BANDIRMA ONYEDİ EYLÜL ÜNİVERSİTESİ

HMJ
HTD

HIPPOCRATES MEDICAL JOURNAL
HİPOKRAT TIP DERGİSİ

Volume/Cilt: 3 Issue/Sayı: 3 Year/Yıl: 2023

e-ISSN 2791-9935

CONTENTS/ İÇİNDEKİLER

Hippocrates Medical Journal 2023 December

Hipokrat Tıp Dergisi 2023 Aralık

Değerli araştırmacılar ve bilim insanları,

Dergimizin yayın ve indeks çeşitliliği artarken gönderdikleri çalışmaları, atıfları ile destek olan siz değerli araştırmacılara bir kez daha canı gönülden teşekkür- lerimi ifade etmek istiyorum.
Gelecek sayımızda görüşmek üzere bilim dünyasının tüm araştırmacılarına ba- şarılarının devamını temenni ediyor, keyifli okumalar diliyorum.
Selam ve saygılarımla.

Prof. Dr. Nureddin CENGİZ

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Tel: +90 266 606 4755
Yayın Türü: Süreli / Yılda Üç Kez
Periodical Journal

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GENEL BİLGİLER

Hipokrat Tıp Dergisi;

Acil Tıp, Adli Tıp, Aile Hekimliği, Algoloji, Anatomi, Aneztezi ve Reanimasyon, Beyin ve Sinir Cerrahisi, Çocuk Sağlığı ve Hastalıkları, Deri ve Zührevi Hastalıklar, Enfeksiyon Hastalıklari ve Klinik Mikrobiyoloji, Fiziksel Tıp ve Rehabilitasyon, Fizyoloji, Genel Cerrahi, Göğüs Cerrahisi, Göğüs Hastalıklari, Göz Hastalıklari, Halk Sağlığı, Hava ve Uzay Hekimliği, Hematoloji, Histoloji ve Tıbbi Embriyoloji, İç Hastalıkları, Kadın Hastalıkları ve Doğum, Kalp ve Damar Cerrahisi, Kardiyoloji, Kulak Burun Boğaz Hastalıkları, Nöroloji, Nükleer Tıp, Ortopedi ve Travmatoloji, Plastik ve Rekonstriktif Cerrahi, Radyasyon Onkolojisi, Radyoloji, Ruh Sağlığı ve Hastalıkları, Spor Hekimliği, Sualti Hekimliği ve Hiperbarik Tıp, Tıbbi Biyokimya, Tıbbi Ekoloji ve Hidroklimatoloji, Tıbbi Farmakoloji, Tıbbi Genetik, Tıbbi Mikrobiyoloji, Patoloji, Üroloji Anabilim Dalları ve yukarıda adı geçen tüm bilim dallarının yan dallarıyla birlikte geleneksel ve tamamlayıcı tıp uygulaları ile biyoteknolojik konular da dahil olmak üzere retrospektif, prospektif veya deneysel araştırma, derleme, olgu sunumu, editöryal yorum/tartışma, editöre mektup, cerrahi teknik, ayırıcı tanı, tıbbi kitap değerlendirmeleri, soru- cevaplar ve tıp gündemini belirleyen güncel konuları yayınlayan, ayrıca Diş Hekimliği, Beslenme ve Diyetetik, Sağlık Hizmetleri Yönetimi disiplinleri ile ilgili çalışmalar ancak Koruyucu Hekimlik konularıyla ilgili olduğu takdirde kabul ederek yayınlayan Ulusal ve Uluslararasi tüm tıbbi kurum ve personele ulaşmayi hedefleyen bilimsel bir dergidir.

Dergi yılda üç sayı olarak Nisan, Ağustos ve Aralık aylarında yayınlanmaktadır. Derginin resmi yayın dili Türkçe ve İngilizcedir. İngilizce yazım tercih sebebidir. Dergi ile ilgili her türlü işlem https://dergipark.org.tr/tr/pub/hmj adresinden yapılabilir. Geçmiş sayılarda yayınlanan çalışmalara bu adresten ulaşılabilir.

Bilimsel Politikalar ve Etik Sorumluluğu: Yazıların bilimsel sorumluluğu yazarlara aittir. Tüm yazarların çalışmaya aktif olarak katılmış olması gereklidir. Gönderilen yazıların dergide yayınlanabilmesi için daha önce başka bir bilimsel yayın organında yayınlanmamış olması gerekir. Gönderilen yazı daha önce herhangi bir toplantıda sunulmuş ise; toplantı adı, tarihi ve düzenlendiği şehir belirtilmelidir. Klinik araştırmaların protokolü ilgili kurumun etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. (Etik kurul tarih ve protokol numarası) Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvanhaklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Değerlendirme Süreci:
Dergiye gönderilen yazıların değerlendirilmesi üç aşamada yapılmaktadır. Birinci aşamada makaleler dergi standartları açısından incelenir, yazım kurallarına uymayan makaleler reddedilir. Makale yazım kurallarına göre düzenlendikten sonra aynı isimle yeniden dergiye yüklenebilir. İkinci aşamada makaleyi editör kurulu tarafından içerik ve yöntem açısından değerlendirmeye alınır. İlk iki aşamayı tamamlayan makaleler üçüncü aşamaya geçerek incelenmesi için hakemlere gönderilir.

Tüm yazılarda editöryel değerlendirme ve düzeltmeye başvurulur; gerektiğinde, yazarlardan bazı soruları yanıtlaması ve eksikleri tamamlaması istenebilir. Değer-

lendirme sonucu kabul, minör revizyon, major revizyon, yeniden yazılması gerekli ya da ret kararı çıkabilir. Dergide yayınlanmasına karar verilen makale basım sürecine alınır; bu aşamada tüm bilgilerin doğruluğu için ayrıntılı kontrol ve denetimden geçirilir; yayın öncesi şekline getirilerek yazarların kontrolüne ve onayına sunulur.

Yayın Hakkı:

1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı dergiyi yayımlayan kuruma aittir. Yazarlar, http://dergipark.gov.tr/smj internet adresinden ulaşacakları "Yayın Hakları Devir Formu"nu doldurup (mavi kalemle ve ıslak imzalı olacak şekilde tüm yazarlarca imzalanmış), DergiPark sitemi üzerinden göndermelidirler.

- Olgu sunumu/serisi ve derleme dışındaki bilimsel çalışmalarda etik kurul onay belgesi sisteme yüklenmelidir.
- Veri toplama süreci Aralık 2010 tarihinden önce tamamlanmış çalışmalar kabul edilmeyecektir.
- Bilimsel çalışmalar, çalışmadaki yazarların isim ve soy isimleri (çalışmaya dahil olan tüm yazar isimleri yazılmalı) ile çalışma başlığındaki tüm kelimelerin (bağlaçlar hariç) sadece ilk harfleri büyük harf olacak şekilde DergiPark sistemineyüklenmelidir.
- Yazarların aynı sayıda ilkisim oldukları yalnızca bir çalışmaları yayınlanacaktır.
- SCI, SSCI, SCIE, ESCI veya A&HCI'de indekslenen dergilerde yayınlanmış çalışmalarında Hipokrat Tıp Dergisi'nde yayınlanmış herhangi bir çalışmaya atıfta bulunan yazarların çalışmalarına öncelik verilecektir. (Çalışma bilgilerinin ve varsa linkinin Editöre Sunum Sayfası'nda belirtilmesi gerekmektedir ve hmj@bandirma.edu.tr adresine mail atılarak hatırlatma yapılmalıdır).
- Yazım dili İngilizce olan bilimsel çalışmaların veya yazım dili Türkçe olan çalışmaların İngilizce özetlerinin yazımında akademik düzenleme hizmeti veren profesyonel kurum veya kuruluşlardan yardım alındığının belgelenmesi durumunda bu çalışmalara öncelik verilecektir.

Yazının Hazırlanması

- Derleme türündeki bilimsel çalışmalar için yazar sayısı üçü geçmemelidir.
- Olgusunumları için yazar sayısı altıyı geçmemelidir.
- Yazılar çift satır aralıklı ve 10 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2.5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Arial olmalıdır.
- Yazılar Microsoft Word formatında olmalıdır. (Tablolar dahilolacak şekilde)
- Kısaltmalar, özette ve ana metinde kelimenin ilk geçtiği yerde parantez içinde verilmeli ve tüm metin boyunca o kısaltma kullanılmalıdır. Küçük harflerle yapılan kısaltmalara getirilen eklerde kelimenin okunuşu esas alınır: cm'yi, kg'dan, mm'den, kr.un. Büyük harflerle yapılan kısaltmalara getirilen eklerde ise kısaltmanın son harfinin okunuşu esas alınır: BDT'ye, TDK'den, THY'de, TRT'den, TL'nin vb. Ancak kısaltması büyük harflerle yapıldığı hâlde bir kelime gibi okunan kısaltmalara getirilen eklerde kısaltmanın okunuşu esas alınır: ASELSAN'da, BOTAŞ'ın, NATO'dan, UNESCO'ya vb.
- Editöre sunum sayfası ayrı bir Word dosyası olarak gönderilmelidir. Editöre sunum sayfasında gönderilen çalışmanın kategorisi, eş zamanlı olarak başka bir dergiye gönderilmemiş olduğu, daha önce başka bir dergide yayınlanmamış olduğu, varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ile varsa bu kuruluşların yazarlarla olan ilişkileri belirtilmelidir.
- Kapak sayfası ayrı bir Word dosyası olarak gönderilmelidir. Kapak sayfasında başlık basit ve anlaşılır şekilde olmalıdır (Türkçe ve İngilizce). Başlık 60 karakterden daha uzun olduğu takdirde İngilizce ve Türkçe kısa başlık da kapak sayfasına eklenmelidir. Tüm yazarların adı, soyadı ve unvanları, ORCID numaraları, çalıştıkları kurumun adı ve şehri bu sayfada yer alma-

lıdır. Bu sayfaya ayrıca "yazışmadan sorumlu" yazarın isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

İstatistik Bilgi Notu

- Kullanılan istatistiksel yöntem, orijinal veriye erişebilecek bilgili bir okuyucunun rapor edilen sonuçları onaylayabileceği bir ayrıntıda belirtilmelidir. İstatistiksel terimler, kısaltmalar ve semboller tanımlanmalıdır. Kullanılan bilgisayar programı, istatistiksel yönteme dair açıklama verilmelidir. Çalışma deseni ve istatistiksel yönteme dair kaynaklar mümkünse belirtilmelidir.
- Sonuçların sunumunda, özellikle ortalama ve yüzdelik verirken, ondalıklı hanelerin gösteriminde virgülden sonra sonra 2 hane kullanılmalıdır (112,2 yerine; 112,20 veya 112,21 gibi). P, t, Z değerleri istisnadır ve virgülden sonra 3 hane verilmelidir ($p<0,05$ yerine tam değer $p=0,001$). Tam sayı dışındaki gösterimlerde virgülden sonra iki hane, istatistiksel değerlerin (p,t,z,F,Ki-Kare gibi) virgülden sonra üç hane değerlerin sunulması, p değerlerinin sunumunda $p<0,05$ veya $p>0,05$ yerine test istatistiği ile birlikte tam p değerinin (bu değerin binde birden küçük olması durumunda $p<0,001$ biçiminde) gösterilmesi gerekmektedir.

Yazının Bölümleri

- Çalışmanın gönderildiği metin dosyasının içinde sırasıyla, Türkçe başlık, Türkçe özet, Türkçe anahtar kelimeler, İngilizce başlık, İngilizce özet, İngilizce anahtar kelimeler, çalışmanın ana metini, kaynaklar, her sayfaya bir tablo olmak üzere tablolar ve son sayfada şekillerin (varsa) alt yazıları şeklinde olmalıdır. Tablolar kaynaklardan sonra, her sayfaya bir tablo olmak üzere çalışmanın gönderildiği dosya içinde olmalı ancak çalışmaya ait şekil, grafik ve fotoğrafların her biri ayrı bir imaj dosyası (jpeg ya da gif) olarak gönderilmelidir.

Araştırma Makalesi:

Öz (Abstract): Türkçe ve İngilizce özetler çalışmanın başlığı ile birlikte verilmelidir. Özetler Amaç (Objective), Gereç ve Yöntemler (Materials and Methods), Bulgular (Results) ve Sonuç (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir.

Anahtar Kelimeler (Keywords): Türkçe özetten sonra Türkçe anahtar kelimeler, İngilizce özetten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction): Giriş bölümünün son paragrafında çalışmanın amacını bildiren bir cümle yer almalıdır.

Gereç ve Yöntemler (Materials and Methods): Araştırmanın tipi, etik hususlar (etik onamının alındığı kurum, tarih ve no), kullanılan istatistiksel analiz yöntemleri belirtilmelidir.

B**ulgular (Results)**

Tartışma (Discussion)

Kaynaklar (References)

Makalenin son sayfasında etik onamının alındığı kurum, tarih ve no ayrıca belirtilmelidir.

Olgu Sunumu/Serisi:

Öz (Abstract): Türkçe ve İngilizce özetler makelenin başlığı ile birlikte verilmelidir. Özetler tek paragraflık olmalıdır. (100-150 kelime olmalıdır.)

Anahtar Kelimeler (Keywords): Türkçe özetten sonra Türkçe anahtar kelimeler, İngilizce özetten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction)

Olgu Sunumu (Case Report) Tartışma (Discussion) Kaynaklar (References)

*Olgu sunumlarında, bilgilendirimiş gönüllü olur/onam formunun imzalatıldığına dair bilgiye makalede yer verilmesi gereklidir.

Derleme:

Öz (Abstract): Derleme özetleri kısa ve tek paragraflık olmalıdır (ortalama 100-150 kelime; bölümsüz, Türkçe ve İngilizce) **Anahtar Kelimeler (Keywords):** Türkçe özetten sonra Türkçe anahtar kelimeler, İngilizce özettten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction) Konu İle İlgili Başlıklar Sonuç

(Conclusion) Kaynaklar (References)

Editöre Mektup:

Mektuplar, kaynaklar hariç 500 kelimeyi geçmemelidir. Türkçe ve İngilizce özete gerek yoktur. Kaynak sayısı 5 ile sınırlandırılmalıdır. Bir mektup en fazla 4 yazar tarafından yazılabilir. Editöre mektuplar hakem değerlendirme sürecine alınmaz, ancak editör tarafından gerekli durumlarda yazarlardan mektuba cevap vermeleri istenebilir.

Anahtar Kelimeler

- En az 3 en fazla 6 adet, Türkçe ve İngilizce yazılmalıdır.
- Kelimeler birbirlerinden noktalı virgül (;) ile ayrılmalıdır.
- İngilizce anahtar kelimeler "Medical Subject Headings (MESH)"e uygun olarak verilmelidir (www.nlm.nih.gov/mesh/MBrowser.html).
- Türkçe anahtar kelimeler Türkiye Bilim Terimleri'ne uygun olarak verilmelidir (www.bilimterimleri.com).

Kaynaklar

- Yazarlar yalnızca doğrudan yararlandıkları kaynakları yazılarında gösterebilirler.
- Kaynaklar yazıda geliş sırasına göre yazılmalı ve metinde cümle sonunda noktalama işaretlerinden hemen sonra "Üst Simge" olarak belirtilmelidir.
- Çalışmada bulunan yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 6 isim yazılıp "et al" eklenmelidir.
- Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org).
- Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır.
- Kaynak sayısının araştırmalarda 50 ve derlemelerde 100, olgu sunumlarında da 20 ile sınırlandırılmasına özen gösterilmelidir.
- Kaynakların dizilme şekli ve noktalamalar aşağıdaki örneklere uygun olmalıdır (Noktalamaişaretlerine lütfen dikkat ediniz): Vancouver kaynak sitiline göre kaynaklar yazılmalıdır.

Makale için; Yazar(lar)ın soyad(lar)ı ve isim(ler)inin başharf(ler)i, makale ismi, dergi ismi, yıl, cilt, sayı, sayfa no'su belirtilmelidir.

Örnek: Baser A, Eliaçık S, Baykam MM, Tan FU. Clinical Manifestations of Overactive Bladder With Migraine as a Comorbidity: A Prospective Cross-Sectional Study. Int Neurourol J. 2020;24(4):375-381. https://doi.org/10.5213/inj.2040186.093.

