Systemic Sclerosis

Hidroksiklorokin Kullanımına Bağlı Gecikmiş Başlangıçlı Morbilliform İlaç Döküntüsü: Sistemik Sklerozlu Bir Hastada Klinik Gözlem

Gülşah ÇELİK * 0009-0002-1170-4110

*Antalya Şehir Hastanesi, Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, Antalya

Yazışma Adresi: Gülşah ÇELİK
Antalya Şehir Hastanesi Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, Antalya
E-mail : gulsahberberr@gmail.com

Geliş Tarihi: 02.02.2025
Kabul Tarihi: 15.03.2025

Abstract

Introduction: Hydroxychloroquine (HCQ) is widely used in the treatment of connective tissue diseases such as systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis and Sjögren's syndrome. Although generally well-tolerated, HCQ may cause cutaneous adverse drug reactions, among which morbilliform drug eruptions are most frequently reported. In this report, a case of morbilliform drug eruption developing in the sixth week of hydroxychloroquine treatment in a patient diagnosed with systemic sclerosis is presented.

Case Report: A 70-year-old female patient was diagnosed with systemic sclerosis and initiated on HCQ 200 mg/day by our clinic. After six weeks of regular use, the patient presented with diffuse erythematous papules and plaques, primarily on the trunk and proximal lower extremities. No mucosal or systemic involvement was observed. Laboratory findings were within normal limits. A skin biopsy revealed mild spongiosis, superficial perivascular lymphocytic infiltration, and minimal dermal edema, findings consistent with morbilliform drug eruption. HCQ was discontinued, and the patient was treated with systemic corticosteroids, topical steroid lotion, and oral antihistamines. Complete resolution was achieved within 10 days without residual pigmentation or scaling.

Conclusion: Morbilliform drug eruptions due to HCQ generally occur within 1–2 weeks after treatment initiation. However, this case demonstrates that such eruptions can also develop later in the course of treatment. Clinicians should consider drug-induced reactions even in delayed presentations and discontinue the suspected agent promptly to prevent progression.

Keywords: Hydroxychloroquine, morbilliform drug eruption, systemic sclerosis, cutaneous adverse reaction, delayed onset

Öz

Giriş: Hidroksiklorokin, sistemik lupus eritematozus, romatoid artrit, sistemik skleroz ve Sjögren sendromu gibi bağ dokusu hastalıklarının tedavisinde yaygın olarak kullanılan bir ilaçtır. Genellikle iyi tolere edilmesine rağmen, hidroksiklorokin kullanımına bağlı en sık bildirilen kutanöz advers reaksiyonlardan biri morbiliform ilaç erüpsiyonudur. Bu olguda, sistemik skleroz tanısıyla hidroksiklorokin tedavisi başlanan bir hastada, ilacın altıncı haftasında gelişen morbiliform ilaç erüpsiyonu olgusu sunulmuştur.

Olgu Sunumu: Yetmiş yaşındaki kadın hastaya sistemik skleroz tanısı konulmuş ve tarafımızca 200 mg/gün dozunda hidroksiklorokin tedavisi başlanmıştır. İlacı düzenli kullanan hasta, altıncı haftada gövde ve alt ekstremitelerin proksimalinde yaygın, eritemli papül ve plaklarla başvurmuştur.

Mukozal veya sistemik tutulum izlenmemiştir. Laboratuvar bulguları normal sınırlar içindeydi. Lezyondan alınan biyopside hafif spongiyozis, yüzeyel perivasküler lenfositik infiltrasyon ve minimal dermal ödem izlenmiş; bulgular morbiliform ilaç erüpsiyonu ile uyumlu bulunmuştur. Hidroksiklorokin tedavisi kesilmiş ve sistemik kortikosteroid, topikal steroid losyon ve oral antihistaminik tedavisi başlanmıştır. Lezyonlar 10 gün içinde, kalıcı pigmentasyon veya pullanma olmaksızın tamamen gerilemiştir.

Sonuç: Hidroksiklorokin'e bağlı morbiliform döküntüler genellikle tedavinin ilk 1–2 haftasında ortaya çıkmakla birlikte, bu olguda olduğu gibi daha geç dönemde de gelişebileceği unutulmamalıdır. Klinik şüphe durumunda ilaç hızla kesilmeli ve uygun tedavi başlanmalıdır.