Kitap için; Yazar(lar)ın soyad(lar)ı ve isim(ler)inin başharf(ler)i, bölüm başlığı, editörün(lerin) ismi, kitap ismi, kaçıncı baskı olduğu, şehir, yayınevi, yıl ve sayfalar belirtilmelidir.

Örnek:

- Yabancı dilde yayımlanan kitaplar için;
- Vissers RJ, Abu-Laban RB. Acute and Chronic Pancreatitis. In: Tintinalli JE, Kelen GD, Stapczynski JS (eds.), Emergency Medicine: A comprehensive Study Guide. 6 st ed. New York: McGraw-Hill Co; 2005. p.573-577.
- Türkçe kitaplar için; Gökçe Ö. Peptik ülser. Dilek ON, editör. Mide ve Duedonum.
- 1. Baskı. Ankara: Anıt Matbaası; 2001. s:265- 276.
- On-line yayınlar için format; DOI tek kabul edilebilir on-line referanstır.

Şekil, Resim, Tablo ve Grafikler

- Şekil, resim, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmelidir.
- Şekil, resim, tablo ve grafiklerin açıklamaları ana metnin sonuna eklenmelidir.
- Tablolar her sayfaya bir tablo olmak üzere yazının gönderildiği dosya içinde olmalı ancak yazıya ait şekil, grafik ve fotoğrafların her biri ayrı bir imaj dosyası (jpeg ya da gif) olarak gönderilmelidir.
- Kullanılan kısaltmalar şekil, resim, tablo ve grafiklerin altındaki açıklamada belirtilmelidir.

tten sonra İngilizce anahtar kelimeler belirtilmelidir.

Giriş (Introduction) Konu İle İlgili Başlıklar Sonuç

(Conclusion) Kaynaklar (References)

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- Vissers RJ, Abu-Laban RB. Acute and Chronic Pancreatitis. In: Tintinalli JE, Kelen GD, Stapczynski JS (eds.), Emergency Medicine: A comprehensive Study Guide. 6 st ed. New York: McGraw-Hill Co; 2005. p.573-577.
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RESEARCH ARTICLE / ARAŞTIRMA MAKALESI

Evaluation of the Relationship Between Breast Cancer Subtypes and Serum Inflammatory Markers

Meme Kanseri Alt Tipleri ile Serum Inflamatuar Belirteçleri Arasındaki İlişkinin Değerlendirilmesi

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Geliş Tarihi / Received : 06.08.2023 Kabul Tarihi / Accepted: 05.09.2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3): DOI: https://doi.org/DOI: 10.58961/hmj.1338535

Abstract

Introduction The most widespread type of cancer among women is breast cancer. Luminal A, luminal B, cerbB2 enriched type, Triple negative molecular subtypes have been defined. This study aimed to reveal the relationship between molecular subtypes and inflammatory markers.

Materials and Methods Breast cancer patients who were operated between January 2019 and April 2023 were evaluated. The study included 93 female breast cancer patients. Demographic characteristics, pathology assessments, molecular subtypes and laboratory data of the patients were collected. Systemic Inflammatory Response Index (SIRI), Platelet/Lymphocyte ratio (PLR) and Neutrophil/Lymphocyte ratio (NLR) were calculated from the hemogram. The relationship between molecular subtypes and inflammatory markers was statistically evaluated.

Results The median age of the patients included in the study was 56 years. Among the patients, 82.8% tested positive for estrogen receptor (ER+), while 61.3% tested positive for progesterone receptor (PR+). The most common molecular subtype was luminal A. When the cut-off value for Ki67 was 14, a statistically significant correlation was found between ER status (p=0.047). When Ki67 cut-off value was set to 20, a statistically significant relationship was observed with ER (p=0.002) and a statistically significant relationship with PR (p=0.025). The median of NLR was 1.9 (from a range of 0.7 to 21.3) and the median of PLR was 123 (from a range of 53.3 to 252).

Conclusion We did not find a significant relationship between breast cancer subtypes and inflammatory markers. However, the tendency to show a statistically significant difference between cerbB2 and PLR and SIRI was remarkable (p=0.08, p=0.057, respectively).

Keywords Breast cancer, Systemic Inflammatory Response Index, Neutrophil lymphocyte ratio; Platelet-lymphocyte ratio

Özet

Amaç Meme kanseri kadınlarda en sık görülen kanserdir. Meme kanserinin, luminal A, luminal B, cerbB2'den zengin tip, triple negatif moleküler subtipleri tanımlanmıştır. Bu çalışma moleküler subtipler ile enflamatuar belirteçler arasındaki ilişkiyi ortayı koymayı amaçlamıştır.

Gerec ve Yöntemler Ocak 2019 ve Nisan 2023 tarihleri arasında opere edilen meme kanseri hastaları değerlendirmeye alındı. Hastaların demografik özellikleri, patoji değerlendirmeleri, moleküler alt tipleri ve labaratuvar verileri toplandı. Hemogramdan Nötrofil/Lenfosit oranı (NLR), Trombosit/Lenfosit oranı (PLR) ve Sistemik Enflamatuvar Yanıt İndeksi (SIRI) hesaplandı. Moleküler alt tipler ile enflamatuar belirteçler arasında ilişki istatistiksel olarak değerlendirildi.

Bulgular Çalışmaya dahil edilen hastaların ortanca yaşı 56 idi. Hastaların %82,8'inde östrojen reseptörü (ER+), %61,3'ünde progesteron reseptörü (PR+) pozitif çıktı. En yaygın moleküler alt tip lümen A idi. Ki67 kesme değeri 14 olduğunda ER durumu arasında istatistiksel olarak anlamlı bir ilişki bulundu (p=0,047). Ki67 cut-off değeri 20 olarak alındığında hem ER ile (p=0,002), hem de PR ile istatistiksel olarak anlamlı ilişki (p=0,025) gözlendi. NLR ve PLR'nin ortanca değerleri sırasıyla 1,9 (aralık, 0,7:21,3) ve 123 (aralık, 53,3:252) idi.

Sonuç Meme kanseri alt tipleri ile inflamatuar belirteçler arasında anlamlı bir ilişki bulamadık. Ancak cerbB2 ile PLR ve SIRI arasında istatistiksel olarak anlamlı fark gösterme eğilimi dikkat çekiciydi (sırasıyla p=0.08, p=0.057).

Anahtar Kelimeler Meme kanseri, SIRI, Nötrofil lenfosit oranı, Trombosit lenfosit oranı

INTRODUCTION

Breast cancer incidence rates have increased over the past four decades. Between 2010 and 2019, it increased by 0.5%. It is also still the most common of cause cancer-related death (1,2). Age, disease stage, tumor subtype, histological grade, and receptor status are important factors in breast cancer prognosis. Even in patients with similar known factors, different clinical outcomes can be seen, so there is no uniform behavioral pattern for breast cancer (3). Because breast cancer is a heterogeneous systemic disease consisting of different biological subtypes (4).

When considering all subtypes, Luminal type A has the best prognosis. Many studies show that overall and disease-free survival is shorter in luminal type B (5). Again, compared to the Luminal A subtype, triple negative and HER-2 positive breast cancers have a poor prognosis (5,6). In recent years, the body's inflammatory response has been increasingly emphasized in tumor development and progression. Empirical evidence from multiple studies suggests that inflammation exerts a substantial influence as a determining factor in cancer progression (7-9). It is known that tumors are infiltrated by both inflammatory and lymphocytic cells. Studies have found that the infiltration of inflammatory and lymphocytic cells differs among different tumor types (10,11).

In the scope of our investigation, we sought to examine the associations between the distinct subtypes of breast cancer and inflammatory biomarkers NLR (Neutrophil/Lymphocyte Ratio), PLR (Platelet/Lymphocyte Ratio), and SIRI (Systemic Immune-Inflammation Index).

MATERIAL and METHODS

In this retrospective study, 93 female breast cancer patients who underwent breast cancer in Trakya University Medical Faculty Hospital were evaluated between January 2019 and April 2023. The inclusion criteria comprised patients who had undergone surgery for breast cancer, while those who received neoadjuvant chemotherapy (NACT) were excluded. Additionally, patients with active infection, chronic inflammatory or autoimmune disease, and those under steroid therapy were not included in the study.

The study encompassed the evaluation of the patient's demographic characteristics, hemogram data (including leukocytes, neutrophils, and lymphocytes) obtained one week before the surgical procedure, and post-operative pathology reports. SIRI, NLR and PLR were all derived. NLR was calculated through the dividing of the absolute neutrophil count by the absolute lymphocyte count; and PLR was computed as the quotient of the absolute platelet count divided by the absolute lymphocyte count. The formula SIRI = neutrophil count × monocyte count/lymphocyte count was employed to calculate SIRI.

ER and PR status were accepted as negative/positive according to the results of the immunohistochemical study. Patients with cerbB2 status and immunohistochemistry 3+ were considered (+). 2+ were determined according to the values obtained by fluorescence in situ hybridization (FISH). An evaluation was made with two cut-off values of 20% and 14% for Ki-67 (5,12). Breast cancer subtypes will be evaluated as Luminal A, luminal B, triple-negative, and CerbB2-enriched breast cancer (TNBC).

Statistical analysis

The distribution status of the data was checked using the Shapiro-Wilk test. In comparing two independent groups, the Student's T or Mann-Whitney U tests were preferred depending on the normal distribution. The Pearson chi-square test or Fisher's exact test investigated relationships between qualitative variables. Descriptive statistics were calculated. Mean and standard deviation were used for normally distributed quantitative variables. For those that were not normally distributed, the median and the smallest value-maximum value were used. Frequencies and percentages are given for qualitative variables. The significance level was determined as 0.05 in all statistical analyzes. Statistical analyzes were performed with JAMOVI (version 1.2).

RESULTS

The median age of the individuals enrolled in the research was 56 years old, with a range from 33 to 85 years. Among the patients, 51.6% had cancer in their left breast. The prevailing histological type was invasive ductal carcinoma, accounting for 67.7% of cases. Most breast cancer cases were classified as Grade II. Axillary lymph node involvement was identified in 12 patients, representing 12.90% of the cohort. Breast-conserving surgery (BCS) and sentinel lymph node dissection were the most performed surgical procedures. In cases with axillary lymph node involvement, axillary dissection (AD) was performed, involving 12 patients. However, patients with micrometastases did not undergo axillary dissection. For more detailed demographic features and laboratory findings of the patients, please refer to **Table**

Table 1. Demographic, Clinicopathologic Characteristics data of patients. (Breast conserving surgery: BCS, sentinel lymph node dissection: SLNB, Axillary dissection:AD)

	Median	Min:max
Age	56	33:85
Tumor size (cm)	2,0	0,4:6
NLR	1,9	0,7:6.62
PLR	123	53.3:252
SIRI	0.98	0.28:4.05
	N:93	**%**
Laterality		
Left	48	51.6
Right	44	43.4
Bilateral	1	1
Histological type		
Duktal	63	67.7
Lobuler	11	11.8
Others	19	20.5
Histological Grade		
I	21	22.6
II	49	52.7
III	23	24.7
Metastatic lymph nodes	12	12.90
Operations		
BCS+SLNB	63	67.7
Mastectomy+SLNB	8	8.6
BCS+SLNB +AD	18	19.4
Mastectomy+SLNB +AD	4	4.3

Among the patients, 82.8% tested positive for estrogen receptor (ER+), while 61.3% tested positive for progesterone receptor (PR+). Additionally, 10.8% of the patients were positive for cerbB2 (HER2/neu). The most common molecular subtype was luminal A, followed by luminal B. Detailed immunohistochemical data of the patients can be found in **Table 2.**

Significant statistical relationship were observed between cerbB2 positivity and Ki67 levels (p=0.003). Furthermore, a statistically significant correlation was found between Ki67<14 and ER positivity (p=0.047). When the Ki67 cut-off was set at 20, a statistically significant relationship was observed with ER (p=0.002) and a statistically significant relationship with PR (p=0.025).

Median values of NLR and PLR were 1.9 (range, 0.7:21.3) and 123 (range, 53.3:252), respectively.

Table 2. Immunohistochemical data

	n	%
Hormone receptor status		
ER		
(+)	77	82.8
(-)	16	17.2
PR		
(+)	57	61.3
(-)	36	38.7
CerbB2		
(+)	10	10.8
(-)	83	89.2
Ki67		
< 20	61	65.6
≥ 20	32	34.4
Ki67		
< 14	51	55.4
≥ 14	41	44.6
Moleküler alt tipler		
Lum A	57	61.3
Lum B	20	21.5
triple-negative subtype	14	15.1
CerbB2-enriched subtype	2	2.2

A statistically significant correlation was found between NLR and age (P < 0.05). There was no statistically significant relationship between NLR and size. Similarly, no statistically significant relationship existed between NLR and ER, PR, and Ki67 levels. There was no statistically significant relationship between NLR and CerbB2. We could not able to detect any significant relationship between PLR and hormone receptor status. Similarly, we did not detect a statistically significant relationship between cerbB2 expression status and PLR. A statistically significant relationship was also found between age and SIRI (p<0.05). In our study, NLR, PLR, and SIRI values according to histological subtypes are shown in detail in **Table 3.**

No statistically significant relationship was found between CerbB2 status and PLR and SIRI. However, the p values showing the relationship between both PLR and SIRI and cerbB2 were 0.08 and 0.057, respectively and tended to be significant. The relationship between hormone status (ER, PR), CerbB2 status, and Ki 67 and inflammatory markers are given in **Table 4.**

Table 3. NLR, PLR, SIRI values according to histopathological subtypes.

	NLR		PLR		SIRI	
Histopathological subtype	**Median**	**Min:max**	**Median**	**Min:max**	**Median**	**Min:max**
Luminal A	2.06	0.72:6.62	121	55:247	1.02	0.28: 4.05
Luminal B	1.93	0.91:4.9	131	53,:252	0.91	0.36:3.09
Triple-negative subtype	1.72	1.27:3.76	122	65,8:220	1.05	0.67:2.12
CerbB2-enriched subtype	1.45	1.44:1.46	127	101:154	0.72	0.57:0.9

Table 4. Relationship among hormone status, CerbB2 status, and Ki67 with inflammatory markers

	NLR			PLR			SIRI		
	Mean	**SD**	**p**	**Mean**	**SD**	**p**	**Mean**	**SD**	**p**
ER									
+	2,12	1,06	0,37	134,4	50,6	0,73	1,17	0,6	0,9
-	1,88	0,65		127	46,5		1,06	0,4	
PR									
+	2,14	1,15	0,79	128,6	45,7	0,51	1,12	0,6	0,98
-	2,01	0,8		138,4	54,4		1,18	0,7	
CerbB2									
+	1,98	1,11	0,47	161,7	58,9	**0,081**	0,98	0,78	**0,057**
-	2,093	0,9		129,8	47,9		1,17	0,62	
Ki67									
<20	2,04	0,99	0,67	131,2	50,7	0,4	1,12	0,5	0,99
≥ 20	2,16	1,05		137,1	48,7		1,23	0,8	
Ki67									
< 14	2,09	1,05	1,0	130,1	51	0,33	1,15	0,55	0,37
≥ 14	2,07	0,96		137,7	49		1,15	0,75	

DISCUSSION

There has been growing interest in studying the relationship between hematological components of the systemic inflammatory response and cancer progression in recent years. Preoperative measurements of the NLR and PLR in primary operable cancer have been reported as effective predictors of survival, independent of tumor stage. Specifically, this evidence appears particularly robust in colorectal, stomach, and kidney cancers (13). Similarly, in a separate study involving ovarian cancer patients, it was observed that preoperative mean NLR values were significantly higher (6.02) compared to healthy individuals (14). This increase in NLR has been linked to the inhibitory effect on cytolytic activity of lymphocytes, and activated T cells, thus potentially facilitating the infiltration of tumor cells into circulation and promoting tumor angiogenesis (15).

In recent years, significant advancements have been made in breast cancer research. Among the various treatment approaches, endocrine therapy is now recommended as a priority for patients with hormone receptor-positive breast cancer. Moreover, genetic testing is employed to accurately predict prognosis and identify individuals who may benefit from adjuvant chemotherapy. However, these tests have limited use due to their high cost (16). Consequently, there is an ongoing search for more affordable and accessible tools to predict prognosis and tailor treatment plans.