Anahtar Kelimeler: Hidroksiklorokin, morbiliform ilaç erüpsiyonu, sistemik skleroz, kutanöz advers reaksiyon, geç başlangıç

Introduction

Hydroxychloroquine (HCQ) is a widely used antimalarial and immunomodulatory agent in the management of connective tissue diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (SS). Antimalarial agents are well known to cause adverse reactions, with skin and ocular side effects being the most frequently reported (1). Among cutaneous adverse drug reactions, morbilliform eruptions are one of the most commonly observed. These eruptions present as symmetrical, widespread erythematous maculopapular lesions and are typically expected to occur within 1–2 weeks of drug initiation. Due to their similarity to viral exanthems, they can be challenging to identify clinically and are generally associated with a delayed-type hypersensitivity mechanism (2). Although HCQ-induced morbilliform eruptions have been rarely reported, they are usually observed in the early stages of treatment. In this report, we present a rare case of a patient with SS who developed a morbilliform eruption approximately six weeks after the initiation of HCQ therapy. Written informed consent was obtained from the patient for the publication of this case report.

Case Presentation

A 70-year-old female patient was diagnosed with SS and initiated on HCQ therapy at a dose of 200 mg/day by our clinic. The patient adhered to the medication regularly and presented with a widespread cutaneous eruption approximately six weeks after starting treatment.

Physical examination revealed diffuse erythematous papules and plaques with a tendency to coalesce, predominantly affecting the trunk and proximal lower extremities. Some lesions exhibited urticarial morphology. The rash was symmetrically distributed and pruritic, with no accompanying systemic symptoms (Figure 1). The patient was afebrile, and no abnormalities were found in the face or mucosal surfaces, including oral, genital, and ocular regions. The uvula was midline without edema or erythema. No lymphadenopathy was detected in the cervical, axillary, or inguinal regions.

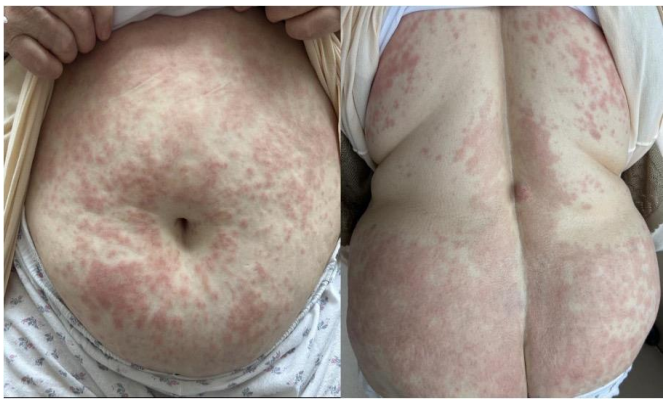


Figure 1. Symmetrical morbilliform rash involving the abdomen and back

Laboratory investigations showed normal complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid function tests, renal, and liver function tests. Eosinophil count was within normal range; no leukocytosis, lymphocytosis, or thrombocytopenia was observed. The patient's known comorbidities included type 2 diabetes mellitus and SS. There was no history of the use of any other medications that could be associated with the eruption.

The patient was referred to the dermatology department for evaluation of the widespread skin lesions. Following a detailed dermatological assessment, a punch biopsy was obtained from a lesion on the lower extremity. Histopathological analysis revealed mild spongiosis in the epidermis, superficial perivascular lymphocytic infiltration in the dermis, and minimal dermal edema. These findings were consistent with a diagnosis of morbilliform drug eruption. While morbilliform reactions are typically seen within the first 1–2 weeks of HCQ therapy, the onset in the sixth week in this case was noted as atypical.

Based on these clinical and histopathological findings, the cutaneous eruption was attributed to HCQ. The medication was discontinued. The dermatology team recommended treatment with bilastine 20 mg twice daily, methylprednisolone aceponate 0.1% lotion applied twice daily to lesions, and intramuscular methylprednisolone 40 mg for four days. The patient was closely monitored and showed complete resolution of lesions within 10 days, without residual pigmentation or scaling.

Discussion

Morbilliform drug eruptions are among the most common cutaneous adverse drug reactions. They typically present as symmetrical, widespread erythematous maculopapular lesions on the trunk and proximal extremities (3). These eruptions generally follow a benign course and are treated with supportive care (4). In our case, both the clinical morphology and lesion distribution were consistent with a morbilliform eruption.