Studies have explored the interaction between the immune system and tumor cells in breast cancer and its association with prognosis (10,11). A meta-analysis conducted by Ethier et al. established the median cut-off value for high NLR (Neutrophil Lymphocyte Ratio) as 2.5 (range 1.9–4.0). This study also reported that NLR has a significant prognostic

impact on both Overall Survival (OS) and Disease-Free Survival (DFS) (17).

In our study, the median NLR values were 1.9 (range 0.7:21.3), and PLR (Platelet Lymphocyte Ratio) was 123 (range 53.3:252). In another investigation by Yersal et al., the median NLR and PLR values for breast cancer patients were reported as 2.01 (range 0.37–37.1) and 137.8 (range 37.1–421.3), respectively (10). Regarding the relationship between NLR and hormone receptor status, Koh et al. did not detect a statistically significant association with ER (Estrogen Receptor) status. However, they reported a significant correlation between NLR and both PR (Progesterone Receptor) and cerbB2 status (p=0.026 and p=0.002, respectively) (18).

Another study found no statistically significant relationship between NLR and HER2 expression or hormone receptor status (10). We either did not find a statistically significant correlation between NLR and ER, PR, and Ki67 levels. Similarly, NLR and CerbB2 status had no statistically significant relationship.

It has been shown that breast cancer patients with higher NLR are older and have metastases (19). In our study, NLR showed a positive correlation with age. However, we did not detect a similar relationship with PLR. It has been reported that patients with higher PLR have a worse prognosis and shorter disease-free survival. It was emphasized that 185 could be the cut-off for the PLR-value in predicting the prognosis (2). Although it was not statistically significant between PLR values and cerbB2 status in our study, we found a tendency to have a significant relationship (p=0.08) (Table 4.). However, there was no statistically significant relationship between PLR and hormone status or Ki67. Similarly, we did not find a statistically significant difference between PLR values and breast cancer subtypes.

One study created a nomogram based on grade, TNM stage, and SIRI in breast cancer patients. The overall survival (OS) of patients with a SIRI value less than 0.65 was statistically higher than that of patients with a SIRI value greater than 0.65. In the same study, it has been reported that SIRI predicts 5- and 10-year survival rates more accurately than the TNM stage alone (20). In a study conducted on postmenopausal breast cancer patients, it was found that high SIRI values were associated with progesterone receptor status (16).

We had several limitations in our study. As of the first, we had a limited number of patients. As a second limitation, we evaluated the past five years.

CONCLUSION

In conclusion, we did not find any correlation between the inflammatory markers and the hormone receptors and molecular markers of breast cancer in our limited number of cohorts. There are controversial outcomes in the literature on the prognostic value of inflammatory markers on breast cancer prognosis. However, the search for cost-effective tools to predict breast cancer prognosis and guide treatment decisions continues, with studies highlighting the potential prognostic value of immune-related markers like NLR and PLR. Studies with a larger number of patients with longer follow-ups should be conducted to thoroughly evaluate the association of inflammatory markers with the hormonal and molecular status of the patients to examine their impact on breast cancer prognosis

Ethıcal Declerations

The approval for this study was obtained from Trakya University Health Research Ethics Committee (Protocol no: TÜTF GOBAEK 2023/201).

InformedConsent:

Because the study was designed retrospectively, no written in formed consent form was obtained from patients.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

Financial Disclosure:

The authors declared that this study has received no financial support.

Author Contributions:

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Polypharmacy and Drug-Drug İnteractions Among Patients With Diabetes Mellitus

Diabet Hastalarında Polifarmasi ve İlaç İlaç Etkileşimleri

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Geliş Tarihi / Received : 23.11.2023 Kabul Tarihi / Accepted: 08.12.2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3):7-15 DOI: https://doi.org/10.58961/hmj.1394987

Abstract

Introduction Diabetes mellitus is a chronic disease. The aim of our study was to evaluate drug- drug interactions and polypharmacy in diabetic patients.

Materials and Methods Patients with type 2 diabetes attending our internal medicine and endocrinology policlinics from April 2019 to July 2019 were included to the study. It was designed as a prospective, descriptive and cross-sectional study. The socio-demographic characteristics of diabetic individuals, the drugs they use in the treatment of diabetes, and other accompanying diseases were evaluated according to the ATC classification. In this study, interactions between multiple drugs and polypharmacy were examined.

Results The study population consisted of 526 patients between the ages of 18-87/years (59 ± 11). 69.6% of the patients were women.83.8% of the patients had chronic diseases accompanying diabetes. The most common chronic diseases were hypertension (53.6%), hyperlipidemia (41.4%) and coronary artery disease (27.2%), respectively. 45.01% of the patients were using five or more drugs. The mean number of drugs was found to be 4.49 ± 1.93. Among the drugs used by the patients, 787 drug-drug interactions were found in a total of 429 (81.5%) patients. The average number of interactions was 3.89 ± 3.6 for interaction A 15.2% (n = 81), 16.2% (n = 85) for interaction B, 69.8% (n = 367) for interaction C was, 47.9% (n = 252) for interaction D, and 0.4% (n = 2) for interaction X. The most frequent interaction was found between acetylsalicylic acid and insulin and metformin and angiotensin converting enzyme inhibitors.

Conclusion Both the polypharmacy rate and drug-drug interaction rate are high in diabetic patients. The most common type of interaction is type C and type D drug-drug interaction. Attention should be paid to drug-drug interactions in the treatment of diabetes patients.

Keywords Diabetes Mellitus, Polypharmacy, Drug-Drug Interactions

Özet

Amaç Diabetes Mellitus kronik bir hastalıktır. Çalışmamızın amacı diyabetik hastalarda ilaç-ilaç etkileşimlerini ve polifarmasiyi değerlendirmektir.

Gerec ve Yöntemler Nisan 2019 ile Temmuz 2019 tarihleri arasında dahiliye ve endokrinoloji polikliniğimize başvuran tip 2 diyabetli hastalar çalışmaya dahil edildi. Prospektif, tanımlayıcı ve kesitsel bir çalışma olarak tasarlandı. Diyabetli bireylerin sosyo-demografik özellikleri, diyabet tedavisinde kullandıkları ilaçlar ve eşlik eden diğer hastalıkları ATC sınıflamasına göre değerlendirildi. Bu çalışmada çoklu ilaç ve polifarmasi arasındaki etkileşimler incelenmiştir.

Bulgular Araştırmanın evrenini yaşları 18-87/yıl (59±11) arasında değişen 526 hasta oluşturdu. Hastaların %69,6'sı kadındı. Hastaların %83,8'inde diyabete eşlik eden kronik hastalıklar vardı. En sık görülen kronik hastalıklar sırasıyla hipertansiyon (%53,6), hiperlipidemi (%41,4) ve koroner arter hastalığı (%27,2) olarak belirlendi. Hastaların %45,01'i beş ve daha fazla ilaç kullanıyordu. Ortalama ilaç sayısı ise 4,49±1,93 olarak belirlendi. Hastaların kullandığı ilaçlardan toplam 429 (%81,5) hastada 787 ilaç-ilaç etkileşimi tespit edildi. Ortalama etkileşim sayısı 3,89 ± 3,6, etkileşim A için %15,2 (n = 81), etkileşim B için %16,2 (n = 85), etkileşim C için %69,8 (n = 367), %47,9 (n = 252) idi. Etkileşim D için ve etkileşim X için %0,4 (n = 2). En sık görülen etkileşim asetilsalisilik asit ve insülin ile metformin ve anjiyotensin dönüştürücü enzim inhibitörleri arasında bulundu.

Sonuç Diyabetik hastalarda hem polifarmasi oranı hem de ilaç-ilaç etkileşimi oranı yüksektir. En sık görülen etkileşim türü C tipi ve D tipi ilaç-ilaç etkileşimleridir. Diyabet hastalarının tedavisinde ilaç-ilaç etkileşimlerine dikkat edilmelidir.

Anahtar Kelimeler Diabetes Mellitus, İlaç ilaç etkileşimleri, polifarmasi

INTRODUCTION

The prevalence of Type 2 diabetes mellitus (T2DM) is increasing worldwide [1,2]. In parallel to this increase in diabetes accompanying comorbidities are also more frequently observed in the last years. This leads to consumption of a lot of medicaments, which is called polypharmacy [3,4]. Accompanying microvascular and macrovascular complications are important. Especially, cardiovascular system diseases are frequently observed in diabetic patients. In addition, hypertension, hyperlipidemia, depression, anxiety disorder and immune system diseases are among the chronic diseases frequently seen in individuals with diabetes. Therefore, this condition increases the risk of drug interactions and, accordingly, undesirable drug effects in individuals with diabetes [1,3,5]. The excess of the number of drugs used in the treatment is defined as the concept of polypharmacy. In the literature, polypharmacy is generally defined as the simultaneous use of five or more drugs [6,7]. Therefore polypharmacy may cause important clinical problems in terms of drug interactions, adverse drug reactions, drug errors and increased risk of hospitalization, which may develop in the patient, in terms of pharmacoeconomics [8]. Multi-drug treatments can inevitably cause drug-drug interactions. This situation may cause serious health problems and makes physicians responsible for malpractice if patients are harmed. When two drugs are used together, the situation that occurs as a result of changing the pharmacological effect of one of the drugs by the other is defined as "drug-drug interaction". Polypharmacy, which is the most important reason for the prevalence of drug interactions, is the use of multiple drugs at the same time [9,10]. The principles of rational drug use aims to be able to treat a disease with few drugs or single drug or to plan effective treatment with the least drug and lowest cost, and to keep drug interactions to a minimum [11]. In our study, it was aimed to analyze the active ingredients of drugs used to treat chronic diseases in individuals with diabetes, to detect the presence of polypharmacy, and to determine interactions between drugs.

MATERIAL and METHODS

Our study is a prospective study, and 526 diabetic individuals with a history of drug use, and who applied to our Internal Medicine and Endocrinology Outpatient Clinics between April 2019 and July 2019, were recruited. Questionnaires including sociodemographic characteristics of diabetic individuals such as age and gender, medications used, comorbidities and family histories were asked. Those who were not diagnosed with diabetes mellitus, had no history of drug use, diabetic individuals under the age of 18, and those who did not volunteer to participate in the study were excluded from the study.For our study, permission was obtained from the Local Ethics Committee (Ethics Committee No/Date:2019-04/19.03.2019). The drugs used were divided into groups according to anatomical, therapeutic and chemical classification (ATC).While evaluating the definition of polypharmacy, the use of five or more drugs was evaluated as polypharmacy in the light of the information in the literature [12,13]. Lexi-Comp (Lexi-Comp.Inc.Hudson, Ohio) electronic database was used for potential drug-drug interactions (pDDI) [14]. Mean, standard deviation, percentage, maximum and minimum values were used as descriptive statistics. Chi-square test was used to compare non-numerical categorical variables. Statistical analyzes and demographic data tables were made. The results were evaluated at the 95% confidence interval, at the $p<0.05$ significance level.

RESULTS

A total of 526 diabetic patients were included in our study.69.6% (366) of DM individuals were female and 30.4% (160) were male. The ages of the patients were (18-87) and the mean age was (59±11/years) **(Table: 1).**

The mean age of the women was (59±10/years) and the mean age of the men was (58±12).40.3% (212) of the patients did not have a family history of diabetes, 55.9% (294) of the patients had a history of diabetes in their first-degree relatives and 3.8% (20) in their distant relatives.83.7% (440) of the patients were married, 14.3% (75) were widowed, and 2.1% (11) were single. There was an accompanying disease in 83.8% (441) of diabetes patients. The most common chronic diseases were hypertension 53.6% (282), hyperlipidemia 41.4% (218), coronary artery disease 27.2% (143), depression 5.3% (28), osteoporosis 4.2% (22), COPD 3% (16), and cancer 1% (6), consecutively. Most of our patients had cardiovascular diseases and hyperlipidemia. When polypharmacy was considered as five or more drug use, the sociodemographic data of diabetic individuals with and without polypharmacy are shown in **Table 2.**

Table 1. Clinical information.

Variable	Subgroups	Number (n=526)	Percent (%)
Gender	Male Female	160 366	30,4 69.6
Diabetes history in relatives	None Primer relative Seconder relative	212 294 20	40,3 55,9 3,8
Age (years) 18-87 (59±11)years	Male Female	(58±12) (59±10)	
Diabetes Duration (years)	Under 10 years 10 years and above	309 213	58,7 41,3
Treatment Type	OAD OAD and Insulin together Insulin	283 157 86	53,8 29,8 16,4
Education	Illiterate Primary education High school University	51 383 79 13	9,69 72,8 15,0 2,47
Marital status	Married Single Divorced	440 11 75	83,65 2,09 14,25
BMI	BMI 1 (low) BMI 2 (high)	63 463	88,02 11,97
Total Drugs Number	2367(1-11)	(4,49±1,93)	
Total DDI Number	787 (0-30)	(3,89±3,6)	33,24
Risk category of the interactions	C D X	367 252 2	69.8 47.9 0.4
Pharmacological data	Categories	n	%
	1–4 5–8 9-11	289 217 20	54,94 41,25 3,80
Number of detected interactions	None 1 2 3 >3	98 94 66 42 226	18,63 17,87 12,54 7,98 42,96

Our polypharmacy rate was 45.01%.The drugs used by individuals with DM and the interactions between these drugs were examined. The most commonly used drug in the treatment of diabetes was metformin. Metformin usage rate was 42%.

Oral antidiabetic drugs and insulin usage data used by the patients and other drugs used during diabetes treatment (**Table 3, Table 4**) are shown together with their ATC (Structural therapeutic chemicals classification) codes.

Table 2. Immunohistochemical data

		Polypharmacy			
		Present (n %) (n: 237, %45,01)	**Absent (n %) (n: 289, % 54,99)**	**X2**	**p**
Gender	**Female**	168 (45,9)	198 (54,1)		
	Male	69 (43,1)	91 (56,9)	0,347	0,556
Marital Status	**Married**	192 (43,6)	248 (56,4)		
	Singe	1 (9,1)	10 (90,9)		**0,003***
	Divorced	44 (58,7)	31 (41,3)	11,71	
Education	**İlliterate**	31 (60,8)	20 (39,2)		
	Primary School	175 (45,7)	208 (54,3)		
	High School	26 (32,9)	53 (67,1)	10,09	0,018*
	University	5 (38,5)	8 (61,5)		
Family type	**Core Family**	180 (43,2)	237 (56,8)		
	Cowded family	52 (54,2)	44 (45,8)	4,09	0,132
	Fragmented Family	5 (38,5)	8 (61,5)		
Diabetes Year	**0-10 years**	122 (39,5)	187 (60,5)		
	11 years and above	113 (53,1)	100 (46,9)	9,38	**0,002***
Age	**0-64 years**	156 (42,2)	214 (57,7)		
	65- years and above	81 (51,4)	75 (48,1)	4,22	0,040*
BMI	**BMI 1**	42 (33,3)	21 (66,7)		
	BMI 2	247 (46,7)	216 (53,3)	3,97	0,046*
Income Status	**Low**	20 (40,8)	29 (59,2)		
	Moderate	205 (46,4)	237 (53,6)	2,30	0,315
	Good	12 (34,3)	23 (65,7)		
Additional Diseases	**Yes**	226(51,2)	215 (48,8)		
	None	11 (12,9)	74 (87,2)	42,24	**0,000***

The most commonly used drug group is diabetes drugs by 48.24% (n=1142).The patients used a total of 2367 active substances. The mean number of active substances used was (4.49±1.93). Patients were using(1 to 11) drugs, of which 3.4% were using one drug, 10.7% using two drugs, 19.7% using three drugs, and 21.6% using four drugs. One patient was using eleven drugs, 18 patients were using one drug. The number of drugs used by the patients is shown in (Figure-1). 787 drug-drug interactions were found in 429 (81.5%) of 526 patients included in our study. Mean number of drug

interactions was (3.89±3.6) (0-30). Interaction A was 15.2% (n=81), interaction B was 16.2% (n=85), interaction C was 69.8% (n=367), interaction D was 47.9% (n=252), interaction was X 0.4% (n=2) **(Table 5).**

Table 3. Drugs used in the treatment of diabetes and ATC (Anatomic Therapeutic Chemical Classification) (Structural classification of therapeutic chemicals codes)