Gülşah ÇELİK

HCQ is a key component of treatment guidelines for autoimmune conditions such as RA, SLE, SS, and primary Sjögren's syndrome. Along with chloroquine, HCQ exists as R and S enantiomers and has a complex pharmacokinetic profile due to its large volume of distribution and prolonged half-life. HCQ binds with high affinity to melanin, allowing accumulation in melanin-rich tissues like the skin and eyes (1).

The most frequently reported cutaneous adverse reactions to HCQ include maculopapular, erythematous, and urticarial eruptions. Such reactions occur in approximately %10 of patients receiving the drug (5). Morbilliform eruptions usually develop within the first 1–2 weeks of treatment and are often associated with a cumulative dose below 100 grams (1). In most cases, the lesions resolve spontaneously within weeks of drug withdrawal. Pruritus is a common feature (6).

Histologically, these eruptions are characterized by superficial perivascular lymphocytic infiltrates in the dermis, occasionally accompanied by eosinophils. Systemic corticosteroids may be required to accelerate symptom resolution (1).

Ezquerra et al. reported a case of a 47-year-old woman with HLA-B27 positive ankylosing spondylitis who developed erythema multiforme five days after discontinuing HCQ due to gastrointestinal intolerance (1). Kumar et al. presented another case involving a 55-year-old woman who developed maculopapular rashes and bullous lesions on multiple body regions while on HCQ for joint pain.

The diagnosis was confirmed by excisional biopsy, and the patient was successfully treated with systemic and topical corticosteroids and immunosuppressants for one month (7).

In our case, the morbilliform eruption occurred approximately six weeks after initiating HCQ, diverging from the typical 1–2 week timeframe. The widespread distribution, clinical morphology, histopathological features, and rapid resolution with treatment all supported the diagnosis of an HCQ-induced morbilliform drug eruption. This case highlights a rarely reported delayed-onset presentation, contributing to the differential diagnosis of cutaneous eruptions in patients receiving HCQ therapy.

Conclusion

Although HCQ is generally considered a safe and effective agent for the treatment of autoimmune diseases, it may occasionally lead to cutaneous adverse drug reactions. Morbilliform eruptions typically occur within the first few weeks of treatment but, as demonstrated in this case, may also present later. Early clinical suspicion, prompt drug discontinuation, and appropriate therapy can lead to complete resolution without permanent sequelae. Therefore, clinicians should consider morbilliform drug eruptions in the differential diagnosis of patients developing skin rashes while on HCQ therapy.

References

1.Rojas Pérez-Ezquerra P, de Barrio Fernández M, de Castro Martínez FJ, Ruiz Hornillos FJ, Prieto García A. Delayed hypersensitivity to hydroxychloroquine manifested by two different types of cutaneous eruptions in the same patient. Allergol Immunopathol (Madr). 2006 Aug;34(4):174–5.

2.Barailler H, Milpied B, Chauvel A, Claraz P, Taïeb A, Seneschal J, et al. Delayed hypersensitivity skin reaction to hydroxychloroquine: Successful short desensitization. J Allergy Clin Immunol Pract. 2019 Jan;7(1):307–8.

3.Khandpur S, Ahuja R. Drug-Induced vs. Viral Maculopapular Exanthem—Resolving the Dilemma. Dermatopathology. 2022 May 7;9(2):164–71.

4.Muzumdar S, Rothe MJ, Grant-Kels JM. The rash with maculopapules and fever in adults. Clin Dermatol. 2019 Mar;37(2):109–18.

5.Mates M, Zevin S, Breuer GS, Navon P, Nesher G. Desensitization to hydroxychloroquine--experience of 4 patients. J Rheumatol. 2006 Apr;33(4):814–6.

6.Gisondi P, Piaserico S, Bordin C, Bellinato F, Tozzi F, Alaibac M, et al. The safety profile of hydroxychloroquine: major cutaneous and extracutaneous adverse events. Clin Exp Rheumatol. 2021 Aug 31;39(5):1099–107.

7.Sunil Kumar S, Elumalai K, Eluri K, Elumalai M, Mallu K, Srinivasan S, et al. A case report on hydroxychloroquine induced maculopapular rashes: The immunosuppressant and corticosteroid therapy. Precision Medical Sciences. 2020 Nov;9(2):98–101.