ATC Code: Oral Antidiabetic Drug		Prescription Frequency %	Number of drugs prescribed n
(A10BA02)	**Metformin**	42	221
(A10BH02)	**Vildagliptin**	25,66	135
(A10BB09)	**Gliclazid**	21,48	113
(A10BD07)	**(Metformin+Sitagipti**	9,31	49
(A10BH01)	**Sitagliptin**	9,12	48
(A10BK01)	**Dapagliflozine**	8,74	46
(A10BH05)	**Linagliptin**	7,03	37
(A10BF01)	**Acarbose**	4,18	22
(A10BG03)	**Pioglitazone**	3,23	17
(A10BK03)	**Empagliflozin**	3,04	16
(A10BJ01)	**Exenatide**	2,66	14
(A10BH03)	**Saxagliptin**	0,95	5
(A10BB12)	**Glimepiride**	0,57	3
(A10BX03)	**Nateglinide**	0,57	3
(A10BB01)	**Glibenclamid**	0,19	1
ATC Code: İnsülin			
(A10AE04)	**İnsülin Glargine**	29,84	157
(A10AB05)	**İnsülinAspart**	17,87	94
(A10AD30)	**İnsülinlispro+ İnsülinAspart**	15,72	83
(A10AB06)	**İnsülinGlusiline**	7,41	39
(A10AE05)	**İnsülinDetemir**	4,75	25
(A10AD06)	**İnsülinAspartand Degludec**	2,66	14

Table 4: Drugs used in non-diabetes treatment and ATC codes

ATC Code: Other drugs		Prescription Frequency %	Number of prescribed drugs (n)
(C10)	**Lipid metabolism drugs**	**44,10**	**232**
(C09)	**Medicines that regulate blood pressure**	**31,93**	**168**
(N02)	**Analgesics**	**17,87**	**94**
(C07)	**Beta Blockers**	**17,11**	**90**
(H03)	**Thyroid Drugs**	**15,58**	**82**
(C08)	**Calcium channel blockers**	**12,54**	**66**
(C03)	**Diuretics**	**5,70**	**30**
(B01)	**Antithrombotic**	**5,70**	**30**
(N06)	**Psycho- analeptics**	**5,13**	**27**
(A02)	**Proton pump inhibitors**	**4,75**	**25**
(R03)	**Respiratory System Drugs**	**2,47**	**13**

Table 5. Drug-Drug interactions

Interacting drug pair	Patient number (%)	Risk Classification (A-X)	Probable effects
ASA-Insulin	54(10,26)	C	Increase in hypoglycemia risk
Metformin-ACE inhibitor	52 (9,88)	C	Lactic acidosis and increase in hypoglycemia risk
Gliclazide-Vildagliptin	49 (9,31)	D	Increase in hypoglycemia risk
ASA-ACE inhibitor	37 (7,03)	C	Decrease in ACE inhibition activity and increase in nephrotoxicity risk
Linagliptin-Insulin	36 (6,84)	D	Increase in hypoglycemia
Metformin-ASA	36 (6,84)	C	Increase in hypoglycemia
Metformin + Sitagliptin-ASA	32 (6,08)	C	Increase in hypoglycemia
ASA-Gliklazid	24 (4,56)	C	Salicylates can enhance the hypoglycemic effect of agents that lower blood sugar
Metformin+ Sitagliptin-Atorvastatin	14 (2,66)	C	Increased adverse / toxic effects , Rhabdomyolysis
ASA-Clopidogrel	13 (2,47)	C	Increase in the antiplatelet effect
Sitagliptin-Atorvastatin	12 (2,28)	C	Increased adverse / toxic effects , Rhabdomyolysis
Carvedilol-Insulin	10 (1,90)	C	Increased hypoglycemia
Thioctic acid-Insulin	7 (1,33)	C	Increased hypoglycemia
Metformin-Sertraline	7 (1,33)	C	Increased hypoglycemia
Atorvastatin-Fenofibrate	5 (0,95)	C	Increased adverse / toxic effects
ASA-Diclofenac	3 (0,57)	C	Increase in the antiplatelet effect, bleeding risk
Paroxetine-Rasagiline	1 (0,19)	X	Seratonin syndrome
Etodolac-Dexketoprofen	1 (0,19)	X	Increase adverse / toxic effects

Gender distribution results are shown in **(Table 6).**

Table 6. Drug-drug interaction: Gender distrubition

		Interaction A		Interaction B		Interaction C		Interaction D		Interaction X	
		n	%	n	%	n	%	n	%	n	%
Gender	Female	66	81,2%	62	72,9%	258	70,3%	175	69,4%	2	0,4 %
	Male	15	18,8%	23	27,1%	109	29,7%	77	30,6%	0	0,0%

We aimed to draw the attention of clinicians to this issue by revealing polypharmacy and potential drug-drug interactions in diabetic patients who applied to the internal medicine and endocrinology outpatient clinic.

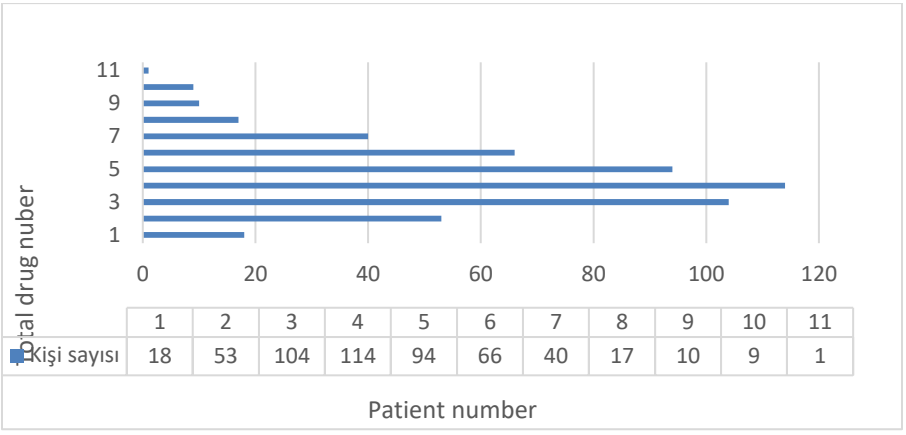

Figure 1. Number of drugs used by patients

DISCUSSION

Polypharmacy is a common condition in patients with diabetes. In terms of pharmacoeconomic, adverse drug reactions, drug-drug interactions, drug-nutrient interactions, it paves the way for serious clinical consequences for patients. When polypharmacy was defined as the number of drugs used daily as 5 or more, the rate of polypharmacy was found to be 45.1% in our study. Polypharmacy was 31.9% in female patients and 13.1% in males. No significant difference was observed in the presence of polypharmacy between men and women. Polypharmacy rates in patients with diabetes are reported to be between 26.7% and 56.5% in the literature. We can say that the rate we found is similar to the literature data [15-18]. Of the diabetic individuals included in our study, 69.6% were female and 30.4% were male. Although there are different results regarding the incidence of DM in the literature, we found that diabetes is more common in women [18, 20-23]. The mean age of our study group was (18-87) and the mean age was (59±11). The mean age of the women was (59±10) and the mean age of the men was (58±12). According to studies, we can say that our average age is higher [22, 23]. Additional diseases seen with aging lead to the use of multiple drugs. Feng and colleagues' studies have revealed that polypharmacy is common in those with additional diseases. Polypharmacy was more common in those with non-diabetic additional diseases in the study group (p=0.000).

Polypharmacy was observed more frequently in individuals aged 65 years and older compared to younger age groups and this was statistically significant (p=0.0040). When we evaluate the relationship of marital status and polypharmacy, the rate of polypharmacy was higher in those who divorced their spouse (p=0,003). As in the whole world, the vast majority of polypharmacy patients in our study were patients aged 65 and older [24]. Polypharmacy is reported to be more common in patients with low levels of education. The fact that those with low levels of education also have low health

literacy explains this situation. It is pointed out in the literature that low level of education is associated with polypharmacy. In our study, polypharmacy rate was high in the illiterate group [20,25]. The number of drugs used in diabetic individuals enrolled in the study was the lowest 1, the highest 11. Our study group used drugs on average (4.49±1.93).

Although the average number of drug use varies between 5.3 and 8.1 in the literature, it is recognized that there is a significant risk for polypharmacy of diabetes. Our results are similar to literature [21,22, 26-28]. In patients with diabetes, the age of diabetes is an important criterion for the development of complications. The incidence of polypharmacy in our patients with diabetes age under 10 years was 39.5%, while this rate was 53.1% in those with diabetes age over 10 years. Polypharmacy was found to be more common in patients aged 11 years and older with diabetes (p=0.002). This can be explained by the use of more medications for diabetic patients to prevent diabetes [29].

High body mass index (BMI) in patients with DM is one of the underlying factors for polypharmacy reasons such as insulin resistance and accompanying diseases. In our study, it was found that the frequency of polypharmacy was higher in those with high BMI. In our study, 918 of antidiabetic drugs were used by individuals under the age of 65, while 329 were used by individuals over the age of 65. Studies indicate that the frequency of antidiabetic drug use decreases as age increases in patients with diabetes [29, 30].

Doctors explain that liver and kidney function in the elderly works more slowly than in young people, and again, because more frequent episodes of hypoglycemia occur in the elderly, they use fewer medications. This also indicates that young people use more antidiabetic drugs to prevent complications that can develop due to diabetes. The results of our study are similar to the literature [31]. 83.8% of our patients with diabetes had a concomitant disease. The most common accompanying disease was 53.6% hypertension and 41.4% hyperlipidemia. Other drugs used during the treatment of diabetes included 44.10% lipid-lowering drugs, 31.93% antihypertensive drugs, 17.84% analgesics decayed. Atorvastatin was most commonly used in lipid-lowering drugs [20]. 42% of our study group was on Metformin. Although this rate was reported as 11.2% in Prado et al studies, the percentage of metformin use was lower than in other studies [19-22]. Hypertension and hyperlipidemia increase the incidence of cardiovascular diseases in patients with diabetes, leading to more drug use. Studies indicate that cardiovascular disease is the most common cause of death in 80% of patients with diabetes [32]. In our study, the most commonly used group of drugs other than diabetes drugs was found to be lipid-lowering and cardiovascular system drugs. Potential drug drug interaction (pDDI) is the simultaneous prescribing/taking of two interacting drugs, regardless of whether an adverse outcome occurs in the patient. In the literature [33] , it is reported that there is a relationship between the presence of polypharmacy and pDDI. In our study, a statistically significant association was found between polypharmacy and pDDI (p=0.000).

The average number of active substances used in the study was (4.49±1.93), while the pDDI value per patient was (0-30), (3.89±3.6). It is mentioned as 5 in the work of Marusic et al [34].

Our pDDI incidence was 33.4%. This value is thought to be a predisposing factor for pDDI in patients with polypharmacy. It bears similarities to the studies carried out [35, 36].

In Type C interactions, it is recommended to follow on the treatment, if the benefit from the joint use of the two interacting drugs is usually greater than the risk caused by the interaction. According to the literature, Type C interactions are most commonly observed in pDDI interactions [37, 38]. In our study, it was also shown that the most common type interaction is Type C interaction with a percentage of 69,8% (367). In different studies, Type C interaction is the most common form as reported in the Savran et al study (47.5%) [39].

In D-type pDDI interactions, it may be necessary to modify the treatment by evaluating the risks and benefits caused by simultaneous use of drugs. Among p DDI's, our rates of D- and X-type interactions, which are considered important for their association with clinical manifestations, were found to be 47.9% (252) and 0.4% (2) . Type D p DDI interaction rates in the literature range from 5.1% to 21.4% in diabetic patients [19,29,40].

In our study results, we found that both Type C and Type D interactions were high compared to the values stated in the literature. Aspirin was one of the most interacting drugs in our study. There is an interaction between Aspirin and antidiabetic drugs such as insulin, metformin, gliclazide. The effect of hypoglycemia may occur when used together. Again, there is an interaction between Aspirin and angiotensin Converting enzyme inhibitor drugs. Aspirin leads to a decrease in the effectiveness of acei medications.Important drugs that cause Group D interaction were found between gliclazide-vildagliptin and linagliptin-insulin. Group X interactions that we identified in our study are between Paroxetine-rasagiline and Etodolac-Decketoprofen. An increase in the number of chronic diseases with aging increases the incidence of both polypharmacy and drug-drug interactions.

CONCLUSION

In our study, in diabetic patients, the rate of chronic disease is high and the associated polypharmacy rate is high. A higher percentage of Type C drug-drug interactions were observed compared to other studies when drug-drug interactions were grouped together. Our D-type drug interaction rate was found to be higher than in other studies. Both patients and physicians have great responsibility for the prevention of polypharmacy and drug-drug interactions. Before issuing a prescription, doctors should check websites, textbooks and databases according to the age, education and knowledge levels of patients and evaluate the medications they will use in treatment.

Ethıcal Declerations

The approval for this study was obtained from Kütahya Health Sciences University Non-invasive Clinical Research Ethics Committee19.03.2019 (Protocol no: 2019/04).

InformedConsent:

Because the study was designed retrospectively, no written in formed consent form was obtained from patients.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

Financial Disclosure:

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Author Contributions:

All authors contributed to the study's conception and design. FO, TPK, KO, and FO, TPK performed study preparation, data collection, and analysis. FO, KO wrote the first draft of the manuscript, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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RESEARCH ARTICLE / ARAŞTIRMA MAKALESI

The Effect of the Covid-19 Pandemic on Emergency Department Forensic Admission

Covid-19 Pandemisinin Acil Servis Adli Başvurularına Etkisi

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Geliş Tarihi / Received : 11.10.2023 Kabul Tarihi / Accepted: 15.12.2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3):16-23 DOI:https://doi.org/10.58961/hmj.1374572

Abstract

Introduction The COVID-19 epidemic, which affected the whole world, also affected judicial events. This study will examine how the epidemic affected the forensic cases admitted to the emergency service.

Materials and Methods In this study, the files of all patients whose forensic records were opened in the Emergency Service between 2019 and 2022 were retrospectively scanned. Patient admissions were classified according to March 2020, when our country's first COVID-19 case was seen. They were divided into 3 groups: pre-pandemic, pandemic and post-pandemic period, and the data obtained were compared within themselves.

Results The files of 17,323 patients on the specified dates were reviewed. 81.7% of the patients were male. 16.6% were foreign nationals. It was observed that the highest rate was during the pandemic period (38.7%) and patients who were admitted for forensic examination (83.0%). It was determined that most of the patients were discharged from the emergency department (98.2%), and most inpatients were followed up in the internal services (35.8%). The rate of patients referred was determined to decrease during the pandemic compared to the previous period. Forensic admissions were at the lowest rate after the declaration of a pandemic, and in the post-pandemic period, they exceeded the pre-pandemic level. It was observed that the number of patients who attempted suicide decreased during the pandemic and did not increase in the post-pandemic as much as in the pre-pandemic. However, it was observed that this rate increased during the period when strict quarantine rules were implemented. Even though the rate of traffic accidents and assault patients decreased during the pandemic, it more than doubled during the post-pandemic compared to the pre-pandemic.

Conclusion It is seen that the flow of forensic cases to emergency department does not decrease even in pandemics. Since most forensic cases have a traumatic process, emergency department admissions can guide the number, character, and prognosis of forensic cases. In another pandemic, forensic events can be controlled.

Keywords Emergency Department, Forensic admissions, COVID-19, Pandemic Effect

Özet

Amaç Tüm dünyayı etkisi altına alan COVID-19 pandemisi, adli olayları da etkilemiştir. Bu çalışmada; çoğu zaman adli başvuruların ilk başvuru yeri olan acil servislerin, salgında nasıl etkilendiği incelenmeye çalışılacaktır.

Gerec ve Yöntemler Çalışma için; 2019-2022 yılları arasında, Acil Servis'te adli kayıt açılmış tüm hastaların dosyaları geriye dönük tarandı. Hasta başvuruları ülkemizde ilk COVID-19 vakasının görüldüğü Mart 2020 tarihine göre sınıflandırıldı. Pre-pandemi, pandemi ve pandemi sonrası dönem olarak 3 gruba ayrıldı ve elde edilen veriler kendi içinde kıyaslandı.

Bulgular Belirtilen tarihlerdeki 17,323 hastanın dosyası incelendi. Hastaların %81,7'si erkek cinsiyette idi.. En fazla oranda pandemi döneminde (%38,7) ve adli muayene nedeni ile başvuran hastaların olduğu görüldü (%83,0). Hastaların büyük bir kısmının acilden taburcu olduğu (%98,2), yatan hastaların ise en fazla oranda dahili servislerde (%35.8) takip edildiği tespit edildi. Sevk olan hastaların oranının; pandemi döneminde bir önceki döneme göre azaldığı tespit edildi. Adli başvuruların, pandemi ilan edildikten sonra en düşük seviyede olduğu, pandemi sonrası dönemde ise pandemi öncesi dönem seviyesini geçtiği gözlendi. Suicid girişimi olan hastaların sayısının pandemi döneminde azaldığı ve normalleşme döneminde bile pandemi öncesi dönemdeki oran kadar artmadığı gözlendi. Ancak katı karantina kuralları uygulandığı zaman diliminde bu oranın arttığı gözlemlendi. Trafik kazası ve darp hastalarının oranı pandemi döneminde azalsa bile normalleşme döneminde pandemi öncesi döneme kıyasla 2 katından fazla artmıştı.

Sonuç Salgınlarda bile adli vakaların acil servislere akışının azalmadığı görülmektedir. Adli vakaların çoğunda travmatik bir süreç yaşandığı için adli olayların sayısı, karakteri, prognozunun değerlendirilmesinde acil servis başvuruları yol gösterici olabilir, başka bir salgında adli olayların kontrolünü sağlayabilir.

Anahtar Kelimeler Acil Servis, Adli başvurular, COVID-19, Pandemi etkisi

INTRODUCTION

During the COVID-19 pandemic, isolation was necessary. People were confined to their homes. For this reason, the course of forensic events has changed, as in every other issue. Studies report that the number of events in which more than one person is affected, such as accidents and assaults, has decreased due to stay-at-home rules, travel restrictions, and strict social distance rules (1, 2).

Emergency physicians have forensic medicine duties as well as curative medicine duties (3). Emergency departments (ED) are units that are always open to injuries without an appointment. Therefore, in forensic cases, the person can be admitted to the emergency service themself or be accompanied by security forces. The patient profile has changed due to the pandemic in the ED, where there are often unnecessary admissions. This situation also affected the urgent admissions of forensic events. In the studies, it has been determined that the rate of work accidents, traffic accidents, and harm to others decreased (4). In addition, it can be said that admissions to the ED have decreased due to the fear of disease (5).

Many studies in the literature have data obtained before and during the pandemic. Still, there are a limited number of studies, including data on the normalisation period, in which the effect of the pandemic has passed. This study examined the ED admissions of forensic cases before, during the pandemic (the peak period of the pandemic, when the vaccination became widespread, and its effect was observed) and when its effect decreased. Thus, the effect of the pandemic on forensic cases admitted to the ED was tried to be understood.

MATERIAL and METHODS

Patient Selection

In the study, the files of all national patients whose forensic records were registered in the ED of Kırklareli Training and Research Hospital between 2019 and 2022 were scanned retrospectively.

According to the ICD code, V00-V99 diagnoses were classified as a traffic accident, W50-51 as assault, W26 as sharp injury, and X60-X84 as a suicide attempt. Moreover, it has been selected from the patients with Z00 ICD code files whether an examination before being taken under custody and released, or it was noted whether there was a work accident.

Patients' demographic characteristics, time of admission, definition of the forensic event, diagnosis, prognosis in the emergency room, hospitalisation, number of days hospitalised and prognosis were examined. The files were analysed using the archive and hospital electronic record system.

Time Interval

Patient admissions were classified based on March 2020, when the first case of COVID-19 was seen in our country. The one year before this date was considered pre-pandemic. The period until July 2021, when the 2nd dose of vaccination was completed, as a pandemic, and the period when quarantine practices were relaxed was considered the normalisation period.

Pre-pandemic: January 1, 2019 - March 11, 2020 (15 months)
Pandemic: 12 March 2020-30 June 2021 (16 months)
Post-pandemic (Normalization): 1 July 2021-31 March 2022 (9 months) was accepted and the files were examined.

In addition, the dates between April 29 and May 17, 2021, when strict quarantine regulations were admitted during the pandemic period, were compared with the previous year (when gradual quarantine practices were implemented) and the pre-pandemic period.

Statistical Analysis

In the descriptive statistics of the data, mean, standard deviation, median minimum, maximum, frequency and ratio values were used. The distribution of variables was measured with the Kolmogorov-Smirnov test. The Kruskal-Wallis test was used in the analysis of quantitative independent data. The Chi-Square test was used to analyse qualitative independent data, and the Fischer test was used when the Chi-square test conditions were not met. SPSS 28.0 program was used in the analysis. $P<0.05$ was considered significant.

RESULTS

The files of 17,323 patients whose forensic records were registered in the hospital system on the specified dates were examined. 81.7% of the patients were male. It was observed that the highest rate was during the pandemic

period (38.7%) and patients who were admitted for forensic examination (83.0%). It was found that most of the patients were discharged from the ED (98.1%), and most inpatients were followed up in the internal services (35.8%) (Table 1).

Table 1. Demographic characteristics of patients and results in the ED

		Min-Max	Median	Mean.±SD n-%
Age		1.0 - 96.0	33.0	34.78 ± 14.12
Gender	Female			3175 18.3%
	Male			14148 81.7%
Period	Pre-Pandemic			5688 32.8%
	Pandemic			6710 38.7%
	Post-Pandemic			4925 28.4%
Reason for admission	Assault			1195 6.8%
	Traffic accident			1077 6.2%
	Sharp Injury			138 0.7%
	Suicide attempt			503 2.9%
	Forensic exam			14385 83.0%
	Other			25 0.4%
Result in the ED	Discharged			16950 97.8%
	Referred			61 0.3%
	Hospitalised			307 1.8%
	Exitus			5 0.02%
Inpatient service	Internal Service			110 35.8%
	Surgery Service			106 34.5%
	Intensive Care Unit			91 29.6%
Number of days hospitalised		1.0 - 30.0	2.0	3.23 ± 3.43

SD: Standart Deviation, Other: Myocardial infarction (at work), arrest of unknown cause, abuse, asphyxia, electric shock

It was determined that there were 223766 ED admissions to our hospital in the pre-pandemic period, 181487 during the pandemic, and 124453 in the post-pandemic period. According to this result, forensic admission rates were calculated as 2.5% in the pre-pandemic period, 3.6% during the pandemic period, and 3.9% in the post-pandemic period. The age of the patients in the pre-pandemic and pandemic groups was significantly higher (p=0.000) than the post-pandemic group. The rate of male patients in the pandemic period was significantly higher (p=0.001) than the other groups **(Table 2).**

When examined in terms of the reason for the admission, the rate of patients admitted due to assault and traffic accidents in the post-pandemic was significantly higher (p=0.000) than in the pre-pandemic and pandemic periods. The number of patients who were diagnosed with forensic examination in all periods was found to be higher than other patient groups. The rate of patients presenting with the cause of suicide in the pre-pandemic period was significantly higher (p=0.000) than in the pandemic and the post-pandemic period. In addition, the number of patients discharged from the ED in all periods was higher than those who were referred, hospitalised, and ex-groups. The rate of patients referred from the ED was significantly higher (p=0.000) in the pre-pandemic and pandemic periods. The hospitalisation day was significantly higher (p=0.013) in the pandemic group than in the others **(Table 2)**

Table 2. Classification of Patients According to Periods

Mean±SD/n-%

	[1]Pre-pandemic		[2]Pandemic		[3]Post-Pandemic		p	
Age	35.66±14.17		35.26±14.18		33.12±13.83		**0.000[k]**	
Gender								
Female	1124[2,3]-19.8%		1152-17.2%		899-18.3%		**0.001[x2]**	
Male	4564-80.2%		5558-82.8%		4026-81.7%			
Reason for admission								
Assault	360	6.3%	285	4.2%	549	11.1%	***0.000***	x^2
Traffic Accident	242	4.3%	295	4.3%	541	10.9%	***0.000***	x^2
Sharp Injury	51[3]	0.8%	55 [3]	0.8%	32	0.6%	*0.348*	x^2
Suicide attempts	220[2,3]	3.8%	141[3]	2.1%	142	2.9%	***0.000***	x^2
Forensic exam	4799[2,3]	84.3%	5926[3]	88.3%	3660	74.3%	***0.000***	x^2
Other	16[2,3]	0.2%	8	0.1%	1	0.0%	***0.002***	x^2
Result in ED								
Discharged	5545[2]	97.5%	6583	98.1%	4822	97.9%	0.056	
Referred	31	0.5%	30	0.4%	0	0.0%	**0.000**	
Hospitalised	110	1.9%	94[1,3]	1.4%	103	2.1%	**0.011**	X2
Exitus	2	0.0%	3	0.0%	0	0.0%	**p>0.005**	
Inpatient Service								
Internal Service	18	0.3%	33	0.5%	59	1.2%	***0.000***	
Surgery Service	55[2,3]	1.0%	36[3]	0.5%	14	0.3%	***0.000***	x^2
ICU	37	0.7%	24[1,3]	0.4%	30	0.6%	0.050	
Number of days hospitalised	3.81 ± 3.98		3.39 ± 4.01		2.46 ± 1.63		***0.013***	K

SD: Standard Deviation, [K]Kruskal-Wallis (Mann-Whitney U test) /[X²] Chi-Square test (Fischer test)
Other: Myocardial infarction (at work), arrest of unknown cause, abuse, asphyxia, electric shock
ICU: Intensive Care Unit
[1]Difference with Pre-Pandemic Group p<0.05,
[2]Difference with Pandemic Group p<0.05,
[3]Difference with Post-Pandemic Group p<0.05

The number of admissions remained unaffected despite the quarantine practices and patient classification changes (Table 3).

Table 3. Admissions according to quarantine periods

Mean.±SD/n-%

	[1]Pre-pandemic		[2]Non-strict quarantine		[3]Strict quarantine		p	
Age	33.38 ± 14.58		35.05 ± 14.80		35.42 ± 15.23		0.237	K
Gender								
Female	57	19.4%	21	17.5%	58	24.4%	0.225	X^2
Male	237	80.6%	99	82.5%	180	75.6%		
Reason for admission								
Assault	17	5.7%	7	5.8%	11	4.6%	p>0.05	X^2
Traffic Accident	10	3.1%	7	5.8%	14	5.8%	p>0.05	X^2
Sharp injury	0	0.0%	0	0.0%	4	1.7%	p>0.05	X^2
Suicide attempts	7	2.3%	2	1.7%	11	4.6%	0.203	X^2
Forensic exam	259	88.1%	104	86.7%	198	83.2%	0.262	X^2
Other	1	0.3%	0	0.0%	0	0.0%	p>0.05	X^2
Result in ED								
Discharged	288	98.0%	118	98.3%	227	95.4%	0.142	X^2
Hospitalised	4	1.4%	2	1.7%	10	4.2%	0.090	X^2
Referred	2	0.7%	0	0.0%	1	0.4%	p>0.05	X^2
Inpatient Service								
Internal service	2	0.7%	1	0.8%	5	2.1%	p>0.05	X^2
Surgery service	1	0.3%	1	0.8%	2	0.8%	p>0.05	X^2
ICU	1	0.3%	0	0.0%	3	1.3%	p>0.05	X^2
Number of days hospitalised	0.04 ± 0.35		0.07 ± 0.53		0.08 ± 0.42		0.098	K

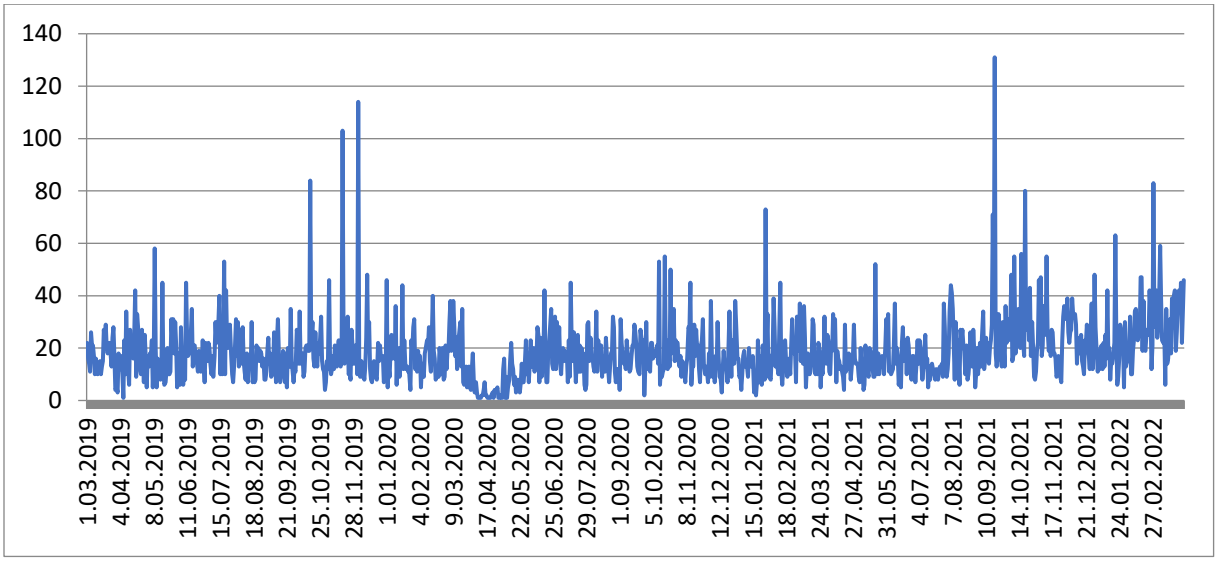
SD: Standard Deviation, [K] Kruskal-Wallis (Mann-Whitney U test) /[X^2] Chi-Square test (Fischer test)

Other: Myocardial infarction (at work), arrest of unknown cause, abuse, asphyxia, electric shock

ICU: Intensive Care Unit

It was determined that forensic admissions were at the lowest level after the declaration of a pandemic, and in the post-pandemic period, they exceeded the pre-pandemic level **(Figure 1).**

Figure 1: Distribution of forensic cases by months



DISCUSSION

In this study, the pre-pandemic, pandemic and post-pandemic periods are compared. The number of cases is thought to have decreased sharply at the beginning of the pandemic. Still, it is seen that the number of forensic cases generally increased during the pandemic period and continued to increase in the post-pandemic period. It has been determined that the number of patients in the suicide group decreased relatively during the pandemic period compared to the pre-pandemic period, and the number of assault and traffic accident patients increased more than twice in the post-pandemic period compared to other periods.

A study in the emergency service admissions of forensic cases found that male patients' rate was higher than female patients before and during the pandemic (6). In this study, similarly, it was found that male patients were admitted at a high rate in all periods. It can be said that men are more likely to be involved in forensic events than women. Studies have shown that the rate of involving pediatric patients in the ED with a forensic incident decreased during the pandemic (7). This study shows that the average age remained the same in the pre-pandemic and pandemic periods but decreased in the post-pandemic period. Therefore, this results align with the literature, namely that forensic incidents involving pediatric patients were less during the pandemic and increased in the post-pandemic period.

The literature has determined that the number of trauma patients and the hospitalisation rate decreased significantly during the pandemic (8). The most important factor causing this situation may be staying home and away from crowded. Due to social distance rules, the number of cases such as fights, injuries and attacks has decreased. In this study, during the pandemic, it was determined that the rate of patients who were assaulted decreased. If all trauma patients are taken together, it is seen that the rate increases significantly in the post-pandemic period. This situation can be expected during the normalisation period. Still, the increase in the number of patients more than before can be called the 'new normal'. This study reveals a high discharge rate from the ED across all periods. The discharge rate was

even higher during the pandemic, while the number of hospitalised patients was lower than in other periods. Moreover, the rate of trauma patients was also lower during the pandemic. Following the pandemic, there has been an increase in the number of trauma patients, which, in turn, has led to a parallel increase in the hospitalisation rate. It was determined that the hospitalisation rate increased proportionately to the rate of trauma patients when strict quarantine rules were implemented. The suicide attempt patient rate increased during this period. Because this period was short, it is worth noting that this observation cannot be generalised. In addition, the decrease in the rate of inpatient forensic cases during the pandemic may be due to the clinicians' focus on the treatment of COVID-19 patients and the transformation of our hospital into the only pandemic hospital in the province. The fact that the referral rate during the pandemic period is higher than the post-pandemic period explains this situation.

CONCLUSION

EDs are the first place of admission for all victims of violence. Emergency physicians must confidently protect the patient's rights, meticulously preserve the evidence without any risk of corruption, and promptly report the incident (9). It is seen that the flow of forensic cases to EDs does not decrease even during the pandemic. Since most forensic cases have a traumatic process, it may be a good idea to evaluate ED admissions. Since the data of our study was obtained from the archive of the largest and sole hospital in the city centre it can represent the general population.

Limitations of the Study

The main limitation is a retrospective study. When the patient files were examined one by one, it was observed that the diagnoses of some patients were entered as a general title instead of the event-specific ICD code, or the diagnosis made at discharge was entered into the system. In addition, since the reports of the forensic cases from the district hospitals could not be found in the system, the diagnoses entered the system were taken as a basis to maintain the study method.

Ethical Declerations:
Kırklareli University Medical School Ethics Committee (P202200030-04/14.09.22) has approved this study.

Informed Consent:
Because the study was designed retrospectively, no written in formed consent form was obtained from patients.

Conflict of Interest Statement:
The authors have no conflicts of interest to declare.

Financial Disclosure:
The authors declared that this study has received no financial support.

Author Contributions:
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Kalp Cerrahisinde Pulsatil ve Nonpulsatil Akımların Preoperatif ve Postoperatif Etkilerinin Karşılaştırılması

Comparison of Preoperative and Postoperative Effects of Pulsatile and Non-Pulsatile Currents in Cardiac Surgery

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Geliş Tarihi / Received : 05.12.2023 Kabul Tarihi / Accepted: 18.12.2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3): 24- 28 DOI:https://doi.org/10.58961/hmj.1400797

Abstract

Introduction Two different flow patterns, pulsatile or nonpulsatile, are used during cardiopulmonary bypass (CPB) in open heart surgery. However, there are uncertainties about the differences and superiorities of these two models. The aim of this study was to compare the biochemical and clinical outcomes of pulsatile and nonpulsatile flow types in isolated coronary artery bypass surgery (CABG).

Materials and Methods This prospective study was conducted between June 2019 and June 2020. 30 patients who underwent isolated CABG surgery were included. Patients received pulsatile (Group I; n=15) and nonpulsatile flow (Group II; n=15) were divided into two groups. The groups were divided into preoperative, postoperative 24.hour and 72.hour postoperative hemogram samples and creatinine levels; pre-CPB, cross Lactate levels were recorded at 5 minutes after clamping, at the end of CPB and 2 hours postoperatively. For both groups postoperative 24th hour drainage and diuresis, intensive care unit extubation, intensive care unit discharge and hospital discharge times were compared.

Results There was no significant difference between the two groups in terms of hemogram and other blood samples ($p>0.05$). Extubation time, ICU discharge and discharge times were similar between the groups ($p>0.05$). However, there was a significant difference between the groups in terms of drainage ($p<0.05$).

Conclusion It was found that pulsatile and nonpulsatile flow model did not show a major difference in terms of biochemical and clinical outcomes in isolated coronary artery bypass surgery.

Keywords Cardiopulmonary bypass, pulsatile flow, nonpulsatile flow

Özet

Amaç Açık kalp cerrahisinde kardiyopulmoner bypass (KPB) sırasında pulsatil veya nonpulsatil olmak üzere iki farklı akış modeli kullanılmaktadır. Ancak bu iki modelin farklılıkları ve üstünlükleri konusunda belirsizlikler vardır. Bu çalışmada izole koroner arter bypass cerrahisinde (CABG) pulsatil ve nonpulsatil akış tiplerinin biyokimyasal ve klinik sonuçlarının karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler Haziran 2019 ile Haziran 2020 arasında tarihleri arasında yapılan bu prospektif çalışmaya izole CABG ameliyatı yapılan 30 hasta dahil edildi. Hastalar pulsatil (Grup I; n=15) ve nonpulsatil (Grup II; n=15) akış olarak iki gruba ayrıldı. Gruplardan preoperatif, postoperatif 24.saat ve postoperatif 72.saat hemogram örneği ve kreatinin düzeyleri; KPB öncesi, kros klemp 5.dakika, KPB sonu ve postoperatif 2.saat laktat düzeyleri kaydedildi. Her iki grup için postoperatif 24.saat drenaj ve diürez miktarları, yoğun bakım ünitesi ekstübasyon, yoğun bakım ünitesi çıkış ve hastaneden taburculuk süreleri karşılaştırıldı.

Bulgular İki grup arasında hemogram ve diğer kan örnekleri açısından anlamlı bir farklılık bulunmadı ($p>0,05$). Gruplar arasında ekstübasyon süresi, yoğun bakım çıkış ve taburculuk süreleri benzerdi ($p>0,05$). Bununla beraber gruplar arasında drenaj açısından anlamlı farklılık tespit edildi ($p<0,05$).

Sonuç İzole koroner arter bypass cerrahisinde pulsatil ve nonpulsatil akış modelinin, biyokimyasal ve klinik sonuçlar açısından majör bir farklılık göstermediği tespit edildi.

Anahtar Kelimeler Kardiyopulmoner bypass, pulsatil akış, nonpulsatil akış

GİRİŞ

Kardiyopulmoner bypass (KPB) açık kalp cerrahisi prosedürlerinde, kardiyak manüplasyonu kolaylaştırır ve hemodinamik dengenin korunmasına olanak sağlar (1). KPB kullanımının organ disfonksiyonuna neden olabilecek bazı riskleri mevcuttur. Kalp cerrahisi sırasında organ koruyucu yaklaşımları belirlemek için önemli çabalar sarf edilmektedir. KPB sırasında pulsatil akış bu yaklaşımlardan biri olarak ifade edilmektedir.

Pulsatil olmayan KPB akışı daha yaygın kullanılmasına rağmen, pulsatil akışın daha faydalı olduğu düşünülmektedir. Pulsatil akışın doku sıvısının hücre zarı etrafında hareketini arttırdığı, mikrosirkülasyonu iyileştirdiği, difüzyonu arttırdığı ve sistemik vasküler direnci azalttığı belirtilmiştir (2). Ancak bir grup araştırmacı her iki akış tipinin de aynı klinik sonuçlar ürettiğini savunmaktadır (3).

KPB sırasında pulsatil akış modelinin sık kullanılmamasının en önemli nedenlerinden biri yöntemin etkinliğine ilişkin verilerin yeterli düzeyde olmamasıdır. Bu prospektif çalışmada amaç erişkin kalp cerrahisinde KPB sırasında pulsatil ve nonpulsatil akımlar arasındaki farklılıkları ortaya çıkarmak bu doğrultuda her iki akım modeli arasındaki biyokimyasal ve klinik farklılıkları tespit etmektir.

GEREÇ ve YÖNTEMLER

Hastalar

Bu tek merkezli randomize kontrollü çalışma XXX hastanesinde, Haziran 2019 ile Haziran 2020 tarihleri arasında 08.01.2019 tarihli, 2018-25 karar numaralı etik kurul onayı ile hastaların onamı alındıktan sonra gerçekleştirildi. Otuz hasta bilgisayar yardımıyla rastgele sıralanarak iki gruba ayrıldı. Grup I (n=15) pulsatil akım grubu, grup II (n=15) pulsatil olmayan (nonpulsatil) akım grubu olarak belirlendi.

Çalışmaya 18 yaş üzeri, izole koroner arter bypass greftleme (CABG) uygulanan, elektif şartlarda, ilk kez opere olacak, herhangi bir kanama patolojisi olmayan hastalar dahil edildi. Reoperasyon, acil şartlarda alınan, geçirilmiş serebrovasküler hastalık (SVH) öyküsü olan, düşük kardiyak debiye (Ejeksiyon fraksiyonu < %40) sahip hastalar çalışma dışı bırakılmıştır.

Anestezi ve kardiyopulmoner bypass

Tüm hastalara standart monitorizasyon sonrası, 1mcg/kg fentanil, 0,1 mg/kg vekuronyum, 1-2 mg/kg propofol ile genel anestezi uygulandı. Her 30 dakikada belirtilen ilaçlar ile idame anestezi devam ettirildi. Santral sternotomi sonrası 300-400 Ü/kg heparin ile antikoagülasyon sağlanıp, uygun kanülasyon yöntemi sonrası KPB'ye geçildi.

KPB sırasında hem pulsatil hem de nonpulsatil akış sağlayabilen Stockert s5 (Stockert GmbH, Freiburg, Almanya) kalp akciğer makinesi, erişkin oksijenatör ve erişkin PVC tubing set kullanıldı. Nonpulsatil başlayan KPB sonrası, pulsatil grupta aortik krossklemp işleminden sonra pulsatil akışa geçildi. Pulsatil akış modları kalp akciğer makinesinden erişkin ayarları (Rate; 70-100 dakika, Base % 50 ve Widht % 70) düzenlendi.

KPB sırasında hastalar orta derece hipotermi (30-32 C), 60 - 80 mmHg ortalama arter basıncı ve 1.8 - 2.4 L/m2/dakika kardiyak indeks ile takip edildi. Hiperkalemik ve izotermik kan kardiyoplejisi ile miyokadiyak koruma sağlandı. Prosedürün tamamlanması ve hastaların vücut ısıları 37 C'ye ulaştıktan sonra KPB sonlandırıldı. KPB sonunda heparinin nötralizasyonu için protamin kullanıldı.

Biyokimyasal örnekler ve klinik takipler

Hastalardan ameliyat öncesi dönem, postoperatif 24.saat ve postoperatif 72.saat periyotlarında hemogram kan örneği ve kreatinin düzeyleri kayıt altına alındı. Kan gazı laktat değerleri KPB öncesi dönem, aort klembi 5.dakika, KPB sonu ve postoperatif 2.saat dönemlerinde kaydedildi. Klinik takipte ise postoperatif 24.saat idrar çıkışı ve drenaj miktarları, yoğun bakım ünitesi ekstübasyon süreleri, yoğun bakım ünitesinden çıkış ve taburculuk gün sayıları kaydedildi.

İstatiksel analiz

Verilerin istatiksel analizinde Statistical Package for Social Sciences 22.0 programı kullanıldı. Dağılımın normalliği ShapiroWilk testi ile değerlendirildi. Gruplar arasındaki farklılıklar normal dağılımda bağımsız T testi, normal dağılım olmadığı durumlarda nonparametrik test olan Mann Whitney U ile değerlendirildi. Kategorik değişkenler Chi square ve Fisher exact testi kullanılarak test edildi. P <0,05 olması istatiksel olarak anlamlı kabul edildi.

BULGULAR

Çalışmaya dahil edilen hiçbir hastada mortalite görülmedi. Gruplar arasında demografik veriler (yaş, cinsiyet, BSA) ve operatif veriler KPB ve AKK süreleri açısından istatistiksel bir farklılık bulunmamıştır (p>0,05; Tablo 1).

Gruplar arasında preoperatif, postoperatif 24. ve 72.saat hemogram (hemoglobin, trombosit, eritrosit) değerleri, aynı periyotlarda kreatinin düzeyleri ve KPB öncesi, AKK 5. dakika, KPB sonu ve postoperatif 2.saat laktat düzeyleri benzerdi (p>0,05; Tablo 2).

Tablo 1: Demografik ve Operatif Veriler

	Grup I (n=15)	Grup I (n=15)	p
Cinsiyet (Kadın)	12	12	1.00
Yaş	56.53±11.26	61.87±8.9	0.161
BSA	1.85±0.13	1.84±0.12	0.765
KPB süresi	106.2±31	93.1±27.5	0.278
AKK süresi	64.9±27.1	49.0±17.9	0.068

BSA; Body Surface Area (Vücut Yüzey Alanı), KPB; Kardiyopulmoner Bypass, AKK; Aortik Kross Klemp

Tablo 2: Kan örnekleri sonuçları

	Grup I (n=15)	Grup II (n=15)	p
Preop HB	13.3±1.7	12.9±2.0	0.349
Post-op 1.gün HB	9.0±1.3	8.9±0.9	0.910
Post-op 3.gün HB	8.7±1.1	8.5±0.8	0.6
Preop PLT	254±78	251±69	0.897
Post-op 1.gün PLT	189±42	188±59	0.969
Post-op 3.gün PLT	172±56	180±66	0.713
Preop RBC	5.1±0.7	4.5±0.6	0.046*
Post-op 1.gün RBC	3.3±0.6	3.2±0.4	0.515
Post-op 3.gün RBC	3.2±0.6	3.3±0.4	0.322
Preop KRE	0.85±0.2	0.91±0.3	0.519
Post-op 1.gün KRE	0.99±0.3	0.92±0.2	0.492
Post-op 3.gün KRE	1.03±0.37	0.95±0.44	0.593
KPB öncesi LAC	1.1±0.4	1.3±0.6	0.128
AKK 5.dk LAC	1.5±0.5	1.6±0.6	0.654
KPB sonu LAC	1.9±0.7	1.8±0.6	0.568
YBÜ 2.saat LAC	2.4±1.1	2.1±0.6	0.230

HB;Hemoglobin, PLT; Platelets (Trombosit), RBC; Red Blood Cells (Eritrosit), KRE; Kreatinin, LAC; Laktat, AKK; Aortik kross klemp, KPB; Kardiyopulmoner Bypass, YBÜ; Yoğun Bakım Ünitesi, * p < 0.05

Postoperatif klinik sonuçlara bakıldığında; drenaj miktarları grup I (451±106 mL) ve grup II (573±90 mL) arasında anlamlı farklılık tespit edildi (p=0,022). Nonpulsatil grupta daha yüksek drenaj miktarı vardı. Diürez miktarları açısından gruplar arasında farklılık yoktu (p>0,05). Gruplar arasında ekstübasyon süreleri (Grup I'de 10,5±2.1 saat, Grup II'de 11,1±1.5 saat), YBÜ kalış süresi (Grup I'de 1,7±0.6 gün, Grup II'de 2,0±0.5 gün) ve taburculuk süresi (Grup I'de 8,5±1.8 gün, Grup II'de 9,9±1.7 gün) açısından anlamlı bir farklılık tespit edilmemiştir (p>0,05 Tablo 3).

Tablo 3: Postoperatif Klinik Sonuçlar

	Grup I (n=15)	Grup II (n=15)	p
Drenaj mL (24.saat)	451±106	573±90	0.022*
Diürez mL (24.saat)	3106±303	3133±305	0.812
Ekstübasyon (saat)	10,5±2.1	11,1±1.5	0.331
YBÜ süresi (gün)	1,7±0.6	2,0±0.5	0.125
Taburculuk (gün)	8,5±1.8	9,9±1.7	0.609

*YBÜ; Yoğun bakım ünitesi, * p<0.05*

TARTIŞMA

Kardiyopulmoner bypass (KPB) geçici de olsa insan fizyolojisini etkilediği bilinmektedir. KPB'nin inflamatuar yanıt, hemodinami, böbrek fonksiyonları, nörolojik fonksiyonlar ve çeşitli organ sistemlerine etkileri inceleme konusu olmuştur. Bu etkilerin olabildiğince minimize edilmesi için KPB ile ilgili çeşitli yaklaşımlar uygulanmıştır. Bu yaklaşımlardan biri KPB akışının vücut fizyolojisine uygun olarak pulsatil uygulanmasıdır. Ancak KPB sırasında uygulanan pulsatil veya nonpulsatil akış konusunda görüş birliği yoktur.

Bugüne kadar, pulsatil perfüzyon lehine artan kanıtlara rağmen KPB'de pulsatil veya nonpulsatil perfüzyonun üstünlüğü konusunda tartışmalar devam etmektedir (4).

Pulsatil perfüzyonun kanın şekilli elemanları üzerindeki etkisinin araştırıldığı bir çalışmada, her iki akış modelinde de KPB sırasında ve sonrasında trombosit düzeylerinin benzer olduğu ifade edilmiştir (5). Pulsatil perfüzyon oluşturmak için roller pompanın kullanıldığı çalışmalarda ise hemoglobin, hematokrit ve trombosit sayılarında gruplar arasında fark bulunmadığı bildirilmiştir (6,7).

Çalışmamızda her iki gruptan postoperatif 24.saat ve 72.saat hemogram örnekleri kaydedilmiştir. Elde ettiğimiz verilere göre, belirtilen çalışmalara paralel olarak hemoglobin, trombosit ve eritrosit düzeylerinde gruplar arasında fark bulunmamıştır. Bu durum pulsatil veya nonpulsatil akışın şekilli elemanların sayıları üzerinde benzer etki yaptığını göstermektedir.

Doku perfüzyonun kritik bir belirteci olarak laktat düzeyleri ifade edilmektedir. Geha ve ark. yaptıkları hayvan deney modelinde pulsatil akış modelinde daha düşük laktat

düzeyleri tespit etmişlerdir (8). Çalışmamızda KPB öncesi, aortik kros klemp 5.dakika, KPB sonu ve yoğun bakım ünitesi 2.saat laktat düzeyleri incelenmiştir. Her iki akım grubunda laktat düzeyleri açısından fark bulunmamıştır.

Ölçüm kolaylığı nedeniyle idrar çıkış miktarı, pulsatil ve nonpulsatil akışları karşılaştırırken en sık kullanılan bir parametredir. Yalnızca bir çalışma pulsatil akış grubunda idrar çıkışında bir artış olduğunu gösterdi (7). Farklı çalışmalarda her iki akış modelinde idrar miktarında bir azalma veya anlamlı bir düzeyde artma lehine bir fark olmadığı bildirilmiştir (9).

Serum kreatinin düzeyi iki akış modelini karşılaştıran birçok araştırmada kullanılmıştır. Bu araştırma sonuçlarına göre kreatinin düzeylerinin akış modeline göre bir farklılık göstermediği ifade edilmiştir (9,10,11). Ancak farklı bir araştırmada kreatin klirensi düzeylerinde iyileşme olduğu ifade edilmiştir (5). Çalışmamızda postoperatif 24.saat ve 72.saatte kreatinin değerlerinde gruplar arasında benzerlik olduğu ve postoperatif 24.saat diürez miktarlarında ise farklılık olmadığı tespit edilmiştir.

Göğüs tüpü drenajı konusunda akış modelleri konusunda çelişkili sonuçlar bildirilmiştir. Bazı araştırmacılar akış modelinin drenaj miktarlarını etkilemediğini ifade ederken (12,13) bazıları ise pulsatil akışın göğüs tüpü drenajı miktarını önemli düzeyde azalttığını belirtmektedir (14,15). Çalışmamızda postoperatif 24.saat drenaj miktarları incelendiğinde pulsatil grupta anlamlı düzeyde daha az drenaj miktarı tespit edilmiştir ($p<0,05$). Ancak bu farklılık hastaların yoğun bakım ünitesinde kalış ve taburculuk parametrelerini, postoperatif 24.saat kanın şekilli elemanları düzeylerini etkilememektedir. Çalışmamız mekanik ventilasyondan ayrılma süresi, yoğun bakım kalış ve taburculuk gün sayıları arasında gruplar arasında fark olmadığını göstermektedir. Benzer çalışmalar da akış modelinin hastanede kalış süresi üzerinde bir etkisinin olmadığını bildirmektedir (11).

Çalışmamızın bazı sınırlılıkları mevcuttu. Öncelikle tek merkezli, küçük bir örneklem dahil edilmesine bağlı olarak sonuçların genele yayılması güçlüğü vardı. Bu çalışmada kanın şekilli elemanlarının sayısal analizi yapılmıştır, hemoliz, uç organ perfüzyonu ve miyokard koruma açısından klinik etkisi değerlendirilmemiştir.

SONUÇ

Literatürde iki akış modeli arasında net bir görüş birliği olmamakla beraber bazı hususlarda pulsatil akış lehine sonuçlar mevcuttur. Çalışmamızda kanın şekilli elemanları, kreatinin ve laktat düzeyleri açısından her iki akış modeli benzer sonuçlar göstermektedir. Ek olarak klinik parametreler açısından iki akış modeli arasında majör bir farklılık yoktur. Çalışmamızın bulguları doğrultusunda, daha detaylı tetkikler ve geniş ölçekli deneysel çalışmalar ile bu iki akış modelinin kıyaslanması gerektiğini önermekteyiz.

Etik Beyanname:

Çalışmanın etik kurul onayı, İstanbul Mehmet Akif Ersoy Göğüs, Kalp ve Damar Cerrahisi Eğitim ve Araştırma Hastanesi'nden alınmıştır (Onay Tarihi: 08.01.2019 - Onay numarası: 2018-25).

Bilgilendirilmiş Onam:

Çalışma proretrospektif olarak tasarlandığından hastalardan yazılı onam formu alınmıştır.

Çıkar Çatışması:

Yazarların herhangi bir çıkar çatışması yoktur.

Financial Destek:

Finansal destek alınmamıştır.

Yazar Katkısı:

Tüm yazarlar çalışmaya eşit katkı sunmuşlardır.

Bu çalışma 12-15 Kasım 2020 tarihleri arasında dijital kongre olarak düzenlenen TKDCD 2020 Ulusal Kongresi'nde sözlü bildiri olarak sunulmuştur.

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High-Grade Dysplasia in Giant Tubular Adenoma

Yüksek Derece Displazili Dev Tubüler Adenom

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Geliş Tarihi / Received : 3 Eylül 2023 Kabul Tarihi / Accepted: 15 Aralık 2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3) 29-33 DOI: https://doi.org/10.58961/hmj.1354554

Abstract

Rectal adenomas with a high risk of cancer frequently occur in anal bleeding and mucus discharge. The risk of malignancy is greater than 50% in polyps larger than 2 cm and includes areas of dysplasia, and the likelihood of dysplasia is correlated with the excess of the villous component ratio, the proximity of the polyp to the anal region, and the increase in size. Large, lumen-encircling polyps are difficult to treat with endoscopic or transanal intervention and necessitate surgical intervention. In this article, we present a female patient who had rectal mucus discharge and had a lower anterior resection and coloanal anastomosis after developing a tubular adenoma with high-grade dysplasia and no villous component.

Keywords Adenomatous polyps, biopsy, colonoscopy, colectomy

Özet

Malignite riski yüksek olan rektal adenomlar sıklıkla anal kanama ve mukus akıntısıyla görülür. Displazi alanları içeren 2 cm'den büyük poliplerde malignite riski %50'den fazladır ve displazi olasılığı villöz komponent oranının fazlalığı, polipin anal bölgeye yakınlığı ve polip boyutunun artışı ile displazi olasılığı korele seyreder. Büyük, lümeni çevreleyen poliplerin endoskopik veya transanal girişimle tedavisi zordur ve cerrahi müdahale gerektirir. Bu yazıda; rektal mukus akıntısı ile başvuran tetkiklerinde yüksek dereceli displazili ve villöz komponent içermeyen tübüler adenomu olan kadın hastamızı, alt anterior rezeksiyon ve koloanal anastomoz yaparak tedavi ettiğimiz olguyu sunuyoruz.

Anahtar Kelimeler Adenomatöz polipler, biyopsi, kolonoskopi, kolektomi

INTRODUCTION

The prevalence Polyps are growths that protrude from the mucosa of the colon into the lumen and are frequently asymptomatic. They may bleed when they get ulcerated on the outside, have tenesmus if they are in the rectum, or become blocked if they become significantly larger. Two-thirds adenomas with neoplastic potential comprise about 2/3 of all polyps, depending on whether they are histologically categorized as neoplastic or non-neoplastic. The presence of one adenoma indicates the presence of a 30-50% synchronous second adenoma [1]. Independent of histological characteristics and size, age is a risk factor for the development of dysplasia [2]. Colon adenoma prevalence is 25-30% in the fifth decade, reaching 50% by the age of 70 [3], increasing the chance of having a high body mass index [4]. The average growth rate of polyps is 0.5 mm per year, and only 5% of minor polyps progress to cancer within 7– 10 years [5]. High-grade dysplasia, an increase in size, and the villous component ratio are all risk factors for the development of cancer. At the time of diagnosis, 3-5% of adenomas had invasive malignancy, and 5-7% had high-grade dysplasia[6]. The majority of adenomas are less than 1 cm in diameter and can be sessile, flat, pedicled, or depressed based on their endoscopic appearance. Hardness, ulceration, and fragility are signs of malignancy. Based on histological characteristics, it is categorized as tubular, villous, or tubulovillous. Tubular adenomas, which comprise 80% of all adenomatous polyps, are defined as having at least 75% of the polyp in tubular components. High-grade dysplasia is characterized by atypical cellular regions that are confined to the crypt epithelium and do not invade the lamina propria. The lamina propria does not promote metastasis because it lacks a lymphatic network. Invasive carcinoma is seen in tubular adenomas larger than 2 cm in 35% of cases[7].

Polypectomy should be used to remove all polyps. In cases where the polyp size is 2 mm or less, endoscopic mucosal resection procedures should be tried. In contrast, in cases where the size is greater, it should be treated with polypectomy with a snare and electrocautery (cold polypectomy)[8]. Endoscopic treatment of an adenoma with high-grade dysplasia with clean resection margins is sufficient and does not require additional intervention. Adenomas with villous components should undergo surgery if they cover a large portion of the colon wall, cannot be removed endoscopically, contain high-grade dysplastic regions, and have villous components.

In this article, the findings of a case with high-grade dysplasia, no villous component, and a tubular adenoma are presented.

CASE REPORT

Our Informed consent was obtained from the patient for this case report.

A 59-year-old female patient was admitted to the outpatient clinic with complaints of involuntary defecation, sporadically bleeding from the anal region, and feeling unable to completely clean over the previous three months. The body mass index (BMI) was 36 kg/m2. A rectal examination revealed a palpable lump in the ampulla recti. Computed tomography showed a mass lesion in the rectum that measured 17 mm at its thickest point and had an approximate 11 cm diameter (Figure 1).

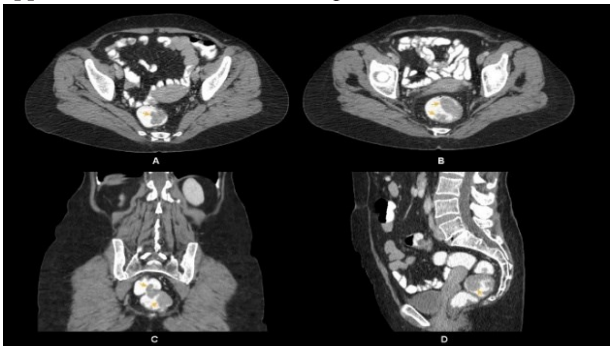

Figure 1. Intravenous and rectal contrast-enhanced Axial (A, B), sagittal (C), and coronal (D) computed tomography images demonstrate a polypoid mass lesion (arrows) originating from the posterior wall of the rectum, extending from the proximal anal canal to the rectum lumen, and generating an intraluminal filling defect

No infiltration of diseased lymph nodes and nearby visceral organs was found in the mesorectal planes of the phased sequential magnetic resonance imaging carried out for this purpose (Figure 2).

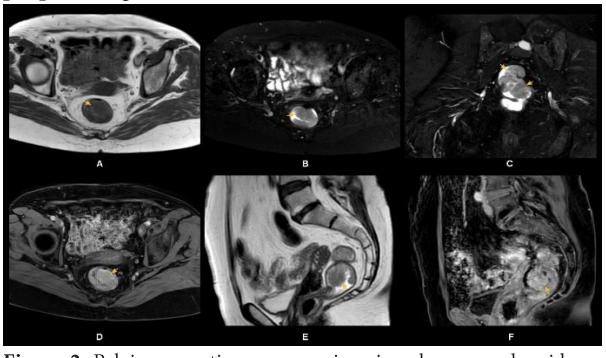

Figure 2. Pelvic magnetic resonance imaging shows a polypoid mass lesion (arrows) that is hypointense on T1 weighted images (WI) (A), iso-hypointense on axial (B) and coronal (C) T2 fat-saturated images, iso-hypointense on T2-WI (E), and minimal heterogeneous enhancement on post-contrast series (D, F). The lesion originates frcm the posterior wall of the rectum, extends from the proximal anal canal to the rectal lumen, and causes the intraluminal filling defect.

Colonoscopic examination indicated a mass lesion that began approximately 4 cm from the anal entrance and progressed up to 15 cm, encircling the lumen but not obstructing it (Figure 3).

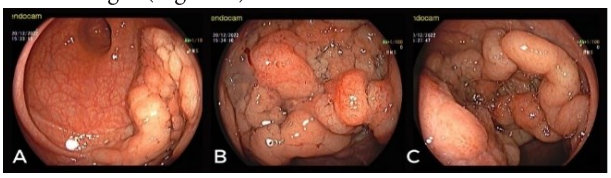

Figure 3. Colonoscopy revealed a giant lobular polyp (A-C) that surrounds the lumen and does not produce obstruction in the lumen, beginning from the 4th cm to the 15th cm from the entrance of the anal canal.

Biopsy samples revealed a high degree of dysplasia. The interdisciplinary oncology council made the decision to treat the patient surgically, which included an ultra-low anterior resection, coloanal anastomosis, and diverting ileostomy. The surgical margins were found to be tumor-free by frozen inspection (Figure 4).

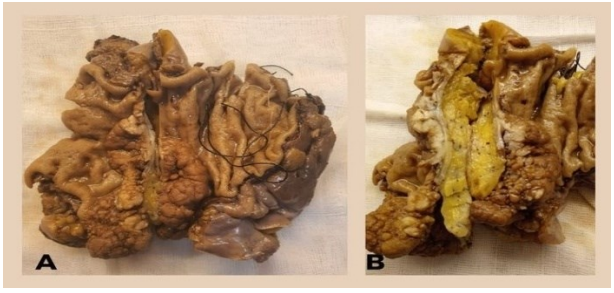

Figure 4. Evaluation of the lower anterior resection piece for a frozen examination.

The ileostomy was closed four weeks after the surgery. Based on pathological analysis, the tumor was a 12x8 cm tubular adenoma with high-grade dysplastic regions (Figure 5). The radial surgical margin was found to be 4 cm, the proximal surgical margin to be 6 cm, and the distal surgical margin to be 2 cm. The nine lymph nodes inspected were found to be clear of tumoral lesions, indicating that the mesorectal excision was finished. The patient had no extra care, and outpatient control was advised.

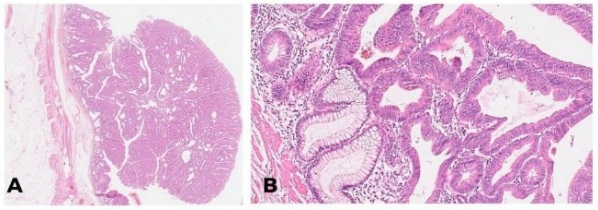

Figure 5. Microscopic examination (A) Hematoxylin and Eosin x4, tubular adenoma; (B) Hematoxylin and Eosin x100, dysplasia of the tubular epithelium.

DISCUSSION

Colorectal cancers develop from epithelial cells that line the mucosa of the colon. The mucosal stem cells at the base of the crypt structures give rise to the short-lived colon lining epithelial cells, which frequently undergo apoptosis on the mucosal surface to end their lives. These cells come into close contact with substances that are harmful and can cause cancer, such as substances found in food, bacteria, and the compounds those organisms make. The rate of epithelial cell renewal is accelerated by both these variables and a few hereditary genetic factors. Rapidly proliferating cells can convert into dysplastic and neoplastic cells as a result of maturation deficits, and adenomas can develop during this process. In the early stage, "dysplastic" changes, also known as neoplastic changes, might be observed in a single crypt.

These malignant cells primarily grow on the basement membrane's surface, where they produce adenomatous polyps that spread into the intestinal lumen. In the advanced stage, dysplastic cells that produce adenomatous polyps override the basement membrane and enter the "lamina propria" regions, the tissue that supports the mucosa, leading to the development of colorectal cancer. The "two-stroke theory" explains how adenoma-carcinoma develops. Therefore, multiple variables occur at different times to produce alterations in the mucosa and the development of cancer. Adenomatous polyps can sometimes indicate advanced growth when this change does not take place. Giant polyps are those that are larger than 3 cm and are removed using endoscopic mucosal excision methods [9,10]. As in the present case, polyps larger than 10 cm are uncommon, and the available research on the best way to treat them is scant.

The malignant degeneration of adenomatous polyps depends on the type and diameter of the polyp. Villous polyps have an eight times greater likelihood of developing cancer than tubular adenomas. Similar to this, although adenomatous polyps less than 1 cm have a malignancy rate of less than 5%, those larger than 2 cm have a malignancy incidence of 50% [11].

Bains et al. presented a review of the literature on large rectal polyps and their histological findings [12]. The average polyp diameter in the patients reviewed was 13.2 cm, and all were villous adenomas. The polyp found in our case is a 14 cm diameter tubular adenoma without a villous component and with high degree dysplasia in some locations.

The majority of adenomatous polyps are asymptomatic and are found during screening or follow-up colonoscopies. Complete excision and biopsy are both possible during a

colonoscopy, in addition to the ability to observe polyps of all sizes. The most effective course of action is polypectomy because most polyps are elevated from the mucosa. The effectiveness of this treatment can occasionally be hampered by the size, location, and difficulty of reaching the polyp. The removal of large colon polyps during endoscopy raises a number of concerns, including the risk of the procedure and the possibility of inadequate polypectomy. The latter is particularly concerning since large polyps have an increased risk of harboring invasive carcinoma. Endoscopic resection of large polyps, especially laterally spreading sessile polyps, is also more time-consuming and requires more resources compared with polypectomy of smaller lesions. Because of these issues, surgical resection is often performed, particularly for large sessile polyps and for those in locations that are difficult to manage endoscopically. However, some large polyps can be successfully removed with endoscopic methods, provided that an endoscopist who is experienced in large polyp removal is available. Thus, some patients can avoid surgery. Large, medium, and distant rectal polyps can be operated on with transanal endoscopic microsurgery. In the literature, the mean polyp diameter for this procedure has been reported as 5.2 cm [13]. Due to the possibility of stricture development, per-anal endoscopic resection is not advised in polyps larger than 6 cm in which circumferential full involvement is seen and the villous component is predominant. Carditello et al. found 10% of invasive cancer in rectal polyps larger than 3 cm after local or broad excision, with recurrence occurring in 23% of patients during a six-year follow-up [14]. Giant rectal adenomatous polyps with a predominately villous component have a 50% accuracy rate for biopsies. Furthermore, invasive carcinoma is found in 1 in 8 polyp excision specimens where malignancy is not expected. These facts make surgical intervention the preferred course of action in such situations. It can be done laparoscopically or openly, with a 0.3% mortality rate and a 1.4% chance of an anastomotic leak [15]. Although there was no villous component in the present case, it was an instructional example and contributed to the literature because a tubular adenoma with a high degree of dysplasia was found and remained asymptomatic for a long time despite its advanced size. Because it was positioned up to the level of the proximal rectum, there was no need for anal intervention, and aggressive surgical intervention was undertaken. The fact that a whole mesorectal ultra-low anterior resection was done and no invasive malignancy was found as a consequence of the pathology is thought-provoking.

Ethical Declerations

Not applicable, because this article does not contain any studies with human or animal subjects. An informed consent was obtained from the patient for this case report.

Conflict of Interest Statement:

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, shareholding and similar situations in any firm.

Financial Disclosure:

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Author Contribution

Surgical and Medical Practices: S.A. Ç.K., Concept: Ç.K., Design: S.A., Data Collection or Processing: S.A. Ç.K., Analysis or Interpretation: S.A. Ç.K., Literature Search: Ç.K., Writing: S.A.

Acknowledgements

Thanks to Dr Nurten Küçükmetin for his support in the treatment process of the patient. Thanks to Dr Sevil Karabağ for his support in the pathology images of the specimen. Thanks to Dr Hadi Sasani for his support in the radiology images of the case

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Three Important Anatomists in the Transition from the Ottoman Empire to the Turkish Republic: Hasan Mazhar, Berkol and Zeren

Osmanlı İmparatorluğu'ndan Türkiye Cumhuriyeti'ne Geçiş Dönemindeki Üç Önemli Anatomist: Hasan Mazhar, Berkol ve Zeren

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Geliş Tarihi / Received : 6.11.2023 Kabul Tarihi / Accepted: 18.12.2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3)34-38 : DOI: https://doi.org/10.58961/hmj.1387053

Abstract

Aim The aim of this study is to examine the change and development of medical anatomy through the short autobiographies of three respected anatomists (Hasan Mazhar Pasha, Nurettin Ali Berkol and Zeki Zeren), who shed light on anatomy education with their studies in the field of medical anatomy in the last periods of the Ottoman Empire and the establishment of the Republic of Türkiye. These three intellectual scientists have worked devotedly for the development of the country at the scientific, political, social, and cultural level in the country under wars and change of management.

Keywords Hasan Mazhar Paşa, Nurettin Ali Berkol, Zeki Zeren, anatomi, tarih, Türkiye

Özet

Amaç Bu çalışmanın amacı, anatomi alanındaki çalışmalarıyla anatomi eğitimine ışık tutan üç saygın anatomistin (Hasan Mazhar Paşa, Nurettin Ali Berkol ve Zeki Zeren) kısa otobiyografileri üzerinden Osmanlı İmparatorluğu'nun son dönemlerinde ve Türkiye Cumhuriyeti'nin kuruluşunda tıbbi anatominin değişim ve gelişimini incelemektir. Bu üç aydın bilim insanı, savaşlar ve yönetim değişikliği altında ülkenin bilimsel, siyasi, sosyal ve kültürel düzeyde kalkınması için özveriyle çalışmışlardır.

Anahtar Kelimeler Hasan Mazhar Pasha, Nurettin Ali Berkol, Zeki Zeren, anatomy, history, Turkey

INTRODUCTION

The last periods of the Ottoman Empire faced many problems in the fields of medicine and education, as in every other field. The reasons for this situation are diverse and multidimensional. During this difficult period, physicians and medical educators have worked devotedly to modernize medical education and practice in the country. These studies continued increasingly during the transition to the Republic of Türkiye and they pioneered the development of today's medical discipline. The aim of this study is to evaluate and present the development and change of medical anatomy is to examine the short autobiography of three respected anatomists (Hasan Mazhar Pasha, Nurettin Ali Berkol and Zeki Zeren) who have shed light on anatomy education with their studies in the field of medical anatomy in the last periods of the Ottoman Empire with the establishment and continuation of the Turkish Republic.

In the Ottoman Empire, education in medical schools in the Madrasa period, which included the period starting from the establishment of Gevher Nesibe Dârüşşifâ and Medical School in Kayseri in 1205 and ending with the opening of the Tıbhane and Cerrahhane-i Amire on 14 March 1827. Education was carried out within the master-apprentice relationship in this period. It was maintained within the framework of its social structure and religious beliefs. Therefore, anatomy education from the beginning of the Madrasa period to the middle of the period could not progress much (1,2). Şemseddin-i İtakî, who lived in the 17th century, and Mehmed Atâullah Efendi (Şânizâde), who lived in the 18th century, were among the leading figures in the field of medicine of this period. Teşrîhu'l-Ebdân and Tercümân-ı Kıbâle-i Feylesûfân, the first illustrated anatomy book written in Turkish by Şemseddin-i İtakî in 1632, is also known for the first use of Turkish anatomical terms. His work, "Hamse-i Şânizâde", which is considered the most important of Şânizâde's works, had a great share in laying the foundations of modern medicine in these lands. The first volume of the work, prepared in five volumes, is Mir'atü'l Ebdân Fi Teşrih-i A'za'i'l-i İnsan, the first anatomy book prepared in a modern sense. The reason why this book was met with interest and followed by Western medical authorities is that it is a work that pioneers the transition from the classical Ottoman understanding of medicine to modern medicine in the Ottoman geography (1-4).

In the period from the Medicine School opened in 1827 to the 1870s, many problems had to be faced in order for medical education to reach a certain standard. These include problems related to the location of the medical faculty, insufficiency of the teaching staff and the fact that instructors are brought from abroad, prejudices that need to be broken for cadaver dissections in anatomy education, difficulties in determining and maintaining the training curriculum and programs, the uncertainty of the language of education, the inadequacy of educational materials generally procured from abroad, and difficulties in acquisition can be considered. During the 100-year period, from the 1870s to the 1970s, these three anatomists played an active role in the modernization of medicine and the establishment of terminology in the country (1,2).

HASAN MAZHAR PASHA (1845 – 1920)

After graduating from Istanbul Darülfünun (University), Faculty of Medicine, he specialized in anatomy and surgery in Paris between 1871-1874. Hasan Mazhar, who returned to his country immediately after becoming a specialist, participated in the Montenegrin, Serbian and Russian wars as a surgeon. In 1878, he returned to the Istanbul Military Medical School and was appointed as an assistant dissection (Associate Professor). In 1879, he was given the title of dissection teacher (Professor of Anatomy) (Figure 1[14]) (2,5-8).

When Mazhar Pasha returned to his homeland, medical education was given in French. He and a group of his friends made studies on this subject, arguing that the lessons should be given in Turkish. He provided an important service in the preparation and use of "Lügat-ı Tıp" (Medical Dictionary) by finding the Turkish equivalents of many medical terms, especially anatomy. Turkish anatomy has been under the influence of Mazhar Pasha's anatomy terms for many years. Hasan Mazhar Pasha is the person who had a say in the establishment of modern anatomy in Türkiye (2, 8-14)

Figure 1. Hasan Mazhar Pasha (14)

NURETTİN ALİ BERKOL (1881 – 1955)

After graduating from Istanbul Darülfünun (University), Faculty of Medicine, he was entitled to receive the rank of captain. He went to France in 1907 to increase his knowledge of anatomy and worked at the Paris Medical Faculty for two years. While abroad, he learned the methods of storing cadavers in ice rooms and protecting them with formol injection from the jugular vein (Figure 2[12]) (2,15,16).

After the Balkan War started in 1912 and the faculty was suspended, he joined the army and worked in various hospitals in the country (Skopje, Thessaloniki, Hadımköy, Çanakkale, Kabataş, Haydarpaşa). Later, he left his military service and was appointed as the chief of the Medical Faculty Dissection (Anatomy) Laboratory. With the start of World War I, he joined the army again and worked in hospitals in Konya and Istanbul. Returning to the university in 1917, he was appointed as a professor. He was elected as a deputy from Istanbul in 1927 and returned to the Faculty of Medicine in 1931 after serving as the deputy chairman of the Turkish Grand National Assembly for three years. In 1933, with the University Reform in Türkiye, he chaired the board formed to translate the terms in the field of anatomy into Turkish. His book titled "Osmanlıca Anatomi Sözlüğü ve Türk Anatomi Terimleri (Ottoman Anatomy Dictionary and Turkish Anatomy Terms)", published in 1946 made a great contribution to Turkish anatomy terminology (2,15-18).

Berkol, who was a student of Hasan Mazhar Pasha, who pioneered the establishment of modern anatomy in the country, was influential in the development of anatomy teaching and research, and became the leader in the development of cadaver dissection by modernizing the dissection room, especially in the Republican period (18).

Figure 2. Nurettin Ali Berkol (12)

ZEKİ ZEREN (1900 – 1973)

He graduated from Istanbul Darülfünun (University), Faculty of Medicine in 1923. Between 1923-1927, he worked as an assistant and chief assistant in anatomy and then surgery clinics. Afterwards, he worked as a surgeon and chief physician in city hospitals in Çankırı and Zonguldak. He returned to Istanbul University Faculty of Medicine with the University Reform in 1933 and worked at the Anatomy Institute under the direction of Nurettin Ali Berkol. In the same year, he was included in the board formed for the Turkish translation of Anatomy terms (Figure 3[19]) (2,17,20,21).

Going abroad for educational purposes in 1939, Dr. Zeren worked for six months at the Paris Faculty of Medicine. During his academic life, he regularly visited various medical faculties in Europe and exchanged views on innovations in the field of anatomy (2,19,21).

Zeki Zeren is one of the faculty members who were expelled from the universities in the 1960 coup. At that time, he undertook the duties of the 12th term deputy in the Turkish Grand National Assembly and the Chairman of the Health and Social Assistance Commission (19,20).

Figure 3. Zeki Zeren (19)

Zeki Zeren has accomplished a great deal in determining and using Turkish equivalents for Latin Anatomy terms instead of Ottoman Turkish. Zeren has made important contributions to the teaching, research, and development of anatomy in Türkiye and to the development of practical dissection studies. He made efforts to establish academic relations with the anatomists of European countries, editorial duties with internationally respected journals, and for Türkiye to take part in international scientific

organizations. He lexicalized these terms by publishing his important book "Latin-Turkish-Ottoman Anatomy Dictionary and Turkish Anatomy Terms" in 1946. At the same time, Dr. Zeren should also be considered as an activist in the fields of culture and civilization in his own time (2,20, 22-24).

CONCLUSION

From the perspective of history, Türkiye, which ended an empire and passed to the republic, has realized a rapid renewal and change. Three anatomists living in this transition period not only received medical education in the European countries where they went for education but also analyzed the socio-cultural structure of these countries and tried to put modernized medical education into practice in Türkiye right after they returned to the country. These three intellectual scientists have worked devotedly for the development of the country at the scientific, political, social, and cultural levels in the country under wars and regime change. They were very influential in the formation of an identity in the new Republic of Türkiye, especially with their contributions to the development of Turkish terminology in the field of medicine.

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The Utility of Platelet-Related Parameters for Assessing COVID-19 Severity and Prognosis

COVID-19 Şiddetini ve Prognozunu Değerlendirmede Trombosit İle İlgili Parametrelerin Faydası

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Geliş Tarihi / Received : 13.12.2023 Kabul Tarihi / Accepted: 14.12.2023

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Hippocrates Medical Journal / Hippocrates Med J 2023, 3(3), 39-41 ***DOI: 10.58961/hmj.1404332***

Dear Editor;

We have read with great interest the research article by Ergenç et al, titled 'Relationship Of Platelet Subgroups With Prognosis And Mortality İn Patients With Mild, Severe And Critical COVID-19' published in the second issue of your journal in 2023 (1). We would like to express our appreciation to the authors and the editorial board for this insightful and highly informative article.We intend to cover particular aspects in this letter, which we believe will contribute to a more comprehensive discussion of the article.

It is worth highlighting that in a pandemic with a simple and rapidly deployable intervention requirement, a basic hemogram test, as also suggested by Ergenç and colleagues, can be a highly beneficial and effective method for determining disease severity and prognosis. Such a straightforward diagnostic tool can play a crucial role in the early identification and intervention of severe cases, potentially improving patient outcomes. Similar to the current study, a meta-analysis that encompassed 17 studies and included 4549 patients highlighted the elevation of mean platelet volume (MPV) in both the mortal group and the poor outcome group (2). MPV is considered not only a marker of platelet activation but is also associated with platelet aggregation and the release of thromboxane A2. One of the significant points that we would like to underscore is the absence of a precise definition for 'severe COVID-19' within the study. Notably, the study lacks both clinical and laboratory criteria to distinctly define severe cases of COVID-19, making it challenging to thoroughly examine the effects on platelets and related markers on prognosis.

Another outcome inferred from the study is the lower platelet count in the group exhibiting a fatal course. This phenomenon can be elucidated by the direct involvement of the coronavirus in bone marrow, leading to platelet consumption and aggregation in response to inflammation (3,4).In a meta-analysis encompassing 19 studies, it has been demonstrated that the likelihood of thrombocytopenia is higher in severe cases, highlighting the possibility of drawing the inference that thrombocytopenic COVID-19 patients may experience a heightened risk of adverse outcomes (4). We think that it would be appropriate to mention that despite the study by Ergenç and colleagues reinforcing this outcome, the potential for achieving more robust results existed by incorporating clearer exclusion criteria and the exclusion of concurrent factors, such as the usage of NSAIDs and antibiotics, which are known to precipitate thrombocytopenia.

In conclusıon platelet count and platelet-related parameters can be effectively utilized for the assessment of COVID-19 severity and prognosis.We would like to express our gratitude to the authors for this study, which includes patients from two separate centers, providing a broad perspective on this subject.

Acknowledgments

The authors declared that this study recieved no financial support.

No conflict of interest was declared by the authors.

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